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ABSTRACT

Background: To evaluate whether the treatment of the pregnant women associated with a lack of monitoring for toxoplasmosis seroconversion affected the prognosis of the patients

Methods: - Cohort study with 292 newborns at risk for congenital toxoplasmosis, in Goiânia-GO (Brazil), between October 2003 until October 2011. We carried out statistical analysis in order to test the efficacy of maternal treatment with spiramycin.

Results and discussion: - 40.74% were born seriously affected. Mother-to-child transmission associated with reactivation during pregnancy occurred in 4.94% (8/162), 25% showed a severe infection. The presence of specific immunoglobulins (fetal IgM and IgA) suggested the worst prognosis. The treatment of pregnant women resulted in an asymptomatic condition in the newborns and it also protected against the severity of the disease. The children of untreated patients showed the worst outcome. The fetal IgM was associated to an ocular impairment in 48% of the fetus and the neonatal IgA-specific was related to neuro-ophthalmologic and systemic forms. The maternal treatment with spiramycin decreased significantly the incidence of the most severe modalities of the disease.

Conclusion – It is necessary to enhance primary prophylactic measures and to improve the secondary prophylaxis in order to treat the fetus.

PALAVRAS CHAVE - Congenital Toxoplasmosis; Toxoplasmosis during pregnancy; Treatment of pregnant women with acute toxoplasmosis.
BACKGROUND

Congenital Toxoplasmosis is an important cause of eye, hearing and mental deficiencies [1,2,3,4,5,6]. This feature was unknown up to 2010 when a mandatory reporting was implemented requiring the assessment of a program to control congenital toxoplasmosis throughout the country [7].

Goiânia, capital of Goiás is located in the Central-Western Region of Brazil. It has a high prevalence of toxoplasmosis in women of reproductive age (65.8%). Moreover, the pregnant women in this city show one of the highest serological conversion rates in the world (8.6%) [8]; situation which predisposes to congenital toxoplasmosis once a seronegative pregnant woman undergoing immunological changes - typical of pregnancy - and living in a place with a high prevalence of the disease is more likely to acquire the infection [9,8,5].

This epidemiological risk stimulated a program of the state in order to control the congenital toxoplasmosis in October 2003. It was linked to a pregnant women care program in order to protect them from the mother-to-child transmission through primary and secondary prophylactic measures; these programs were created as an attempt to reduce vertical transmission and the severity of the congenital infection.

We performed a serological screening for toxoplasmosis and other infections such as Syphilis, Rubella, Cytomegalovirus (CMV), Hepatitis B (HBV) and C (HBC), HTLV, HIV and Chagas disease, at the first prenatal appointment. Although serological conversion follow-up is recommended in a high prevalence of the infection we have not performed it [10,5].
Analyzing the screening programs effectiveness is essential for the decision-making within public health politics, once even in an environment with a low incidence of the infection, toxoplasmosis have proved its importance [11,12,13]. Prophylactic strategies against Toxoplasmosis adopted by different public health systems are not always homogeneous; they differ even within the same country. There is a high prevalence of the infection in France [14], Austria [15] and seroconversion surveillance is performed monthly in those countries. They implemented a program of prenatal screening in Slovenia [16] and some other countries with a low incidence have adopted a program of neonatal screening, Denmark [17] and Poland [18] for example. In the United States [19] and United Kingdom [20] congenital toxoplasmosis is a rare condition, so they do not have a program of serological screening.

There had been much discussion concerning the significance of these government programs to control toxoplasmosis in pregnancy [14,15,21,18,22,16,20,10,17,23,12,24,13,7].

There are several circumstances that hinder the enforcement of these protocols: it is difficult to identify the acute phase of the infection in pregnancy when seroconversion is not performed; a proper interpretation of the results of the IgG avidity test is difficult to achieve if it is carried out after 16 weeks of pregnancy [25,26,27]; treatment compliance problems; inappropriate newborn assistance according to the reference service; the treatment provided for the pregnant patients does not prevent the vertical transmission of the protozoan infection [23]; the type of drug used in order to treat infected women causes international controversy as well [25,21,16,11,28].
Therefore, this study aimed to assess whether the treatment of the mother and the lack of serological conversion surveillance in the seronegative pregnant woman affected the prognosis.

