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RESEARCH ARTICLE

Prematurity and Low Birth Weight did not Correlate with Anti-*Toxoplasma gondii* Maternal Serum Profiles – a Brazilian Report

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Abstract

Gestational *Toxoplasma gondii* infection is considered a major risk factor for miscarriage, prematurity and low birth weight in animals. However, studies focusing on this topic in humans are scarce. The objective of this study is to determine whether anti-*Toxoplasma gondii* maternal serum profiles correlate prematurity and low birth weight in humans. The study examined 213 pregnant women seen at the High-Risk Pregnancy Hospital de Base, São José do Rio Preto, São Paulo, Brazil. All serological profiles (IgM-/IgG+; IgM-/IgG-; IgM+/IgG+) were determined by ELISA commercial kits. Maternal age, gestational age and weight of the newborn at birth were collected and recorded in the Statement of Live Birth. Prematurity was defined as gestational age <37 weeks and low birth weight $\leq$ 2499 grams. The *t*-test was used to compare values ($p < 0.05$). The mean maternal age was 27.6±6.6 years. Overall, 56.3% (120/213) of the women studied were IgM-/IgG+, 36.2% (77/213) were IgM-/IgG- and 7.5% (16/213) were IgM+/IgG+. The average age of the women with serological profile IgM+/IgG+ (22.3±3.9 years) was different from women with the profile IgM-/IgG+ (27.9±6.7 years, $p = 0.0011$) and IgM-/IgG- (27.9±6.4 years, $p = 0.0012$). There was no statistically significant difference between the different serological profiles in relation to prematurity ($p = 0.6742$) and low birth weight ($p = 0.7186$). The results showed that prematurity and low birth weight did not correlate with anti-*Toxoplasma gondii* maternal serum profiles.

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Introduction

Toxoplasma gondii is an obligate intracellular parasite that causes toxoplasmosis, one of the most widespread zoonotic diseases in the world. In all countries there is a high number of humans and animals infected with *T. gondii*. In some regions, about 30–60% of the population is positive for toxoplasmosis in serological tests [1–4].

The *T. gondii* life cycle alternates between intermediate hosts (mammals and birds), where the asexual stage occurs, and definitive hosts (felines), harboring the sexual stage. The infection in the intermediate host occurs by eating raw or undercooked meat containing cysts, and water or food contaminated with oocysts secreted in the feces of infected cats [2].

In the acute phase, rapid replication of tachyzoites predominates and in approximately 60–90 days the infection becomes chronic. As the immune response is effective in controlling the infection, tachyzoites differentiate into bradyzoites, which divide more slowly and form cysts in various cells, particularly in the brain, heart and muscles. About 80% of chronically infected individuals are asymptomatic although in some cases eye injuries occur [2,5–11].

When the primary infection occurs during pregnancy, the parasites can infect the fetus through the placenta, causing birth defects and ocular complications. The consequences of maternal and fetal infection depend on the degree of exposure of the fetus to parasites, the virulence of the strain and the gestational period in which there was infection, and the classic signs of congenital toxoplasmosis are: hydrocephalus; chorioretinitis; cranial calcifications and mental retardation [1,12–23].

Contemporary research on *T. gondii* infection in humans has been directed to risk groups such as patients with immunodeficiency, transplant patients, patients with eye injuries and even normal individuals. In addition to these, pregnant women and newborns are targeted for medical attention given the risks of congenital transmission and the sequelae [14,24–30].

The prevalence of *T. gondii* infection was investigated in different Brazilian states in recent decades and the results revealed great variability in its contents, including previous studies by our group [2,31–34]. In addition to these studies, we were able to establish that the congenital transmission rate in the region reaches 2.3% [32]. The interest in conducting proper screening for *T. gondii* infection in risk groups has grown considerably in recent years, as well as the interest in studies to establish some relation to the conditions presented by newborns, such as prematurity and disease severity [5,18,35–42].

Toxoplasmosis thus constitutes a serious public health problem, especially in pregnant women who were not infected by *T. gondii*, and may cause neurologic damage the baby, being a disease of epidemiological significance to pregnant women and women of childbearing age and recently included in the list of by the CDC of neglected diseases [43,44].

The aim of this study was to correlate prematurity and low birth weight with the serological profile of pregnant women for toxoplasmosis.

Materials and Methods

Ethical aspects of the study

This study was approved by the Ethics Committee in Research of the Faculty of Medicine of São José do Rio Preto–FAMERP (protocol 168/2007). The need for a written consent of patients was waivered as all the data were retrospectively collected from the patients' hospital records and was anonymized.

Data analysis

Data records were consulted for 310 pregnant women who met at the Clinic of High Risk Pregnancy and Fetal Medicine from the Hospital de Base de São José do Rio Preto, Brazil from 2005 to 2007. Complete data were found for 213 women regarding serological screening for toxoplasmosis during the prenatal period; weight data, gestational age and maternal age were collected from their Statement of Live Birth.

