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Clinical Evaluation of Gestational and Congenital Toxoplasmosis in Two Health Institutions in the City of Monteria, Colombia from 2015 To 2021

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Abstract

Introduction: Toxoplasmosis is a zoonotic disease widely distributed throughout the world, caused by T. gondii, which infects various tissues and organs. Infection during or just before pregnancy can cause congenital toxoplasmosis and cause serious damage, especially at the CNS level. Objective: To evaluate the clinical characteristics of toxoplasmosis in pregnant women and new-borns in two health institutions in the city of Montería.

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Results: 76 clinical histories of neonates, children of mothers with gestational toxoplasmosis, diagnosed by IgM were analyzed. 50% of the pregnant women were treated and congenital toxoplasmosis was confirmed in 8 neonates: 5 with positive IgG and IgM, 2 with positive IgG and indeterminate IgM, with negative IgA and one with negative IgG and IgM symptoms. The clinical findings were hepatosplenomegaly and jaundice; eye disorders; ventriculomegaly and intraparenchymal calcifications in the brain and dilation of the left heart chamber. 62.5% of neonates with a clinical and/or serological diagnosis were treated with pyrimethamine / sulfadiazine plus folinic acid or pyrimethamine / sulfadoxine.

Conclusions: The diagnosis of gestational and congenital toxoplasmosis was made mainly by serology. Most of the pregnant women received treatment; however, there is still inefficiency in it. More than 60% of neonates with congenital toxoplasmosis received treatment at discharge; even so, there should be no limitations to access it.

Keywords: Gestational toxoplasmosis; congenital toxoplasmosis; Toxoplasma gondii; Ocular toxoplasmosis; Colombia

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Introduction

Toxoplasmosis is a zoonotic disease widely distributed worldwide, caused by Toxoplasma gondii (T. gondii), an obligate intracellular protozoan parasite that infects various tissues and organs, including skeletal muscle, intestine, nervous system, among

others [1]. Felines harbour this protozoan in their intestinal tract and excrete it through feces, infecting other warm-blooded animals and humans [2, 3].

Primary infection in pregnant women during or just before pregnancy can cause infection of the fetus (congenital toxoplasmosis) [4] and cause serious damage, especially to the central nervous system [5, 6].

Congenital toxoplasmosis is an acute disease caused by haematogenous transmission of the parasite through the placenta, although cases of congenital toxoplasmosis have been reported in infected mothers up to 3 months before gestation. [7, 8]. At the time of birth, it is generally asymptomatic, but with time alterations may occur, which will depend largely on the gestational age of the maternal infection [9].

In the first trimester of pregnancy transmission rates are low to less than 10%, but involvement is usually severe in up to 60% of cases, and can result in encephalomyelitis, macrocephaly, hydrocephalus, ocular disorders, psychomotor retardation and even miscarriage. However, if the pregnant woman contracts the disease in the second or third trimester of pregnancy this vertical transmission rate usually increases to 55-80% respectively, but fetal involvement is usually less at the ocular and CNS level. Lesions with late manifestations such as epilepsy, chorioretinitis, cerebral calcifications, and blindness, mental or psychomotor retardation may occur [10, 11]. Transmission rates are usually higher in pregnant women due to down- regulation of cellular immunity to prevent maternal rejection of the fetus, which increases susceptibility to intracellular organisms [12].

The infection is widely distributed worldwide, and its prevalence differs geographically in different regions, due to risk factors; it has been reported that approximately more than 60% of some populations are infected with Toxoplasma, being areas with warm and humid climates and low altitudes the most affected, because the oocytes of this parasite survive better in this environment. On the other hand, some authors consider that the prevalence of this disease is different among regions of the world because economic, social, and cultural factors also play a role. The 1988 National Health Study in Colombia found the highest prevalence in the Atlantic Coast region (63%), and the lowest in the Central region (36%) [13].

The worldwide rate of primary toxoplasmosis infection during pregnancy varies widely, with a reported prevalence of 1-15/1,000, the highest incidence having been described in

France at 8.1/1,000. In Colombia, approximately half of pregnant women have IgG antibodies for Toxoplasma, and 0.6-3% are expected to acquire the infection during pregnancy. [14] Of these, 90% will develop the infection asymptomatically; however, 50% of pregnant women will transmit the disease to the fetus [15] hence the concern for adequate screening during gestation, which reduces the risk of fetal transmission and therefore the squeal that can be left in these children both at birth and in the long term.

In Colombia, in 2012 the Ministry of Health and Social Protection and Colciencias, in association with expert groups, developed the Guide for comprehensive care for the prevention, early detection and treatment of complications of pregnancy, childbirth and puerperium, and included a section on the management of infections in pregnancy, such as toxoplasmosis. In the search for efficient screening during pregnancy, the guidelines recommend testing the pregnant woman for IgG and IgM antibodies for toxoplasma at the first prenatal check-up to determine the presence of toxoplasma infection, and according to the results, continue monthly screening or order confirmatory tests, early treatment and diagnostic aids to determine the severity of fetal involvement [16, 17].