**METHODS**

The present research is a cohort study with 292 newborns at risk for vertical transmission of congenital toxoplasmosis because either their mothers were seronegative or they showed specific IgM anti-*Toxoplasma gondii* (*T. gondii*) in their peripheral blood after the obligatory serological screening that was performed at the first visit of prenatal care. The patients were monitored in the Reference Service of the Federal University of Goiás (UFG) Clinical Hospital (CH), in Goiânia, state capital of Goiás, between October 2003 and October 2011.

The Association of Parents and Friends of Exceptional Children (APAE) in Goiânia and Anápolis/GO and public maternity Hospitals that participate in the Program for the Protection of Pregnant Women (PPG) were responsible for the selection of mothers and their newborns through collection of peripheral blood and/or umbilical cord blood. The inclusion criteria were babies from IgM positive mothers and babies with IgM-specific detected in peripheral blood or by Guthrie test.

The pregnant patients were labeled as having an acute infection when IgM-specific was confirmed, when the avidity of IgG (<30%) was low. The tests were performed before 16 weeks of pregnancy. These criteria are also used by Camargo et al. [26], Jenum et al. [27] and Figueiró-Filho et al. [29].
Acutely infected patients were treated with spiramycin 3g/day (from diagnosis to delivery). Furthermore, underwent amniocentesis and cordocentesis in order to extract biological material with suspected congenital infection (amniotic fluid and fetal blood).

The newborns suspected to have congenital infection underwent serological screening for toxoplasmosis and they were followed-up.

The diagnosis of fetal infection was carried out by the presence of the parasite (polymerase chain reaction or isolation of the parasite in mice), or specific anti-*Toxoplasma gondii* IgM in the amniotic fluid or fetal blood which were obtained by amniocentesis and cordocentesis after the 20th week of pregnancy. The procedure was conducted by a specialized Professional.

The children with suspected congenital toxoplasmosis underwent routine screenings. The protocol for the congenital infection diagnose was approved by the Medical and Animal Research Ethics Committee from the CH/UFG (039/2002). We included in the study children whose mothers have agreed to take part in the protocol for the diagnosis of congenital infection. We excluded the patients when vertical transmission of maternal infection was not confirmed.

Patients were considered infected when: *T. gondii* was isolated by experimental inoculation or the DNA of the parasite was detected in the fetal blood or in the CSF by PCR analysis; we identified the IgM and/or specific anti-*Toxoplasma gondii* IgA in fetal blood or in the newborn blood; we found specific antibodies (IgG and/or IgM) in the CSF of the newborns; the IgG-specific was larger than maternal IgG; IgG-specific of the nursing infant stabilized, showing either a rise in antibody titer (even with the treatment) or an
increase in antibody titer; IgG-specific in the infant remained positive after 12 months of life; a clinical alteration was compatible to the congenital infection such as ophthalmologic, neurological or a widespread impairment; there was diffuse node infarction along with the presence of IgM-specific in the maternal blood; transfontanelar ultrasound revealed hydrocephalus or intracranial calcifications; there was a lack of other diagnostic possibilities (Chagas disease, Syphilis, Rubella, CMV, HIV, HTLV, HVB and HVC).

The eye fundus examination was performed at the Reference Center of Ophthalmology (CEROF), in the Department of Ophthalmology, Faculty of Medicine of UFG.

Newborns infected or suspected of being infected were treated with sulfadiazine (100-150mg/kg/day), in a scheme of four doses a day (every six hours); pyrimethamine (1-2mg/kg/day) in a scheme of two doses (every twelve hours); and folinic acid orally given in daily dose of 3.5 mg. When the protein levels in the CSF were high (>150 mg/dl) or when there was ophthalmologic impairment, we added a daily dose of prednisone (2-3mg/kg/day) to the treatment. These conditions were maintained until we could annihilate the possibility of vertical transmission and for the infected patients the duration of the treatment depended on the presence of clinical abnormalities at birth (two years) or on the absence of clinical signs (one year).

