

Research Article

Congenital Toxoplasmosis: Epidemiological Study in the Marche Region (Central Italy)

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Introduction

Toxoplasmosis is a zoonotic disease caused by an obligate intracellular protozoan parasite, *Toxoplasma Gondii* (TG). The parasite can infect humans and other species of vertebrates but the primary host is members of family Felidae (domestic cats and their relatives). The life cycle of the parasite is limited to the feline intestine where oocysts are created and excreted with feces. Humans can become infected by the ingestion of oocysts through the direct contact with an infected cat or its feces; by ingesting food or water contaminated with oocysts; by consuming raw or undercooked meat containing tissue cysts [1]. Approximately 25-30% of the world populations are known to be infected with TG [2]. The seroprevalence of TG varies incredibly from country to country (from 10% to 80%) and even within the same country or among the different communities of the same region [2]. The seroprevalence is related to different risk factors such as women

Abstract

Background: Toxoplasmosis is caused by *Toxoplasma gondii*, an obligate intracellular protozoan parasite. This parasitic infection in pregnancy congenitally causes severe outcomes to their fetus and newborn.

Objective: The aim of this study was to assess the epidemiological situation of *Toxoplasma gondii* infection in a population of pregnant women and newborns in Marche region (Italy).

Materials and Methods: A prospective study was undertaken between May 2011 and April 2012 in 13 of 15 birthing centres of the region. The women population was investigated on the basis of antenatal screening, the seroprevalence and maternal infection, while newborns were considered for congenital infection.

Results: The total number of pregnant women participated to this study was 10,232 and the serological screenings for *Toxoplasma gondii* infection were performed in 98.6% of women. The overall seroprevalence of pregnant women was 27.5% (28.9% for immigrants). The maternal infection rate was 0.09% of the total women and 1.2/1000 of the susceptible pregnancies. Spiramycin antibiotic were used in all infected women. The prevalence of congenital infection for *Toxoplasma gondii* was 1/10.000 born alive. The unique newborn infect was asymptomatic at birth and was treated for 1 year with Pyrimethamine/Sulfadiazine and Leucovorin. It did not show infection outcomes in the follow-up.

Conclusions: Epidemiological data revealed how the prevalence of congenital toxoplasmosis in Italy is relatively low. However, the results of this study have confirmed the importance of antenatal serological screening to prevent and eventually treat the infection.

Keywords: *Toxoplasma Gondii*; Pregnant Women; Congenital Toxoplasmosis; Prenatal Serologic Screening

in fertile age, consumption of raw meat or food contaminated with cat feces, contact with cats, and low level of education or living in rural areas [1,2]. Parasitemia associated with primary infection during pregnancy may conduct to placental and fetal infection. The fetal infection occurs in around 30% of cases, and the risk rises as the pregnancy progresses from 5% in the 1st trimester to 80% in the 3rd trimester [3]. In contrast, the risk of severe clinical signs in the infected infant is reduced from 60% in the 1st trimester to 5% in the 3rd one [4]. Over 90% of pregnant women are asymptomatic during the acute infection and even the congenital infected newborns. Although most of them do not present clinical signs (over 85% of cases) at birth, they have high risk of developing severe sequel later in life including mental retardation, hydrocephalus, convulsions, sensorineural hearing loss and chorioretinitis, that if untreated may result in blindness [1,5]. In addition to the hygienic measures, antibiotic treatment of the mother during pregnancy is an attempt to

reduce the frequency and severity of fetal infection.

Treatment with Spiramycin in the early stages of pregnancy caused 60% reduction in vertical transmission rate [6,7]. However, once fetal infection has been diagnosed, the combination of pyrimethamine and sulfadiazine should be administered to pregnant women and as postnatal treatment, that significantly contributes to lower the rates of severity of the infection and the sequel in the infected newborns [6,7].

Furthermore, the prevalence of TG-IgG antibody observed in women's reproductive phase, as result of an earlier infection, is decreased in the last decades in most of industrialized countries, leaving women more susceptible to primary infection during the pregnancy. Despite these findings, in some countries where pregnant women undergo routinely antenatal serological screening for TG infection, it has been observed a reduction of the prevalence of congenital infection [8].

The aim of this study was to analyze the epidemiological situation of TG infection in pregnant women and newborns in Marche region (Italy) and to assess the preventive efficacy of prenatal serologic screening.

Materials and Methods

Marche is a region of central Italy with a population of nearly 1.5 million of people. The number of births is around 14000/year and the population of pregnant women consist of 75.5% of Italian and 24.5% of foreign women.

A prospective study was undertaken between May 2011 and April 2012 in 13 of 15 birthing centers of the region. A questionnaire was designed with all the data related to the research and sent to each birth centre that was filling out monthly. In our data were included the number of pregnant mothers, the women attending the antenatal screening, the seropositive women to antibodies anti-TG, those with seroconversions and acute maternal infection and the number of born alive with congenital infection. The number of alive infants has been calculated on the basis of percentage of multiple births in 2010 (1.3%) in the region of Marche [9]. A casual sample of women was used to evaluate the seroprevalence data in foreign pregnant women. On the basis of serological tests the women were classified in:

- Immune or seropositive : Presence of TG-IgG and absence of TG-IgM antibodies
- Non immune or seronegative: Absence of both antibodies,

TG-IgG and TG-IgM

- Seroconversion: Appearance of TG-IgG and/or TG-IgM antibodies during the pregnancy, after a negative test
- Maternal acute infection: Presence of TG-IgM + TG-IgG antibodies associated to TG-IgG with medium-low avidity

Instead, diagnoses of congenital toxoplasmosis were made in fetus, newborn or babies less than one year of age, if it was detected:

- PCR real time (polymerase chain reaction) testing on amniotic fluid
- Specific IgM and IgA antibodies
- Specific IgG antibodies within the first 12 months of life
- Persistent positive of specific IgG antibodies until 1 year of age.