Toxoplasmosis is a very common disease, which presents a risk of vertical transmission to the fetus when it is acquired for the first-time during pregnancy, producing serious short- and long-term squeal, generating concern in the clinical and epidemiological setting. We note that, despite having guidelines, the diagnosis is not properly made, and the respective treatment is not ordered for the indicated case [18].

Currently, the information available on seroconversion in pregnancy is very scarce and its appearance to date is worrying, since, due to different factors, such as poor access to health services, the precariousness of the same and the lack of adherence to the recommendations made in the literature, this could increase, making it necessary to evaluate toxoplasmosis in the pregnant population and therefore in their new-born's, to identify whether patients are being treated early, as required, This could be increasing, making it necessary to evaluate toxoplasmosis in the pregnant population and therefore in their new-borns, to identify whether patients who require it are being treated early, in order to avoid serious sequel in the fetus and new-born.

Therefore, the objective of this study was to evaluate the clinical characteristics of toxoplasmosis in pregnant women and new-borns in two health institutions in the city of Monteria.

Methodology

A retrospective study was conducted in new-borns of mothers diagnosed with toxoplasmosis during pregnancy in 2 tertiaries health institutions in the city of Monteria, Cordoba; Maternal and Child Clinic Casa del Niño of private character and in the ESE Hospital San Jeronimo of the city of Monteria, in the period from January 2015 to May 2021.

A review was made of the database from the individual service delivery records (RIPS) with the diagnostic impression CIE-10 P371 (gestational toxoplasmosis) B589, (congenital toxoplasmosis) and (other infections transmissible in pregnancy) in the case of the hospital San Jerónimo, since, in the latter until the diagnosis is confirmed, the respective CIE 10 is not assigned to the disease.

A total of 76 clinical histories of new-borns potentially infected with toxoplasmosis during pregnancy were obtained, as evidenced by the recording in the neonatal clinical history of positive maternal laboratories for congenital toxoplasmosis. Of these medical records, 61 were obtained from the Clínica Materno Infantil Casa del Niño and 15 from the Hospital San Jerónimo. Subsequently, all the medical records were consulted

and Sociodemographic and clinical variables of the patients in question were extracted. The Sociodemographic variables included the age, origin and social security of the mother, gestational age, socioeconomic stratum and the clinical variables included attendance at the first prenatal check-up, number of prenatal check-ups performed, laboratory tests ordered for the mother during the different trimesters of the gestational period (IgG and IgM serology, avidity test and PCR of IgG and IgM, test and avidity and PCR of amniotic fluid for toxoplasma) and the treatment prescribed for gestational toxoplasmosis, as well as the signs and symptoms of toxoplasmosis in the new-born, serological evaluation of IgG, IgM and IgA for toxoplasma, and treatment performed at the time of birth. The data obtained were analyzed using descriptive statistics.

To establish that the diagnosis and treatment of pregnant women and new-borns were properly carried out, the recommendations of the Colombian guide for comprehensive care for the prevention, early detection, and treatment of complications of pregnancy, childbirth and puerperium were followed: section toxoplasmosis in pregnancy. This states that maternal diagnosis should be made by screening with serology during pregnancy. Women with positive IgG and negative IgM are considered to have had a previous or old infection and rule out the risk of infection during pregnancy. Seronegative women (IgG and IgM negative), i.e., those who have had no previous infection, are recommended to be screened monthly with an IgM test. In case IgG is negative and IgM positive, repeat IgG in 2 weeks is indicated to document acute seroconversion or presence of natural IgM. A second positive IgG test is evidence of recent seroconversion. Patients with negative IgG, i.e., with natural IgM, should have monthly follow-up with IgG. In the presence of positive IgG and IgM, the avidity test is indicated to confirm the antiquity of the infection, if the pregnancy is less than 16 weeks, the avidity test for IgG is indicated, and IgA if it is greater than 16 weeks of gestation. When seroconversion or recent toxoplasma infection test results are found in the pregnant woman and it is necessary to know if the fetal infection is already present, amniocentesis and PCR in the second

Trimester of gestation is suggested as an alternative. Once the diagnosis of toxoplasmosis has been made in the pregnant woman, treatment is indicated to prevent transmission of the infection to the fetus with spiramycin 3 grams per day for the rest of the pregnancy, and pyrimethamine plus sulfadiazine plus folinic acid in case there is confirmation of fetal transmission of toxoplasmosis either by PCR tests or ultrasound scans suggesting neurological involvement in the fetus.

For diagnosis in the new-born, it is recommended to perform IgG, IgM, and IgA together for the diagnosis of congenital toxoplasma infection. Western blot confirmation for toxoplasma infection should be performed in the presence of negative IgA and IgM results. In the presence of a positive IgG result and negative results in all 3 tests (IgM, IgA, and Western blot), monthly follow-up is recommended for 6 months, and then every 3 months until one year of age with IgG to rule out seroconversion.