**Laboratory Techniques**

We performed the neonatal serological screening through the Indirect Fluorescent Antibody Test (IFAT) and the Microparticle Enzyme Immunoassay (MEIA). We performed the IgM detection test for the suspected patients of congenital toxoplasmosis by three techniques - IFAT, MEIA and ELFA.
(Enzyme-Linked Fluorescent Assay). The IgA-specific detection test was performed by the Enzyme-linked immunosorbent assay (ELISA).

We isolated the parasite by inoculation of mice in order to analyze the biological samples suspected of being contaminated (fetal blood, amniotic fluid, neonatal blood and CSF of the newborns). We used the protocol from Silva et al. [30]. We also used PCR techniques which were performed at the Biology, Physiology and Immunology Laboratory for Protozoans of Human Interest in IPTSP/UFG. The PCR was standardized and the DNA from *T. gondii* was extracted as specified by the Pure Link Gennomic Purification kit- for purification of genomic DNA-Invitrogen. Reactions were performed in the MasterCycler Personal thermocycler. The amplification scheme consisted of an initial denaturation at 94°C (5'), 35 cycles of denaturation at 94°C (1'), annealing at 62 °C (1'), extension at 72 °C (1') and a final extension at 72°C (10'). The reactions were performed in duplicate by using a sequence of the gene B1 from the *T. gondii*. We used the following pairs of primer: Toxo-T1 (5'-ATG GTC CGC CCG GTG TAT GAT ATG CGA T-3'); Toxo-T2 (5'- TTC CTA CGT GGT GCC GCA GTT CCT-3'); Toxo-B5 (5' – TGA AGA GAG GAA ACA GGT GGT CG-3') and Toxo- B6 (5'-CCG CCT CCT TCG TCC GTC GTA-3'). The PCR amplified products were analyzed through electrophoresis in polyacrylamide gel (6 %) stained with silver nitrate. We used the peritoneal fluid and blood of mice infected with the RH strain of *T. gondii* for a positive control.

We performed the IFAT test - following the protocol Camargo [31] - at the Biology, Physiology and Immunology Laboratory for Protozoans of Human Interest in IPTSP/UFG. We used the RH strain kept in the laboratory for the analysis of blood (from the mother, the fetus or the newborn), amniotic fluid and
CSF from the newborn. We used Biolab conjugate (Fluoline G and M). The presence of IgM was demonstrated by removing Rheumatoid Factor Positive Serum and we used reagents produced by Biomérieux.

The microparticle enzyme immunoassay (MEIA) was used for the quantitative determination of the antibodies IgG and IgM anti-\textit{Toxoplasma gondii} in the CSF or in the plasma of the pregnant women, newborns and puerperal patients. It was done according to the instructions manual for the AXsYM ABBOTT immunochemical automated analyzer at the Clinical analysis laboratory, CH/UFG.

Enzyme-Linked Fluorescent Assay (ELFA) was used for the quantitative determination of the antibodies IgM anti-\textit{Toxoplasma gondii} in the plasma of the newborns. It was performed according to the instructions manual, at the Clinical analysis laboratory, CH/UFG.

Enzyme-linked immunosorbent assay (ELISA) was used for the determination of IgA. It was also used according to the instructions manual, at the Clinical analysis laboratory, CH/UFG.

\textbf{Statistical analysis}

We computerized the data using Excel 2007 and we used Excel 2007 and Epi Info 3.3.2 for the statistical analyses applying univariate tests. We evaluated whether there was association between each of the variables collected or not. We compared the results to the presence and the absence of maternal treatment with Spiramycin. P values $< 0.05$ were considered as statistically significant and we based our calculation on 95\% confidence interval. We used the Fisher's Exact Test when data were less than five.
RESULTS

Seronegative pregnant women had no primary preventive care guidance in order to avoid acute toxoplasmosis, so they did not follow the seroconversion during gestation period.

Eight women (4.94%) who had *T. gondii* infection before pregnancy gave birth to infected children; 3 (37.5%) of those children developed an asymptomatic form of the disease; 3 (37.5%) had asymptomatic meningitis; 1 (12.5%) developed the systemic form of toxoplasmosis and 1 (12.5%) an ocular form of toxoplasmosis. No patient was infected by HIV or any other infectious disease (Chagas disease, Syphilis, Rubella, CMV, HTLV, HVB and HVC).