Definition of prematurity and birth weight

Preterm birth was defined as gestational age less than 37 weeks and low birth weight as less than or equal to 2499 grams according to the criteria of the World Health Organization [45].

Definition of serological profiles for toxoplasmosis

All serological profiles were determined by ELISA commercial kits (Diasorin, Italy) and all manufacturer's instructions were strictly followed. Three serological profiles were constructed: **I** = IgM positive/ IgG positive; **II** = IgM negative/IgG positive; **III** = IgM negative/IgG negative. The profile IgM positive/IgG negative was not found in the analyzed cases. All maternal serum profiles were identified at the first medical consultation.

Statistical analysis

The *t*-test was used to compare the data according to the serological profiles. The alpha value less than or equal to 5% was considered significant.

Results

The average age of the selected pregnant women was 27.6±6.6 years. The results are shown in Tables 1, 2 and 3. In Table 1, it can be seen that the profile IgM negative/IgG positive (Profile II) prevails over the other.

Table 2 shows the average age of pregnant women according to the identified serologic profiles. No statistically significant differences were observed between the mean age of the women with the profiles II and III ($p = 0.9999$). However, the average age of the women in profile I was lower than those observed for the women in profile II ($p = 0.0011$) and III ($p = 0.0012$).

The average birth weight of newborns analyzed was 1,916 ± 617.1 grams. Table 3 lists the maternal serological profile and weight of the newborn. No statistically significant differences were observed between the different serological profiles (I, II and III) and the low weight of the newborn (I x II: $p = 0.7384$; I x III: $p = 0.5078$; II x III: $p = 0.7250$).

The mean gestational age was 33.7 ± 3.7 weeks. Table 4 shows the relationship between the serological profile and prematurity. Profiles I, II and III when compared showed no statistically

Table 1. Serological profile of pregnant women seen at the Clinic of High Risk Pregnancy and Fetal Medicine of Hospital de Base de São José do Rio Preto, São Paulo, Brazil from 2005 to 2007.

Profile	Serology	N	%
I	IgM+/IgG+	16	7.5
II	IgM-/IgG+	120	56.3
III	IgM-/IgG-	77	36.2
	Total	**213**	

(+) = positive; (-) = negative.

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Table 2. Comparison of serological profile for anti-*T. gondii* antibodies and maternal age.

Profile	Serology	N	Average Maternal Age
I	IgM+/IgG+	16	22.3 ± 3.9
II	IgM-/IgG+	120	27.9 ± 6.7
III	IgM-/IgG-	77	27.9 ± 6.4
	Total	**213**	

I x II: p = 0.0011; I x III: p = 0.0012; II x III: p = 0.9999

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significant difference (I x II: p = 0.7780; I x III: p = 0.7681; II x III: p = 0.7534). Table 5 shows the frequency of birth weight classifications.

Discussion

The objective of this study was to correlate prematurity and low birth weight with the maternal serum profiles in 213 pregnant women for toxoplasmosis the northwestern region of São Paulo State who gave birth a single baby for both sexes, whose data prematurity and low birth were obtained from the official Statement of Live Birth. The decision to use this document as a data source is due to the fact that they constitute an official record established by Brazilian legislation. [41,42,46].

The frequencies of the identified serological profiles in patients in our study are consistent with findings in the literature [47,48]. The prevalence of *T. gondii* infection is high in the northwest of São Paulo State and it has been shown that most pregnant women have the anti-*T. gondii* IgG class. Even so, a large percentage of individuals do not present specific antibodies for this parasite and this may result from having contact with the infective form. The simultaneous presence of anti-*T. gondii* IgM and IgG classes is transient in most cases and therefore the percentage of pregnant women with this profile is smaller than the other mentioned above [14,18,31,47,49,50].

The results showed that the pregnant women's positive containing only anti-*Toxoplasma* IgG antibodies (profile II) have an average age of pregnant women as the negative for both classes of antibodies (profile III). However, the mean age of the women with these serological profiles was higher than that of positive pregnant women for both antibody classes (profile I).

There are reports that the average age of pregnant women at increased risk of congenital infection (IgM+/IgG- and IgM+/IgG+) is lower than those with other serological profiles (IgM-/IgG- and IgM-/IgG+). Pessanha et al. [51] reported that the average age of women who gave birth to children with laboratory indications of congenital infection was lower than those

Table 3. Relationship between low birth weight and maternal serological profile serological profile for anti-*T. gondii* immunoglobulins.