In pregnant women the specific antibodies levels in the serum were determined by immunoenzymatic tests commercially available and performed in specific public and private laboratories. However, the DNA analysis was performed by PCR real time in public laboratories (Roche-Switzerland). Chemiluminescence methods in public laboratories were used to detected specific antibodies in infant and newborns (Diasorin- Italia). The 95% Confidence Interval (CI) were used to evaluate the prevalence and incidence rates.

Results

A total of 10,232 pregnant women participated to this study, 74.9% were Italian and 25.1% of them were foreign. A casual sample of foreign expectant mothers was composed of 357 women. Serological screening for TG infection were performed in 98.6% of women (IC 95%: 98.3-98.8) and the total seroprevalence was found in 27.5% (IC 95%: 26.6-28.4) of pregnant women, while 28.9% (103/357) (IC 95%: 24.2-33.6) was detected in foreign. Nine women, among them 7 Italian, were TG infected; 7 were seropositive for both TG-IgG and TG-IgM antibodies associated to TG-IgG with medium-low avidity, instead, the other 2 cases were positive for appearance of TG-IgM after a negative test. Amniocentesis was carried out, with negative result, in 2 women. All women were treated with Spiramycin as prevention. The incidence of primary infection was 0.09% (IC 95% 0.03-0.15) of the total women and 0, 12% (IC 95% 0.04-0.20) of the most susceptible ones, respectively. Moreover, one asymptomatic Italian newborn presented congenital toxoplasmosis infection for the

Table 1: Italian epidemiological data of toxoplasma gondii infection [13-19].

	Antenatal Screening Rates	Seroprevalence Rates (Foreign Pregnant)	Maternal Infection Rates	Congenital Infection Prevalence
Ricci M, et al. [13]	-	34.4%	3.5%	0.040%
De Paschale M, et al. [14]	-	21.5%	0.9%	-
Stagni L, et al. [15]	-	-	0.24%	0.013%
Tomasoni LR, et al. [16]	-	35.8%	-	-
De Paschale M, et al. [17]	-	20.7%	0.36%	-
Lauria L, et al. [18]	97.7%	-	-	-
Puccio G, et al. [19]	94.8%	17.9% (30%)	0.11%	0.12%
Our data	98.6%	27.5% (28.9%)	0.12%*	0.010%

* Susceptible pregnancies

presence of specific TG anybodies. The case was treated for 1 year with Pyrimethamine/Sulfadiazine and Leucovorin. It did not show infection outcomes in the follow-up.

Although the number of infants born alive based on incidence of multiple births was 10,198, the prevalence of the congenital TG infection was estimated to be 0, 01% (IC 95%: 0.00-0.03).

Discussion

In Italy a prenatal serological screening to detect early infection is highly suggested and consists in a serological analysis in the first prenatal check-up and if the test is negative, it's followed to routine evaluation every 4 to 6 weeks till the end of the pregnancy [10]. In addition, women should be well informed how to implement hygiene measures to prevent TG infection.

Participation of women in antenatal TG screening data, observed in our study and reported by other authors, has demonstrated how the Italian doctors are well aware of toxoplasmosis problem during pregnancy (Table 1). Between 10 to 20% of pregnant women are immune to TG in some countries of the Northern Europe and USA, instead the percentage increase up to 50 percent in France, Poland and some German regions¹⁸. In Italy the seroprevalence goes between 17.9% to 35.8% (Table 1). Our data are in line with other authors and confirm that nearly 70% of pregnant women in our country are susceptible to TG. Therefore, seroprevalence data of other authors in foreign women can be compared with our data (Table 1). Rate of maternal infection is estimated at 1 to 8/1000 susceptible pregnancies, with high levels in France [11]. On the other hand, according to the latest research, in Italy the infection levels involve 1.1 to 9/1000 pregnancies, instead our data, compare to susceptible women, was 1.2/1000 pregnancies, similar to those reported by other authors.

The prevalence of congenital TG infection rages from < 1 to 10/10,000 born alive instead in Italy varies from 1 to 4/10,000 born alive (Table 1). In the last decades, some countries have experienced a reduction of the prevalence of the congenital TG infection, for example, in France the infection had decreased from 10/10,000 born alive in 1995 to 3.3/10,000 born alive in 2007 [8]. Moreover, other Italian epidemiological data have shown how the prevalence of congenital infection was 4 times lower than the last decade. The possible explanations of this reduction are: 1) reduction of the seroprevalence of pregnant women that caused a lower level of circulation of the parasite in the environment and consequently decrease the risk of infection in pregnancy; 2) the use of a universal prenatal screening for TG that allows to diagnose maternal infection and intervene with preventive therapy that reduce the incidence of vertical transmission.

However our study presents some limitations. First, we did not investigate possible risk factors associate with toxoplasmosis in pregnancy. Second, the lack of data on the number of abortions/fetal deaths caused by TG infection in pregnancy. In France, congenital toxoplasmosis was responsible for 4% of pregnancy termination (54.5% abortions and 45.5% fetal deaths) [12].

Conclusion

Epidemiological data on the prevalence of congenital TG infection in our population are in line with current Italian literature

and confirmed the low prevalence of congenital infection in Italy.

Furthermore, it has been demonstrated that antenatal screening is a really important weapon for health care against TG infection because allowed to find out the most susceptible women and provide an accurate primary prevention or, in case of maternal infection, secondary.

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