Table 1 highlights 162 infected patients, 40.74% (66/162) of them were born seriously sick; among the seven patients who showed widespread disease, two also had neurological and optical impairment; 57 seronegative babies of women who did not follow serological surveillance developed congenital toxoplasmosis; neurological and optical forms of the infection were more statistically significant in those mothers.

The positive diagnosis for acute toxoplasmosis during gestation accounted for a 3.25 times higher risk of meningitis due to toxoplasmosis infection.

30.86% (50/162) of the babies were born with ophthalmologic impairment and 76% (38/50) of those had also neurological impairment; 20% (10/50) developed only the optical form while 4% (2/50) only had the systemic form of the disease. Among these children, 52% (26/50) were born with poor eyesight, 50% (13/26) of who were blind and 50% (13/26) with peripheral vision because of bilateral macular impairment; the systemic form was found in 4.32% (7/162);
31.48% (51/162) had intracranial calcifications and 37.25% (19/51) among the latter developed hydrocephalus.

Furthermore, 4.94% (8/162) of the patients were infected with toxoplasmosis and also with cytomegalovirus showing cerebral impairment characteristic of both infections; 4.32% (7/162) of the patients died due to the severity of the toxoplasmosis congenital infection.

Table 2 indicates that there was a higher risk of toxoplasmosis transmission to the child in the third trimester of pregnancy (1.44 times higher).

Table 3 shows that for the time of the prenatal diagnosis, in the third trimester there were no case of intracranial calcification, neither the auditory form nor the nodal one. The ophthalmologic impairment was more frequent (statistically significant) when the mother was aware of the infection only in the end of the gestation period.

Table 4 point out the clinical forms that are seemingly milder at birth (asymptomatic and meningitis) occurred more frequently when the mother was treated during the pregnancy - 1.8 times higher for the asymptomatic infection and 1.9 times higher in meningitis. The neurological-optical form was significant from a statistical standpoint, once it was more frequent among children of women not treated than in the treated group, 36.15% (30/83) for the former and 8.45% (6/71) for the latter. The systemic form was also found more frequently in the absence of treatment 7.23% (6/83); the frequency was 1.41% (1/71) in the treated woman, meaning that no statistical significance exists.

The fetal IgM test was performed in 47/162 (29.01%) of the cases and it and 25/47 (53.19%) have tested positive for it; 48% (12/25) within this group developed ophthalmologic impairment. The neonatal IgM was positive for
38.51% (62/161) of the cases and the neonatal IgA for 20.45% (18/88); patients with specific anti-Toxoplasma gondii IgA - 61.11% (11/18) - developed a severe form of infection; 85.7% (6/7) of the children with widespread disease had IgA-specific.

The parasite was identified in 31.67% (38/120), and in 34.21% (13/38) of the cases developed some sort of severe impairment; CSF was abnormal in 70.9% (78/110) with Toxoplasma gondii-specific IgG associated with nonspecific conditions.

The tests specific anti-T. gondii had a sensitivity of 60.9% for MEIA-IgM; 60.9% for ELFA-IgM; 59.6% for IFAT- IgM and 57.1% for IgA (Rodrigues et al. 2009).

**DISCUSSION**

The Program for Congenital Toxoplasmosis Control made possible the diagnosis of 162 children infected with T. gondii. Those children were sent to the Reference Center in the CH/UFG.

The diagnosis of the congenital disease was difficult to establish - the mother suffered acute toxoplasmosis or a recurrent form of the disease - because of the low sensitivity of congenital infection markers. Both IgM (38.51%) and IgA-specific (20.45%) levels along with of T. gondii identification (31.67%) found in this research were different from the Olariu et al. [19] results. They reported much higher percentages: 86.6% for IgM and 77.4% for IgA, which were also described by Castro et al. [32].
The fetal IgM proved to be a better marker for congenital infection than the same test in the newborn peripheral blood (53.19% and 38.51%, respectively). However it can be considered a poor marker once it failed to diagnose nearly half of the infected patients. An important aspect of it is that 48% of fetuses showed ophthalmologic impairment and we haven’t found any description of it in the literature. Our results imply that scientists should research this kind of infection more, even though there is an international debate on the subject concerning PCR in amniotic fluid being more important than other tests [33,34,35,36].

