

# STUDY ON THE PREVALENCE OF TOXOPLASMOSIS IN INDONESIA: A REVIEW

Srisasi Gandahusada

Department of Parasitology, Medical Faculty, University of Indonesia, Jakarta, Indonesia.

**Abstract.** Congenital toxoplasmosis has been confirmed in Indonesia. Many newborn children in Indonesia have congenital anomalies attributable to *Toxoplasma gondii*. The parasite is widespread, with seroprevalence rates of 2-63% in humans, 35-73% in cats, 75% in dogs, 11-36% in pigs, 11-61% in goats, and less than 10% in cows.

The prevalence of *Toxoplasma* antibodies in pregnant women in the Dr Cipto Mangunkusumo Hospital in Jakarta is 14.3%, and in 50 abortions it is 67.8%. In patients with a history of one or more abortions or stillbirths, the prevalence is 21.5% and 22.8%, respectively. No significant difference has been found in women with or without histories of habitual abortions or stillbirths.

In adults and children with chorioretinitis, the prevalence of antibody is 60%; in patients with other eye lesions, it is 17%. The prevalence in hydrocephalic children is 10.6%; in children with mental retardation, 44.6%; in children with eye lesions, 44.6%; and in children with signs of systemic diseases, 9.5%.

The diagnosis of an acute *Toxoplasma* infection using the ELISA should be based on a significant increase in IgG levels in paired sera or on detection of IgM.

## INTRODUCTION

In Indonesia, many newborns are seen with congenital anomalies, such as hydrocephalus, chorioretinitis, mental retardation and hepatosplenomegaly. It was assumed that *Toxoplasma gondii* was associated with these anomalies. Before 1970 the evidence of this causative correlation was not established. The first evidence of toxoplasmosis in Indonesia was reported in 1962 when 27.4% of those skin tested for the disease in Java and Bali were found to be positive (Catar *et al*, 1962, quoted by Nelwan *et al*, 1975). Surveys for antibodies to *T. gondii* using the indirect hemagglutination test (IHA) were carried out in the 1970s on the major islands of the archipelago and a microtiter adaptation of the IHA test was established in our laboratory in 1977. The prevalence of *Toxoplasma* antibodies is 2-63% in humans, 35-73% in cats, 75% in dogs, 11-36% in pigs, 11-61% in goats, and less than 10% in cows. Congenital toxoplasmosis has been confirmed in Indonesia and is a great financial burden on families because of the very high cost of special care for these handicapped children. This paper reports on the prevalence of toxoplasmosis in several population groups in Indonesia.

## PREVALENCE OF TOXOPLASMOSIS

Before it was suggested that titers of 1:256 or greater indicate a recent exposure to *T. gondii*, many authors elected to consider lower titers as significant. In 1964, de Roever-Bonnet *et al* found a positivity rate of 24% among the autochthonous population aged 10-50 years in the Baliem Valley and Merauke, West Irian, when a dye test titer of  $\geq 1:4$  was considered as positive. Clarke *et al* (1973a, 1973b) and Durfee *et al* (1976) considered IHA antibody titers of 1:16 and 1:32 as positive, with resulting prevalence rates of 51% in 95 adults in several villages in Kresek in West Java, 20% of 314 volunteers aged 0-50 years near Yogyakarta in Central Java and 31% of 1,050 residents of 7 villages aged 1-50 years in South Kalimantan. In another study using the indirect fluorescent antibody technique (IFA), van der Veen *et al* (1974) reported a prevalence rate of 63% of 573 blood donors, students, laboratory personnel and their children aged 1- $\geq 50$  years in Surabaya, East Java, when titers of  $\geq 1:32$  were considered as positive.

In later studies, IHA titers of  $\geq 1:256$  were considered significant since titers at these levels are considered more indicative of recent exposure.