Regardless of whether the mother received treatment, the guidelines recommend that these patients should be treated with pyrimethamine plus sulfadiazine plus folinic acid for one year: pyrimethamine: 1 mg/kg every 12 hours for the first 2 days, followed by 1 mg/kg per day for 1 year, and sulfadiazine at a dose of 50 mg/kg every 12 hours and folinic acid (10 mg 3 times per week) until 1 week after the suspension of pyrimethamine. If this treatment option is not available, other recommendations are: pyrimethamine plus sulfadoxine, or oral pyrimethamine plus clindamycin.

Results

The medical records of 76 children of mothers with a laboratory diagnosis of toxoplasmosis during pregnancy (IgM and IgG serology, avidity test and amniotic fluid PCR), with or without treatment during pregnancy, with a diagnostic impression of gestational toxoplasmosis and/or congenital toxoplasmosis in the RIPS were analyzed.

On analysing the medical records of the 76 children born to mothers diagnosed with toxoplasmosis during pregnancy in the two health institutions, the mean age of the patients on admission to the new-born units was ± 1 day. Of the patients, 52.6% were male. Regarding the service of origin of the patients, 53 new-borns (69.7%) were admitted from the delivery room and/or operating rooms, while the rest were referred from other health institutions.

A total of 72 patients belonged to the subsidized regime, and 42 of the mothers of these new-born's (55.2%) were from rural areas. These belonged to the departments of Córdoba, Antioquia, and Sucre with a percentage of 84.2%, 14.4% and 1.3%, respectively.

The patients coming from the department of Cordoba belonged to the municipalities of Montelíbano 20.3%, followed by Tierralta at 17.2% and the city of Montería at 10.9% followed by the municipalities of Cienaga de Oro, Sahagun, Los cordobas, Panetta Rica, San Pelayo, and Puert Libertador, Ayapel, Cerate, La Apartada, Canalete, Cotorra, Lorica, San Jose de Ure and Valencia. Those from the department of Antioquia corresponded 2 (18.2%) to the municipalities of Turbo, 2 (18.2%) to El Bagre 18.2% and the rest to Arboletes, Carepa, Necoclí, Puerto Claver, San Carlos, San Pedro de Uraba and Caceres. The only patient (1.3%) from Sucre was from the municipality of Tolú. As shown in Table 1, which details the Sociodemographic characteristics of the participants? **(Table 1)**.

Regarding the maternal and perinatal clinical characteristics, the average maternal age was 22.0 ± 5.49 years, 52.6% of the mothers were primigestantes. 75 pregnant women (98.6%) attended prenatal check-ups, with an average of 5 visits during the entire pregnancy; and only 18 pregnant women (23.6%) attended the first visit.

Five pregnant women were diagnosed with toxoplasmosis by serology in the first trimester, 29 in the second trimester and 33 in the third trimester.

During the first trimester of pregnancy, serology results in pregnant women in the hospital showed that only one patient (6.6%) had both IgG and IgM positive, with no additional avidity test. In the clinic, 4 pregnant women (6.5%) were diagnosed:

Table 1. Sociodemographic characteristics.

VARIABLES	Hospital (n:15)	Clinical (n:61	Total (n:76)
Age of newborn	1 ±1day	1 ±1 day	1 ±1 day
Sex of newborn			
Male	60% (9)	50,8% (31)	52,6% (40)
Female	40,0% (6)	49,2% (30)	47,3% (36)
Service of origin of the newborn			
Delivery	-	-	
Room/Operating Room.			69,7% (53)
	60,0% (9)	72,1% (44)	
Referrals	40,0% (6)	27,8% (17)	30,2% (23)
Health system			
Subsidized	93,3% (14)	95,0% (58)	94,7% (72)
Contributory	-	3,2% (2)	2,6% (2)
Prepaid medicine	-	1,6% (1)	1,3% (1)
Linked	6,6% (1)	-	1,3% (1)
Area of maternal origin			
Urban	33,3% (5)	45,9% (28)	43,4% (33)
Rural	60,0% (9)	54,1% (33)	55,2% (42)
Department of maternal origin			
Córdoba	100% (15)	80,3% (49)	84,2% (64)
Antioquia	-	18.0% (11)	14,4% (11)
Sucre	-	1,6% (1)	1,3% (1)
Socioeconomic stratum			
One	100% (15)	98,3% (60)	98,6% (75)
Two	-	1,6% (1)	1,3% (1)
Maternal age	22,4 ± (5,53)	21,9(5,53)	22,0 (5,49)

2 had positive IgG and IgM, and 2 reported positive IgM with unknown IgG, one of the latter had a low avidity test.

In the second trimester of gestation, 3 pregnant women (20%) were diagnosed in the hospital, all with positive IgG and IgM. On the other hand, 26 pregnant women (42.6%) were diagnosed in the clinic: 18 (29.5%) with positive IgG and IgM, of these only 2 had avidity test (one with unknown result and the other reported as positive). Three patients 4.9% reported only positive IgM, and one of these had avidity test with

Unknown result: 5 pregnant women 8.2% had negative IgG and positive IgM, of these only one was followed up with IgG at 2 weeks.

In this gestational trimester, 2 more avidity tests were performed, corresponding to the 2 first trimester patients with positive IgM and unknown IgG (one indeterminate and the other with high avidity).