The IgA-specific was also associated with the worst prognosis of vertical transmission (neural- optical and systemic forms), just like it was described by Rodrigues et al. [37].

A fact has drawn our attention, 4.94% (8/162) of congenital infection cases affected immunocompetent children of women who had acute infection prior to pregnancy. Nevertheless, in 25% of the cases, the vertical transmission of the severe form of the disease occurred (ocular and systemic). We believe that this situation is likely to have resulted from a reduced cellular response of the host during the gestation period. It can interfere with the parasite load and with the clinical course of maternal infection and consequently increase the risk of vertical transmission [38,39,40,41,42,43]. Some authors report that IgG positive pregnant women could not transmit toxoplasmosis except in rare cases of acute toxoplasmosis relapse due to immunodeficiency of the patient [5]. Our results highlight that toxoplasmosis during pregnancy is a complex infection. Even if the mother is immune, the disease can be transmitted in its severe form.
to the child; all pregnant women should pay attention to primary prevention measures, regardless of their immune status.

Our results - 40.74% (66/162) were born severely affected (table 1) - are in accordance with Thiebaut et al. [23] (SYRICOT) this study compared the severity of congenital toxoplasmosis in Brazil and Europe, the most severe congenital cases were in our environment. One should note that those severe forms of the congenital infections occurred more frequently when there was no diagnosis of acute infection in pregnant women. This fact could be explained by either the lack of serological conversion surveillance in seronegative pregnant women or the absence of prenatal care.

The lack of seroconversion surveillance in 57 pregnant women at risk during the eight years of the Program for Congenital Toxoplasmosis Control in Goiania, resulted in the appearance of 37/57 (64.91%) children with severe forms of the infection (neurological, ocular and/or systemic). This number is much higher than the ones described in regions where there is no governmental program for controlling infection. The finding highlights the need for serological surveillance of the pregnant women, as already recognized by the literature [5,44].

As we see on table 2, toxoplasmosis transmission was higher in the third trimester of pregnancy (1.44 times higher), similar to the results of a meta-analysis study [23]. As in the European research, when a mother was diagnosed in the third trimester no intracranial calcification was found in the newborns, different from the ophthalmologic impairment that in this study presented an increase in its incidence.
In the third trimester there was neither the auditory form nor the nodal one. The neurological-optical form was found in all trimesters of the gestation period, indicating that in our country *Toxoplasma gondii* more aggressive to the fetus.

The neurological-optical form affected 36.15% (30/83) of the children of untreated mothers and 8.45% when the mothers underwent treatment with spiramycin. The treatment was a statistically significant protection for this clinical form of toxoplasmosis. Furthermore, maternal treatment decreased the prevalence of the sequelae forms of toxoplasmosis, a reduction from 60.24% (50/83) to 19.72% (14/71). These findings were much higher than those described by Schmidt et al. [17] - 21.8% of untreated pregnant women - in Denmark; confirming once more the increased aggressiveness of the congenital toxoplasmosis in our environment.

Among children with ocular impairment we found that 52% (26/50) were born with poor eyesight, (50% blind and 50% with peripheral vision because of bilateral macular impairment); these results are in accordance with the study of Gilbert et al. [45, who found more intense aggressiveness of toxoplasmosis in Brazil than in Europe. Moreover, we found a higher prevalence of the systemic forms (4.32%) which is considerably higher than the prevalence for other areas; in Europe, for example it is not higher than 1%.

Neurological manifestations, including asymptomatic meningitis, took place in 51.23% (83/162), and 61.44% (51/83) of those developed intracranial calcification (37.25% hydrocephalus). These results are similar to that of Daffos [46] and it is also evidence that the infection is more aggressive in our environment. Moreover, 4.94% (8/162) were infected by toxoplasmosis and
cytomegalovirus together, the cerebral impairment is a characteristic of both infections and it made the prognosis of the infected patients even worse.