Subsequently, the following prevalence rates were recorded from different parts of the country: Surabaya, East Java, 8.9% of 179 healthy adults (Yamamoto *et al*, 1970); Lindu Valley, Central Sulawesi, 7.9% of the total population tested (Clarke *et al*, 1975); Palu Valley, Central Sulawesi, 16% of 1,166 persons aged 0- $\geq$ 50 years (Cross *et al*, 1975a); Soyolali, Central Java, 2% of 693 persons aged 2- $\geq$ 50 years (Cross *et al*, 1975b); North Sumatra, 9% of the population tested (Cross *et al*, 1975c); West Kalimantan, 3% of the population tested (Cross *et al*, 1975d); Jakarta, 10% of 293 medical students at two private universities (Partono and Cross, 1975), 12.5% of 184 medical students at the University of Indonesia and 96 laboratory personnel aged 14-59 years (Srisasi, 1978); and Obano, Irian Jaya, 34.6% of 188 persons 2-54 years of age (Srisasi and Endardjo, 1980). In Manado, North Kulawesi, Kapojos (1988) found a prevalence rate of 60% in 108 persons 0-54 years of age, considering IHA titers of 1:128 or greater as positive (Table 1).

The prevalence of toxoplasmosis in different ethnic groups was investigated and was found to be 18% in Indonesian students and 7% in Chinese students (Partono and Cross, 1975). In another study, the prevalence rate was 14.3% in the Indonesians and 2.3% in the Chinese ethnic groups (Srisasi, 1978).

The prevalence of *T. gondii* IHA antibodies in 288 pregnant women in the Dr Cipto Mangunkusumo Hospital was found to be 14.3% by Sayogo *et al* in 1980. The seropositivity rate of 50 abortions in the Department of Obstetrics and Gynecology at the same hospital was 67.8% (Samil, 1988). In 1985, 810 sera from women at obstetric clinics in hospitals in Jakarta were collected and sent to the Department of Parasitology, Medical Faculty, University of Indonesia to be tested for *Toxoplasma* antibodies. The sera were obtained from 280 women with no history of abortion or intrauterine fetal death, 409 women with habitual abortion or sporadic abortion, and 145 women with a history of intrauterine fetal death. Twenty-four of the 409 women with abortion histories also had a history of intrauterine fetal death. An IHA titer of  $\geq$  1:4 was found in 71.8% (288) women who had never aborted; 67.8% (84) who aborted once; 74.3% (156) who aborted more than once; 76.0% (57)

with habitual abortion; 72.7% (483) with no history of intrauterine fetal death; and 70.4% (102) with a history of intrauterine fetal death. No significant difference could be found between the seropositivity rate of *Toxoplasma* antibodies in the different groups of women tested. When an IHA titer of  $\geq$  1:256 was considered positive, there was also no significant difference between the seropositivity rate in the different groups of women tested ( $\chi^2 < 3.8$ ;  $p > 0.05$ ) (Srisasi, 1985).

Patients with ocular diseases were also tested for *Toxoplasma* antibodies with the IHA test. From 1978 to 1982, sera were obtained from 295 children and adults with ocular disease sent to the Department of Parasitology, University of Indonesia, from the Dr Cipto Mangunkusumo Hospital and private practitioners in Jakarta. Eye lesions were chorioretinitis (226 patients), uveitis (49 patients), cataract (12 patients), microphthalmia (9 patients), anophthalmia (2 patients) and vitreosis (2 patients); four cases had more than one eye lesion. *Toxoplasma* antibodies were detected in 77% of the patients. The highest frequency (60%) was in the chorioretinitis group (Srisasi, 1982). Suhardjo *et al* (1988) found 48 (88.9%) of 54 ocular toxoplasmosis outpatients in Yogyakarta suffering from chorioretinitis.

The actual occurrence of congenital toxoplasmosis in newborns is unknown, but there have been several reports. Partono and Cross (1976) reported a case of blindness in an 18 month old child with microphthalmia and bilateral cataracts, and an IFA titer of 1:1,024. The child's mother had an IFA titer of 1:512. Said *et al* (1978) reported two cases of congenital toxoplasmosis in the Department of Child Health, University of Indonesia: (1) a 13-month old child with mental and growth retardation, microphthalmia, history of frequent fever, cataract in the right eye, a large area of pigmentation in the left fundus, and an IFA titer of 1:2,048; and (2) a 6½-month infant with growth retardation, fever, microphthalmia, cerebral calcification, an IHA titer of 1:4,096, and an IFA titer of 1:2,048.