In the third trimester of pregnancy, 6 (40%) hospital patients were diagnosed with positive IgG and IgM, with no report of avidity test or PCR for toxoplasma in amniotic fluid. In the clinic, 27 pregnant women were diagnosed: 21 (34.4%) with positive IgG and IgM, one of them with negative avidity test; one pregnant woman with negative IgG and positive IgM, without IgG follow-up; and 5 pregnant women with positive IgM and IgG with unknown result. PCR for toxoplasma in amniotic fluid was only performed in this gestational trimester in 2 mothers diagnosed in the second trimester, both with negative results. See Table 3.

Nine of the pregnant women (11.8%); 5 from the hospital and 4 from the clinic reported a diagnosis of gestational toxoplasmosis, but the trimester in which it was made was unknown. A pregnant woman diagnosed in the third trimester of gestation reported fetal splenomegaly in the ultrasound of this same trimester. It was not known if this was performed before or after the serologic diagnosis. Another important clinical aspect assessed was treatment for gestational toxoplasmosis. During the first trimester of pregnancy, no patient received treatment.

In the second trimester of pregnancy, 22 of the 29 patients diagnosed with toxoplasmosis were treated: 3 patients belonged to the hospital (20%) and 19 to the clinic (31.1%). All cases were treated with spiramycin according to the doses indicated by the guidelines; however, only 2 of these pregnant women continued treatment until delivery.

Of the 19 mothers (31.1%) in the clinic who reported having started treatment in the second trimester of gestation, 12 were pregnant women with positive IgG and IgM, 2 with positive IgM and negative IgG, and 3 with positive IgM and unknown IgG. The other 2 pregnant women who received treatment were diagnosed in the first trimester of gestation. Seventeen pregnant women were treated with spiramycin, one with clindamycin, and in the other the treatment administered was unknown. No patient was rotated to pyrimethamine/sulfadiazine. Treatment was complete in 6 patients, incomplete in 6, and 7 had no record of the time of administration. Finally, in the third trimester of gestation, treatment for gestational toxoplasmosis was received by 12 pregnant women; 4 belonged to the hospital and only 2 received complete treatment with spiramycin. The 8 pregnant women from the clinic who received treatment during this trimester of. The indicated treatment was spiramycin in 6 of these pregnant women. Only 4 completed the treatment until the end of gestation.

The pregnant woman with ultrasound during pregnancy with a report of fetal splenomegaly received incomplete treatment. None of the pregnant women had treatment rotation to pyrimethamine/sulfadiazine.

As with the diagnosis, data concerning the treatment indicated during gestation were unknown; one of the pregnant women in the hospital reported starting treatment, but the trimester of gestation, the time and the medication administered were unknown, as was the case with the 3 patients in the clinic. All diagnostic tests and treatment were implemented in the participating patients **(Table 2)**.

Regarding the clinical characteristics of the new-borns (Table 3), sixty-seven (88.1%) of them were at term and with an adequate weight for gestational age, with a mean gestational age of 38.55 with a standard deviation of 1.48 weeks. Within the clinical manifestations at birth, we found jaundice at the expense of direct bilirubin was present only in one patient (1.3%), which belonged to the clinic, as well as manifestations such as hepatosplenomegaly was present in 2 patients (2.6%). No other signs and symptoms related to toxoplasmosis were found. It should be noted that the new-born with ultrasound with fetal

Table 2. Diagnostic tests and treatment in pregnant women

Quarter	First		Second		Third	
Institution	Hospital(n:15)	Clinical (n:61)	Hospital(n:15)	Clinical (n:61)	Hospital(n:15)	Clinical (n:61)
Diagnosed pregnant women	**6,6% (1)**	**6.5 % (4)**	**20% (3)**	42,6% (26)	**40% (6)**	44,2% (27)
IgG (+) IgM (+)	6,6% (1)	3,2% (2)	20% (3)	29,5% (18)	40% (6)	34,4% (21)
IgG (-) IgM (+)	-	-	-	8,1% (5)	-	1,6% (1)
IgM (+)	-	3,2% (2)	-	4,9% (3)	-	8,2% (5)
Greed test	-	-	-	8,2% (5)	-	1,6% (1)
PCR	-	-	-	-	-	3,2% (2)
Initiated treatment	-	-	20% (3)	31,1% (19)	26,6% (4)	13,1% (8)
Treatment						
Spiramycin	-	-	20% (3) *	27,8% (17)	26,6% (4)	9,8% (6)
Clindamycin	-	-	0	1,6% (1)	0	0
Unknown	-	-	0	1,6% (1)	0	3,2% (2)
Treatment Time						
Suitable	-	-	13,3% (2) *	8,2% (5)	-	6,5% (4)
Incomplete	-	-	0	9,8% (6)	13,3% (2)	4,9% (3)
Unknown	-	-	6,6% (1)	13,1% (8)	13,3% (2)	1,6% (1)

splenomegaly was not palpable on physical examination, and it was later ruled out with abdominal ultrasound.