The neurological and ocular aggressiveness - even in the children of treated pregnant women - larger than those found in places lacking prenatal preventive programs, indicate the need for future research, isolation and genetic characterization of the circulating strains in Goiás, and also immune assays of neonates exposed to *T. gondii* in pregnancy.

Despite treatment have been made with Spiramycin, there was a clinical improvement of the congenital infection consequences. The ophthalmologic impairment changed from 45.78% (38/83) to 11.27% (8/71); the neurological-optical from 36.15% (30/83) to 8.45%; intracranial calcifications decreased from 43.37% (36/83) to 15.49% (11/71) and the systemic form from 7.22 (6/83) to 1.4% (1/71). But these results - even in the presence of treatment - are still higher than those found in the absence of treatment in other locations. Schimidt et al. [17], for example, also found higher ocular aggressiveness among untreated women (9.64%) than in those who underwent treatment (2.82%).

This is another study showing the diagnosis of acute infection during pregnancy and its consequent treatment that can reduce the clinical forms of congenital infections [15,14,41,42]. These works emphasize the importance of the preventive programs of congenital toxoplasmosis during pregnancy, including seroconversion surveillance in seronegative pregnant [47]. In Brazil, where the congenital infections are more aggressive (which has been described) than elsewhere in the world, a national program for controlling toxoplasmosis infection during pregnancy is highly recommended.
Our research has also shown the need for improvements in the current program implemented in the state of Goiás. Primary and secondary prophylaxis measures should be intensified (serological surveillance in seronegative pregnant women and change in the treatment of acutely infected patients). We suggest monthly serological screening, such as the French program for control of congenital toxoplasmosis [14]. It is worth mentioning that the money spent on tertiary prophylaxis for severely infected newborn and the maintenance of life without quality exceeds what would be spent to carry out the monthly serological tests in seronegative pregnant women (34.2%). According to second Remington et al. [5] the cost is approximately one million dollars / patient with a severe form of the disease.

Once as the treatment of pregnant women is a very controversial issue in the literature [33,34,35,22,23,12], our study is in accordance with works that demonstrated a reduction in severity of the fetal infection when the mother was treated during pregnancy [33,34,41,42]. We also presented a different result from the meta-analysis published by SYROCOT study group [23]. We found a statistically significant protection in the onset of neurological-optical form in the offspring of women treated during pregnancy.

This study showed that congenital toxoplasmosis is more severe in our area than elsewhere. The infection occurs at much higher levels than in other locations that do not even have a program of prenatal care. We suggest implementing primary preventive measures (measures to control infection with T. gondii). These measures must be performed regardless of the patient immune status against toxoplasmosis; implement monthly seroconversion surveillance for seronegative pregnant women or for patients at risk; replace
spiramycin by sulfadiazine after the 20th week of pregnancy (75 mg/kg/day in the first two days, followed by 50 mg/day in two doses) and folinic acid (10 to 20 mg/day) until a week after withdrawal of drugs (up to the moment of birth). This should be done even without a diagnosis of fetal impairment, once the diagnosis of congenital infections is complex and the aggressiveness of the infection in our country is intense. It is important noting that a negative test does not prevent the vertical transmission.

CONCLUSIONS

1) The IgM in fetal blood must still be studied, once it has proven to be the most common marker for congenital infections; its presence in the fetus may suggest eye impairment.

2) The occurrence of severe forms in pregnant women whose chronic infection is recurrent demonstrated the need to expand the primary prophylactic program to all pregnant women, regardless of their immune state against T. gondii.

3) The severity of the congenital infection in our country shows the need for secondary prophylaxis programs with drugs that treat the fetus and pregnant women acutely infected.