Profile	Serology	Low Birth Weight		Non Low Birth Weight	
		N	%	N	%
I	IgM+/IgG+	02	12.5	14	87.5
II	IgM-/IgG+	25	20.8	95	79.2
III	IgM-/IgG-	18	23.4	59	76.6
	Total	**45**		**168**	

I x II: p = 0.7384; I x III: p = 0.5078; II x III: p = 0.7250

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Table 4. Relationship between prematurity and maternal serological profile for anti-*T. gondii* immunoglobulins.

Profile	Serology	Prematurity		Non-Prematurity	
		N	%	N	%
I	IgM+/IgG+	04	25	12	75
II	IgM-/IgG+	36	30	84	70
III	IgM-/IgG-	25	32.4	52	67.6
	Total	**65**		**148**	

I x II: p = 0.7780; I x III: p = 0.7681; II x III: p = 0.753

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whose newborns did not present signs of infection. Although the mean age of the pregnant women with serological profile I was lower in comparison with those carrying serological profile II and III; we must take in account that IgM+/IgG+ serum profile does not confer risk of congenital toxoplasmosis transmission.

Dias et al. [52], Rodrigues et al. [47] and Ferenzi and et al. [53] reported a higher mean age for positive pregnant women with IgG anti-*T. gondii* compared to those not exposed to the parasite. These observations are supported by the data observed in this study. In fact, chronic infection maintenance and the risk of reinfection contribute to the production of IgG class antibodies and with a higher avidity index [1,4,14,54–56]. The high rates of infection in the region of origin of pregnant women evaluated in this study can contribute to re-exposure to the parasite favoring the prevalence of anti-*T. gondii* IgG class antibodies in the population [2,31,47,57–60].

The average age of pregnant women with serological profile III did not differ from that observed in women with pattern II and this can be a result that the series were selected in a reference center caring for high-risk pregnant women.

This study also explored the relationships between serum maternal profile with low-birth and prematurity since these variables were previously reported [5,30,40–42,59–64]. A report from Moraes et al. [65] showed that the prevalence of low-birth and prematurity for the region in which this study was carried out is equal to 6.5% and 9.0%, respectively. These values are lower in comparison with our data since the medical records were collected from a reference center for high risk pregnancy.

Comparison of birth weight with different serological profiles did not show statistically significant differences. Pessanha et al. [51] observed that birth weight is not correlated with the presence or absence of congenital infection by *T. gondii*. Although Pessanha did not correlate serological profiles of pregnant women with birth weight, their data underlie, at least in part, the results reported in this study.

Prematurity observed in the analyzed sample showed no correlations with the maternal serum profiles found. McLeod et al. found that serotypes of *T. gondii* NE II are associated with

Table 5. Frequency of weight at birth and serological profiles for *T. gondii*, São José do Rio Preto, São Paulo.

Serology	Normal Weight >2.500g	Low Birth Weight <2.500g	Very Low Birth Weight <1.500g	Extremely Low Birth Weight <1.000g	Total
IgM-/IgG-	55	19	1	2	77
IgM-/IgG+	99	16	2	3	120
IgG+/IgM+	14	1	0	1	16
Total	**168**	**36**	**3**	**6**	**213**

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prematurity and/or severity of congenital toxoplasmosis but did not establish correlations of these conditions to the serological profiles of the analyzed pregnant women. [36]

This study present some limitations and therefore their data must be considered as preliminary. First, only ELISA test was performed to detect IgM and IgG anti-*T. gondii* antibodies and it present some limitations. Persistent IgM antibodies can be detected for several months after the primary infection and therefore IgM+/IgG+ serum profile does not correlate acute infection necessarily [1,50,56,66,67]. Secondly, IgG avidity test and Western blot test were not carried out in the pregnant women and their neonates since they are not offered by Brazilian public health system [14,39,68–70]. Studies with large numbers of pregnant women in different Brazilian regions may contribute to the elucidation of the importance of analysis of maternal serum profiles and their potential correlations with low birth weight and prematurity and infection by *T. gondii*.n conclusion, our data show that maternal age is related to the serological profile, but prematurity and low birth weight did not correlate with anti-*T. gondii* maternal serum profiles.

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Author Contributions

Conceived and designed the experiments: CCBM SB MMLF LCM. Performed the experiments: SB MMLF LCJFS DCMVO AHO EAG. Analyzed the data: MMLF LCM CCBM. Contributed reagents/materials/analysis tools: MMLF LCM. Wrote the paper: MMLF LCM CCBM. Head of the FAMERP Toxoplasma Research Group and responsible for concept and design of the study: CCBM. Performed the inclusion of patients, sample collection, and developed the clinical evaluation and clinical analyses: MMLF SB LCJFS EAG. Performed the data analysis, interpreted the data and wrote the manuscript: CCBM LCM MMLF LCJFS AHO DCMVO. Approved the final manuscript: MMLF SB LCJFS DCMVO EAG AHO LCM CCBM.

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