The tests performed on the new-borns were IgG, IgM and IgA. In the hospital, only one patient presented both positive serologies, making a diagnosis of congenital toxoplasmosis, and he was the only patient with clinical signs compatible with the disease. The only Western blot of the patient with both positive serologies was unknown. In the clinic, 2 patients (3.2%) had positive IgG and indeterminate IgM due to borderline results and 4 patients (6.5%) had both positive IgG and IgM, the latter 6 being considered new-borns with a diagnosis of congenital toxoplasmosis. IgA was only performed in 29 neonates (38.1%), of these, 22 were negative and 7 in 7 the result was unknown. Both Western blot and PCR toxoplasma were requested to one patient and the results were unknown. Neonates diagnosed with congenital toxoplasmosis underwent fundus examinations, cerebral ultrasound and Echocardiography, performed during the patients' hospital stay.

The fundus examination was performed by pediatric ophthalmology in 88.1% of the patients, alterations were found in 4 patients (5.3%). One of these patients corresponded to the only new-born with positive serologies for toxoplasmosis in the hospital, the other 3 new-borns who had reported abnormalities in the fundus examination related to congenital toxoplasmosis were perished to the clinic. Brain ultrasound was performed in 93.4% of the patients, with no reports of alterations in the new-borns from both institutions; however, one patient (1.63%) from the hospital reported 1.63% in the brain CT scan performed. Echocardiogram was performed in 41 patients (53.9%), of which one case of left cavity dilatation was found in a patient with positive IgG and IgM serology for toxoplasma, who belonged to the clinic.

Once the tests were performed, 8 patients were diagnosed with gestational toxoplasmosis, one in the hospital both by serology and by clinic, and 7 patients in the Clínica Casa del Niño, of the latter 6 by serology results and one by clinic: of the 4 new-borns with positive IgG and IgM, 3 had clinical signs, the other 2 patients who had positive IgG and indeterminate IgM by ranges within the limit, did not have clinical signs at the time of diagnosis. The only patient diagnosed with clinical signs compatible with congenital toxoplasmosis did not have known serology results.

Regarding the treatment received at the time of discharge, at the hospital it was applied to the only patient with a diagnosis made, which corresponds to 6.6% of the total number of patients, and at the clinic to 4 patients, that is, 6.5% of the total number of new-borns studied: 3 of these patients had positive IgG and IgM at the time of discharge and the other was the patient with a clinical diagnosis. The other 3 new-borns were not indicated for treatment because the results were not available at the time of discharge. The type of treatment received in both entities was adjusted according to Colombian guidelines, with pyrimethamine-sulfadiazine plus folinic acid in 7 of the 8 patients; only the patient in the hospital received the second treatment option of pyrimethamine plus sulfadoxine because the first option was not available.

Finally, the average hospital stay for all patients was 8 days with a standard deviation of 4.37, being lower in the hospital with a mean of 6 days and standard deviation of approximately 6 days except for two outlier records that are greater than or equal to 15 days, while in the clinic an average of 8 days was obtained with a standard deviation of 4 days and with 5 records of outlier data **(Table 3).** The 8 patients who were diagnosed with congenital toxoplasmosis in the two institutions, one belonged to the Hospital San Jerónimo and 7 to the Casa Del Niño mother and child clinic. 100% of these patients were at term at the time of birth. There was one new-born with a history of mothers without prenatal controls during gestation, which belonged to the clinic. The patient from the hospital was male, with a weight greater than 2,500 gr. Of the patients from the Clínica Materno Infantil Casa Del Niño, 5 (71.4%) were male, and 6 (85.7%) had a weight greater than 2,500 gr. The average gestational age for patients diagnosed with toxoplasmosis was 38.13 weeks with a standard

Table 3. Clinical characteristics of the new-born.

Institution	Hospital (n:15)	Clinical (n:61)	Total (n:76)
Gestational age			
Newborn at term (NBT)	86,7% (13)	88,5% (54)	88,1% (67)
Preterm newborn (PTNB)	13,3% (2)	11,4% (7)	11,8% (9)
Mean gestational age	38,5 (1,81)	38,5 (1,41)	38,5 (1,48)
Sex			
Male	60,0% (9)	50,8 % (31)	52,6% (40)
Female	4% (6)	49,1% (30)	47,3% (36)
Weight			
> 2,500 gr	86,6% (13)	88,5% (54)	88,1% (67)
< 2,500 gr	13,3% (2)	11,4% (7)	11,8% (9)
Hospital stays	6 days 6.53)	8 days (3.97)	8 days (4.37)
Clinical Manifestations			
Jaundice	-	1,6% (1	1,3% (1)
Hepatosplenomegaly	6,67% (1)	-	1,3% (1)
Laboratories			
IgG IgM			
IgG (-) IgM (-)	13,3% (2)	8,1% (5)	9,2% (7)
IgG (+) IgM (-)	40,0% (6)	70,4% (43)	64,4% (49)
IgG (+) IgM (Undetermined)	-	3,2% (2)	2,6% (2)
IgG (+) IgM (+)	6,66% (1)	6,5% (4)	5,2% (5)
IgM (-)	-	3,2% (2)	2,6% (2)
IgG IgM Unknown	40% (6)	8,2% (5)	14,4% 11)
IgA			
Positive	-	-	-
Negative	-	36, 1% (22)	28,9% (22)
Unknown	-	11,4% (7)	9,2% (7)
Not performed	100% (15)	52,4% (32)	61,8% (47)
Western Blot Toxoplasma			
Unknown	-	1,64% (1)	1,31% (1)
Not performed	100% (15)	98,3% (60)	98,6% (75)
PCR Toxoplasma			
Unknown	-	1,6% (1)	1,3% (1)
Not performed	100% (15)	98,3% (60)	98,6% (75)
Fundus			
-Performed	60% (9)	95,0% (58)	88,1% (67)
-Alterations	6,6% (1)	4,9% (3)	5,2% (4)
Brain Ultrasound *.			
-Performed	80,0% (12)	96,7% (59)	93,4% (71)
-Alterations	-	-	-
Echocardiogram			
-Performed	40,0% (6)	57,3% (35)	53,9% (41)
-Alterations	-	1,6% (1)	1,3% (1)
Treatment at discharge	6,6% (1)	6.5% (4)	6.5% (5)