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Table 1 Distribution of clinical forms of congenital toxoplasmosis related to the serological screening at the first prenatal visit (2012, Goiânia/GO, Brazil)

<table>
<thead>
<tr>
<th>Maternal screening clinical form</th>
<th>Seropositive %</th>
<th>Seronegative %</th>
<th>N/I</th>
<th>%</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toxoplasmosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) Asymptomatic</td>
<td>30</td>
<td>13</td>
<td>12</td>
<td>21.82</td>
<td>55</td>
</tr>
<tr>
<td>b) Meningitis</td>
<td>29</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>34</td>
</tr>
<tr>
<td></td>
<td>*p= 0.006</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c) Intracranial calcifications</td>
<td>8</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>11</td>
</tr>
<tr>
<td>d) Neural-optical</td>
<td>14</td>
<td>24</td>
<td>0</td>
<td>0</td>
<td>38</td>
</tr>
<tr>
<td></td>
<td>*p= 0.03</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e) Ocular</td>
<td>6</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>f) Systemic</td>
<td>1</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>*p= 0.04</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>g) Auditory</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>h) Nodal</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Sub-total</td>
<td>93</td>
<td>57</td>
<td>12</td>
<td>7.41</td>
<td>162</td>
</tr>
<tr>
<td>no toxoplasmosis</td>
<td>71</td>
<td>43</td>
<td>8</td>
<td>40</td>
<td>130</td>
</tr>
<tr>
<td>Total</td>
<td>164</td>
<td>56.16</td>
<td>108</td>
<td>36.99</td>
<td>292</td>
</tr>
</tbody>
</table>

\[ ^a \text{RR} = 3.25 (1.33<\text{RR}<7.92) \text{ Yates corrected} \quad \chi^2 = 7.35 \]
\[ ^b \text{RR} = 0.51 (0.29<\text{RR}<0.92) \text{ Yates corrected} \quad \chi^2 = 4.48 \]
\[ ^c \text{RR} = 0.13 (0.02<\text{RR}<1.06) \text{ Fisher exact} \quad \chi^2 = 3.55 (\text{Yates corrected}) \]

N/I = no information
Table 2 Distribution of newborns according to the trimester in which we carried out the prenatal serological screening (2012, Goiânia/GO, Brazil)

<table>
<thead>
<tr>
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<th>%</th>
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<th>%</th>
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<td>44.52</td>
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RR= 1.44 (1.21<RR<1.85) X²= 3.67 (Yates corrected)

N/I = no information
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<th>Trim 1</th>
<th>%</th>
<th>Trim 2</th>
<th>%</th>
<th>Trim 3</th>
<th>%</th>
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<th>%</th>
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<td>18.52</td>
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<td>30.59</td>
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<td>3</td>
<td>37.5</td>
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<td>0</td>
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<td>9.41</td>
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<td>50</td>
<td>4</td>
<td>28.57</td>
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<td>21.43</td>
<td>14</td>
<td>16.47</td>
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<td>20</td>
<td>3</td>
<td>60</td>
<td>5</td>
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</tr>
<tr>
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<td>75</td>
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<td>0</td>
<td>4</td>
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<tr>
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<td>100</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
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<td>42</td>
<td>28.77</td>
<td>22</td>
<td>15.07</td>
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Table 4 Relationship between the treatment of toxoplasmosis during pregnancy with spiramycin and the clinical form of vertical transmission, Goiânia (GO)/Brazil, 2012

<table>
<thead>
<tr>
<th>Maternal Treatment</th>
<th>With Treatment</th>
<th>%</th>
<th>Without Treatment</th>
<th>%</th>
<th>N/I</th>
<th>%</th>
<th>Total</th>
</tr>
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<tbody>
<tr>
<td><strong>With toxoplasmosis</strong></td>
<td></td>
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<tr>
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<tr>
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<td><strong>Total</strong></td>
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<td>56.16</td>
<td>108</td>
<td>36.99</td>
<td>20</td>
<td>6.85</td>
<td>292</td>
</tr>
</tbody>
</table>

\(^{a}R^R= 1.80 (1.11<RR<2.93)\) Yates corrected \(x^2 = 5.18\)

\(^{b}R^R= 1.91 (1.01<RR<3.65)\) Yates corrected \(x^2 = 4.10\)

\(^{c}R^R= 0.34 (0.15<RR<0.78)\) \(x^2 = 6.99\) (Yates corrected)

\(^{d}R^R= Cornfield not accurate Fisher exact (Tailed) 0.03\) \(X^2 = 3.12\)

N/I = No information