*Toxoplasma* antibodies were found in 7 (10.6%) of 66 hydrocephalic children in Jakarta, aged 1 day to 12 years, when an IHA titer of  $\geq$  1:256 was considered positive. Five infants, aged 1-11 months had persistent high titers of 1:2,048 and

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Table 1  
Serological surveys for *Toxoplasma* antibodies in Indonesia.

Area	Investigator	Test	Pos titers	Result (%)
West Irian (Wamena, Merauke)	De Roever-Bonnet <i>et al</i> , 1964	DT	$\geq 1 : 4$	24
Kresek West Java	Clarke <i>et al</i> , 1973a	IHA	$\geq 1 : 32$	51
Yogyakarta Central Java	Clarke <i>et al</i> , 1973b	IHA	$\geq 1 : 32$	20
South Kalimantan	Durfee <i>et al</i> , 1976	IHA	$\geq 1 : 16$	31
Surabaya East Java	Van der Veen <i>et al</i> , 1974	IFA	$\geq 1 : 32$	63
Surabaya East Java	Yamamoto <i>et al</i> , 1970	HA	$\geq 1 : 256$	8.9
Lindu Valley Central Sulawesi	Clarke <i>et al</i> , 1975	IHA	$\geq 1 : 256$	7.9
Palu Valley Central Sulawesi	Cross <i>et al</i> , 1975a	IHA	$\geq 1 : 256$	16
Boyolali Central Java	Cross <i>et al</i> , 1975b	IHA	$\geq 1 : 256$	2
North Sumatra	Cross <i>et al</i> , 1975c	IHA	$\geq 1 : 256$	9
West Kalimantan	Cross <i>et al</i> , 1975d	IHA	$\geq 1 : 256$	3
Jakarta	Partono and Cross, 1975	IHA	$\geq 1 : 256$	10
Jakarta	Srisasi 1978	IHA	$\geq 1 : 256$	12.5
Obano	Srisasi and Endardjo, 1980	IHA	$\geq 1 : 256$	34.6
Manado North Sulawesi	Kapojos, 1988	IHA	$\geq 1 : 128$	60

1:8,192. Two infants also suffered from chorioretinitis and cerebral calcifications. In all seven cases, the mothers were positive for *Toxoplasma* antibodies. Toxoplasmosis was suggested as the cause of hydrocephaly in the five cases described above, but it could not be ascertained in the other two cases (Srisasi and Mahjuddin, 1981).

Over a period of two and a half years (1986-1988) 99 infants, aged 1 day - 6 months old) with congenital anomalies were examined in the Department of Parasitology by ELISA. Eighteen infants (18.2%) were considered to be congenitally infected; specific IgM antibodies were detected in eight infants; at autopsy, one infant was found to have *T. gondii* in the brain and other organs; and rising or constantly elevated IgG levels were seen in nine infants. Thirty-nine infants (39%) were most likely infected because they had IgG antibodies. Forty-two of the remaining infants were not considered infected because no IgG or IgM antibodies were detected (Srisasi, 1988).

Harun *et al* (1989) reported a case of congenital toxoplasmosis in a 15-day old infant with hydrocephaly, cerebral calcifications, and chorioretinitis. Serology of a single specimen revealed a high IgG titer by ELISA. The final diagnosis was established at autopsy where *T. gondii* tachyzoites and cysts were detected in the brain, testicular tissue, liver, spleen and striated muscle. Lazuardi *et al* (1989) found rising or constantly elevated IgG levels in 37 infants (15.3%), aged 0-1 year, among 242 children aged 0-12 years with the following clinical signs: 108 with growth retardation, 14 with convulsions, 108 with eye lesions, 34 with head anomalies, 5 with deafness, and 23 with systemic diseases. Widyantoro (1989) found seven cases of congenital toxoplasmosis out of 18 infants born to mothers with high IgG levels: two infants, one with hydrocephaly and the other with microcephaly, both with positive IgG and IgM titers (ELISA); two premature infants with positive IgG titers in paired sera taken at birth and at 6 months, and a positive IgM titer in one infant; three clinically normal infants with positive IgG titers in paired sera taken at birth and at 6 months and a positive IgM titer in one infant.