deviation of 1.64 weeks; it should be noted that there was only one patient diagnosed with toxoplasmosis in the hospital, the average is the age of the patient and since there is no variability, the standard deviation is zero (0). See table 4.

In addition, only one mother of these 8 new-borns (12.5%) received adequate treatment with spiramycin during pregnancy; 3 had incomplete treatment, and the other 4 did not receive treatment. Regarding the results of the laboratories of these patients, it was found that both IgG and IgM for toxoplasma were positive in the neonate in the hospital, this patient did not have IgA and the result of the Western blot taken was unknown at the time of discharge. On the other hand, 85.7% (6) new-borns attended in the clinic had positive IgG, in 14.2% [1]. of these patients the results were unknown. Of these 7 patients, IgM was positive in 4 (57.1%), indeterminate in 2 (28.5%) and unknown in one patient. IgA was performed in 4 of these patients, of which 2 were negative and in 2 patients the result was unknown. Western blot was performed in only one patient and for toxoplasma, in both cases without results.

Regarding the clinical manifestations related to toxoplasmosis, 2 new-borns (25%) had hepatosplenomegaly, one of whom belonged to the hospital and the other to the clinic. Among other pathologies recorded in the clinical histories, the risk of sepsis and heart murmur were most frequently found in 2 patients (25%). Half of the new-borns diagnosed with congenital toxoplasmosis had alterations in the fundus. Bilateral lens opacity and macular scarring were found in the hospital patient, and 3 patients in the clinic had the following findings: left eye with 2 lesions in the temporal retina with no signs of activity and

Diagnosis of sequelae of congenital toxoplasmosis in one patient, scar in macula of the left eye by TORCH with questioned diagnosis in another new-born, and finally chorioretinitis in both eyes in another neonate. Regarding brain ultrasound, it should be noted that 100% of the patients did not present alterations in this, however, the hospital patient showed ventriculomegaly and intraparenchymal calcifications in the simple cranial CT, however, there was no record in the clinical History of previous transfontanelar ultrasound. With respect to the echocardiogram, only one patient showed important alterations in it, presenting dilatation of the left cavity perimenbranous atrial septal defect (ASD) which required treatment.

In relation to the treatment received, 5 (62.5%) of these 8 patients were prescribed treatment for congenital toxoplasmosis before discharge, one from the hospital and 4 new-borns from the clinic. Three patients from the clinic (42.8%) did not receive treatment because at the time of discharge the results of the toxoplasma antibodies were not yet available. The only hospital patient with a diagnosis of congenital toxoplasmosis was given the second treatment option, with pyrimethamine/sulfadoxine plus folinic acid because the first option was not available at the time of discharge, while the other 4 clinic patients received treatment with pyrimethamine plus sulfadiazine plus folinic acid, in accordance with the latest Colombian guidelines, according to the stipulated doses. The mean hospital stay was 16 days with a standard deviation of 6.17 and depended to a great extent on the difficulty of securing the treatment at discharge.

Finally, 100% of the patients diagnosed with congenital toxoplasmosis at the time of discharge were referred for follow-up with the infectious disease, neurology, and pediatric ophthalmology services; and potentially infected patients who were not confirmed for toxoplasmosis were also referred for follow-up by the outpatient clinic to rule out or confirm the diagnosis during this period. Finally, no correlation was found between positive clinical variables for diagnosis of the disease **(Table 4)**.

Table 4. Clinical characteristics of patients diagnosed with congenital toxoplasmosis.

Institution	Hospital (n:1)	Clinical (n:7)	Total (n:8)
Gestational age			
Newborn at term (NBT)	-	100% (7)	87,5% (7)
Preterm newborn (PTNB)	-	-	-
Gestational age in weeks (mean)	40 (0,00)	37,8 (1,57)	38,1 (1,64)
Sex			
Male	-	71,4% (5)	62,5% (5)
Female	100% (1)	28,5% (2)	37,5% (3)
Weight			
> 2,500 gr	100% (1)	85,7% (6)	87,5% (7)
< 2,500 gr	-	14,2% (1)	12.5% (1)
Hospital stays	21 days (0)	10.5 days (4.82)	16 days (6.17)
Clinical manifestations (signs/symptoms)			25% (2)
Hepatosplenomegaly	100% (1)	-	12.5% (1)
Jaundice	-	14,2% (1)	12.5% (1)
Other pathologies	-	42,8% (3)	37,5% (3)
Fundus findings	100% (1)	42,8% (3)	50% (4)
-Bilateral lens opacity	100% (1)	-	12.5% (1)
-Temporal retinal lesions	-	14,2% (1)	12.5% (1)
-Macular matrix	100% (1)	14,2% (1)	25,0% (2)
-Chorioretinitis	-	14,2% (1)	12.5% (1)
Findings in brain ultrasound	-	-	-
Echocardiogram findings	-	14,2% (1)	12.5% (1)
-Left cavity dilatation + atrial septal defect (ASD)	-	14,2% (1)	12.5% (1)
Treatment at discharge	100% (1)	57,1% (4)	62,5% (5)
Type of treatment			
-Pyrimethamine/ sulfadiazine + folinic acid	-	100% (7)	87,5% (7)
-Pyrimethamine/ sulfadoxine	100% (1)	-	12.5% (1)
-Pyrimethamine/ clindamycin	-	-	-

Discussion

The results of our work on gestational and congenital toxoplasmosis in two health institutions in the city of Monteria, showed in terms of Sociodemographic characteristics, that our findings are like Colombian studies, where this population belongs to low socioeconomic strata to low socioeconomic strata. More than 50% of the patients included in the study come from rural areas of the departments of Córdoba, Sucre, and Antioquia, 90% of which are from the department of Córdoba, which provides us with a more reliable approximation regarding the diagnosis in children of mothers screened during pregnancy in Córdoba, a department not included in the first multicentre study in newborns for congenital toxoplasmosis in Colombia [19].

Regarding maternal and perinatal clinical characteristics, despite the deficiencies in access to health services in our country, approximately 99% of the mothers of these newborns attended an average of 5 prenatal visits during gestation. However, the percentage of pregnant women who attended prenatal check-ups in the first trimester recorded in the medical records did not exceed 25%, and a large percentage of the data for this period were not recorded, which indicates that the opportunity for screening during this period was deficient in our study.

The average maternal age was like a study conducted in Brazil that included 39 newborns potentially infected with toxoplasmosis [20]. In this study, 46.9% of the pregnant women underwent amniocentesis for PCR for T. gondii, in contrast to ours, where it

was performed only in a small percentage of pregnant women, since the diagnosis was made mainly based on IgG and IgM serology. The reason for not performing the PCR for toxoplasma, as well as the avidity test for confirmation of the diagnosis is not clear since there was no clarification in the medical records. However, since only one pregnant woman was diagnosed with gestational toxoplasmosis by seroconversion in the second trimester, and the highest percentage of diagnoses were in the third trimester of gestation, it is evidence not only of little or no attendance of pregnant women during the first trimester of gestation, but also of poor screening, including serology during the same.

Regarding the treatment of pregnant women with toxoplasmosis, the evidence available in Latin America differs from our results. We found that in the meta-analysis performed in Brazil; only 22.5% of pregnant women did not receive any drug for the treatment of toxoplasmosis during pregnancy [21]. This shows that in our country there is still a lack of efficient strategies in the follow-up of pregnant women with toxoplasmosis, compared to countries with a clear characterization of patients and well-established governmental guidelines.

Our results are like the Colombian study published by Gómez-Marín et al. in which they found that of the 143 pregnant women with a history of toxoplasmosis diagnosis during pregnancy, 82 (57%) received antibiotics, 96.3% with spiramycin; however, unlike our study, 3 of them received combinations of pyrimethamine-sulfadoxine. In these only two children whose mothers were treated had positive IgM anti-Toxoplasma test in umbilical cord blood, however, at follow-up both children became negative. This clearly lower incidence of congenital toxoplasmosis in their study is most likely due to the methods used for screening these newborns. The importance of treatment of gestational toxoplasmosis to avoid transmission to the newborn should be emphasized.

In the Brazilian study like ours, the diagnosis of congenital toxoplasmosis was made in 28% of the newborns potentially infected during gestation; however, in our investigation only 10.5% of the neonates were diagnosed at birth, and only one patient per clinic. This difference could be due to the greater number of patients with clinical diagnosis in the presence of severe symptoms in the Brazilian study, since the strains of T. gondii in that country are phenotypically and genetically different from those in Europe and North America, reflected in a greater proportion of children with congenital infection with severe disease, and with earlier onset of clinical symptoms than cases in the rest of the world [22, 23].