## DISCUSSION

In some of the studies discussed, the data showed a decrease in seropositivity rates at higher altitudes. This observation was also reported from Central and South America (Remington and Desmonts, 1982). A seropositivity rate as low as 2% was found in several villages located at elevations of 900 to 1,900 meters along the slopes of Mt Merapi and Mt Merbabu, Boyolali Regency, Central Java (Cross *et al*, 1975b). Low prevalence rates were also found in North Sumatra (9%) (Cross *et al*, 1975c) and West Kalimantan (3%) (Cross *et al*, 1975d). The villages in these areas were located at higher elevations than the villages with higher prevalences. Wallace *et al* (1974) found a prevalence rate as low as zero, or less than 2%, in Lakes Plain, Central Highlands, Southern Coastal Plain, Great Plateau in New Guinea, and a high rate of 14-34% in the Eastern highlands and Rossel Island. The low prevalence rates were found in areas where there were no cats, higher rates were found in areas where cats were numerous. In Obano, in the district of Paniai, situated at an altitude of 1,745-2,100 meters above sea level, a prevalence rate as high as 34.6% was found. No cats were found in this area. It appeared that the source of toxoplasmosis in this area was raw or undercooked pork. To further substantiate the role of raw or undercooked pork in transmission of the disease were three patients with significant *Toxoplasma* antibody titers who suffered from epileptic seizures of cerebral cysticercosis, and *Taenia solium* infections have been shown to be endemic in this area (Desowitz *et al*, 1977). From these observations it can be concluded that there is no correlation between prevalence of *Toxoplasma* antibodies and altitude, but *Toxoplasma* antibodies are correlated with the presence of cats and with eating raw or partly cooked meat in the areas described above.

The prevalence of *Toxoplasma* antibodies was lower in Chinese than in Indonesian students. Lower prevalence rates in Chinese than in other ethnic groups were also found in Singapore (Zaman and Goh, 1969), Taiwan (Tsai and Cross, 1972; Durfee *et al*, 1975), Malaysia (Tan and Zaman, 1973), and Canada (Seah, 1974). However, Wallace *et al* (1974) reported a prevalence

rate of 86% in Chinese in Tahiti and compared to 70% in Tahitians. The low prevalence of *Toxoplasma* antibodies in Chinese in Southeast Asia is difficult to explain. In the studies in Jakarta no correlation could be found between positive titers and ownership of cats or eating raw or partly cooked meat. The reason for this difference in the two groups could not be determined.

In a study of women with a history of habitual abortion or sporadic abortion and intrauterine fetal death, and in women with no such history, no significant difference could be found in their seropositivity rates. This same observation was reported in 25 cases of abortion by Southern (1972), 73 cases of habitual abortions by Kimball *et al* (1971), and in 46 cases of habitual abortions and 61 sporadic abortions by Stray-Pedersen *et al* (1977). Other studies, however, suggested a cause-and-effect relationship between *Toxoplasma* infection, abortion, and intrauterine fetal death. Because of inconsistent reports from different laboratories, Remington and Desmonts (1982) suggested that more studies be done.

*Toxoplasma* antibodies in patients with ocular diseases were found to be highest in the chorioretinitis group (Srisasi, 1982; Suhardjo *et al*, 1988). Remington and Desmont (1982) indicated that toxoplasmosis is one of the most common causes of chorioretinitis. Moreover, toxoplasmic chorioretinitis in older children and adults is considered to be the result of a congenital infection.

Various serological surveys have been done for congenital toxoplasmosis, indicating the importance of this infection and confirming its high prevalence rate.

The diagnosis of toxoplasmosis in our laboratory is done by detection of specific IgM and IgG antibodies using the ELISA. The diagnosis of an acute infection should be based on a significant increase in IgG levels in paired sera or on detection of IgM. When IgM antibodies are not found, it is necessary to detect elevation of IgG in paired sera. Detection of antigen in serum and body fluids with monoclonal antibodies for a rapid, direct diagnosis of active infection would be desirable to identify women who acquire infection during pregnancy

and to identify congenital toxoplasmosis in newborns so that treatment can be considered.

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