The diagnosis of congenital toxoplasmosis in our 8 newborns was made mainly based on positive IgM, since IgA for toxoplasma, as well as Western Blot and PCR were performed in few patients, and those that were performed lacked results at the time the patients were discharged from the institutions. The only patient with a clinical diagnosis did not have the results recorded in the clinical history. However, in the case where IgM was negative, it is important to note that this is probably due to the timing of sampling after infection, and that IgM production may have ceased at birth. In addition, up to 20% of infants with congenital toxoplasmosis may have negative anti-Toxoplasma IgM at birth, because in utero treatment may shorten both anti-IgM and IgA responses [24]. However, up to half of the cases with congenital infection could have anti-Toxoplasma IgA antibodies, and this immunoglobulin can be found in the absence of specific IgM [25]. Hence the importance of performing the latter, and of serological follow-up of patients during the first year of life, despite the absence of clinical signs or positive serology for toxoplasmosis at birth.

A study conducted in Temeke, Tanzania, where 371 pregnant women were studied, showed that the overall prevalence of signs and symptoms typical of toxoplasmosis was 13%. These neonates presented ocular alterations in 4.8% and hydrocephalus in 3.2% [26]. This is consistent with our findings, with ocular findings being the most prevalent. Although one of the newborns in our study reported Ventriculomegaly and intraparenchymal calcifications in the simple cranial CT, there was no record in the clinical history of previous transfontanelar ultrasound, however, its use is justified by the presence of positive serological tests, alterations in the physical examination at the time of admission, and the lack of nuclear magnetic resonance in the institution.

Treatment for congenital toxoplasmosis was indicated in a timely manner to 5 (6.57%) of the 76 potentially infected newborns, which disagrees with data from other studies as shown in the systematic review from Brazil where 17.94% (n=7/39) of the newborns were treated for congenital toxoplasmosis. The treatment of these newborns was adjusted to the clinical evidence available in the different guidelines, given that all symptomatic or asymptomatic children with para clinical or clinical criteria compatible with gestational toxoplasmosis, as well as all those with confirmed fetal infection during gestation, regardless of whether their mother received treatment, should be treated with a pyrimethamine- sulfadiazine/folinic acid regimen for one year. And if this scheme is not available, there are other equally effective options, despite the risk of adverse effects and doubts about the therapeutic levels during administration at weekly intervals, as in the case of oral pyrimethamine + sulfadoxine. Regardless of the treatment used, the main objective of treatment will be the same: in symptomatic cases it is to reduce ocular and neurological sequelae, as well as mortality; in asymptomatic children with positive tests for toxoplasma, to prevent the appearance of retinochoroiditis lesions and/or the development of hydrocephalus [27, 28].

We emphasize that the present study had no cases of mortality due to congenital toxoplasmosis in the short term, unlike children studied in Poland [29] and Porto Alegro [30].

The incidence of congenital toxoplasmosis could differ by socioeconomic, age or geographic factors as evidence shows, however, in our study these variables did not determine the significant differences in the presentation of congenital toxoplasmosis in the health institutions studied.

This study conducted in 2 institutions in the city of Monteria, should provide representative data on the presentation of congenital toxoplasmosis in those patients whose mothers were diagnosed with toxoplasmosis during gestation, since they are

the public and private reference centers where patients from the department of Cordoba and some surrounding municipalities of the departments of Antioquia and Sucre are referred. However, there are limitations since the confirmation of the diagnosis in most of the patients was obtained only through the detection of anti- Toxoplasma antibodies in the new-born, due to the lack of other confirmatory tests in time. It would be useful in subsequent studies to diagnose congenital toxoplasmosis using neonatal screening that is considered a true indicator of the presence or absence of the disease [31].

Conclusions

The newborns born to mothers diagnosed with gestational toxoplasmosis during pregnancy in these 2 institutions, despite belonging to low socioeconomic strata and coming from rural areas, mostly in the department of Córdoba, received 98% of prenatal care, with an average number of adequate prenatal visits.

In our study we found that the diagnosis of gestational toxoplasmosis was based on IgG and IgM serology. Although half of the pregnant women were treated, only one third of them received treatment with pyrimethamine at the doses and time established by the guidelines of the Ministry of Health of the country. This should be considered due to the reduction in transmission if treatment is initiated in the first 3 weeks of seroconversion, according to clinical evidence so far. This makes it necessary to study pregnant women to determine the lack of access to complementary diagnostic tests, but also the opportunity to access treatment during pregnancy, which ultimately reduces the transmission of the disease to the fetus.

The percentage of newborns diagnosed with congenital toxoplasmosis in this study is above the evidence of research in our country; however, it should be considered that this is a retrospective study with limitations in the collection of information in the clinical histories, probably differences in the screening techniques and in the collection of samples. Although also because serological tests only provide transient results, and may not detect early immunoglobulin, the number of infected patients in our study population could be underestimated.

In addition, because this infection can be asymptomatic and clinical signs are nonspecific, serological tests should be used to differentiate between maternal or self-antibodies. Therefore, it would be necessary to implement a prospective study like the reference multicentre study in Colombia to clinically characterize the population of the department of Cordoba.

In relation to the treatment of these newborns diagnosed with congenital toxoplasmosis, a greater opportunity is required at the time of receiving them by the corresponding entities, since there are still many limitations at the time of accessing these drugs, as well as the multidisciplinary follow- up of these patients. Therefore, ocular and neurological sequelae and mortality would be reduced, both in the short and long term, especially those of the CNS, which affect the integral development of the child.

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