The Lancet Regional Health - Americas 1 (2021) 100010

Contents lists available at ScienceDirect

The Lancet Regional Health - Americas

journal homepage: www.elsevier.com/locate/lana

Research paper

Evaluation of the impact of the first evidence-based guidelines for congenital toxoplasmosis in Armenia (Quindío) Colombia: An observational retrospective analysis

Manuela Mejia-Oquendo[1], Elizabeth Marulanda-Ibarra[2], Jorge Enrique Gomez-Marin[3,*]

GEPAMOL group, Centre for Biomedical Research1, Faculty of Health Sciences, Universidad del Quindío, Colombia

ARTICLE INFO

Article history:
Received 11 April 2021
Revised 22 May 2021
Accepted 25 May 2021
Available online 13 July 2021

Keywords:
Toxoplasmosis
pregnancy
treatment
diagnosis
guidelines

ABSTRACT

Background: Colombia implemented the world's first evidence-based guidelines for congenital toxoplasmosis in 2013, no evaluation of its impact has been reported.

Methods: We reviewed the clinical charts of cases referred to the specialized consultation of the health care centre at Universidad del Quindío during an 18-year period (2001-2019), where the diagnosis criteria and the correlation between prenatal treatment and symptoms at birth were analysed. Additionally, we described the diagnosis criteria and treatment for mothers during pregnancy at a primary prenatal care centre in the city of Armenia during 2018. Institutional consent was obtained to review clinical charts.

Findings: At the referral centre, we found that before the implementation, 27.3% did not have prenatal diagnosis but after implementing the clinical practice guidelines, all mothers were diagnosed during pregnancy. In addition, we observed that prenatal treatment was associated with fewer symptoms and this improved significantly over time after implementing the guidelines. At the primary health care centre in 2018, we found that all mothers were diagnosed and treated, as recommended by the national guideline.

Interpretation: The national guideline has had a positive impact by improving early diagnosis and treatment of prenatal toxoplasmosis and reducing severe forms, as observed at the referral centre.

Funding: Colombian Ministry of Science.

Research in context

Evidence before this study

We performed a search in Pubmed with the terms "Guideline" [Publication Type] AND "Toxoplasmosis"[Mesh], "toxoplasmosis guidelines evidence based", "impact evaluation toxoplasmosis guidelines". We found five publications of guidelines for toxoplasmosis with GRADE evaluation, but without analysis of socioeconomic nor impact evaluation. In SIGN website (https://guidelines.ebmportal.com/) a search with the term "toxoplasmosis" do not found any guideline.

Added value of this study

Our study is the first to evaluate the impact of evidence-based guidelines for toxoplasmosis during pregnancy. The implementation of recommendations on clinical practice improved substantially the number of mothers with diagnosis and treatment and for the first time in Colombia mothers were diagnosed at the time of seroconversion, a critical step to initiate early treatment with the best benefit for the children at risk of congenital infection.

* Corresponding author
E-mail address: mmejiao@uqvirtual.edu.co (J.E. Gomez-Marin).
[1] https://orcid.org/0000-0001-5812-184X.
[2] https://orcid.org/0000-0003-2418-6287.
[3] https://orcid.org/0000-0001-6472-3329.

https://doi.org/10.1016/j.lana.2021.100010

Implications of all available evidence

Implementation of evidence based clinical guidelines for toxoplasmosis during pregnancy should be done in prenatal control programs.

Data sharing

Data collected for the study, including individual participant data and a data dictionary defining each field in the set, will be made available to other researchers upon request to authors. Data available will be the deidentified participant data and data dictionary data when publication will be available without restriction.

This translation in Spanish was submitted by the authors and we reproduce it as supplied. It has not been peer reviewed. Our editorial processes have only been applied to the original abstract in English, which should serve as reference for this manuscript.

Resumen

Antecedentes: Colombia implementó las primeras guías de práctica clínica basadas en evidencia para toxoplasmosis congénita en el mundo en el 2013. No se cuenta con una evaluación de su impacto.

Métodos: Se revisaron las historias clínicas de los casos de toxoplasmosis congénita remitidos a la consulta especializada de toxoplasmosis en el Centro de Salud de la Universidad del Quindío durante un período de 18 años (2001-2019). Se analizaron los criterios diagnósticos y la relación entre el tratamiento prenatal y la clínica al nacer. Adicionalmente, describimos el proceso diagnóstico y tratamiento de mujeres en embarazo en un centro de atención primaria de atención prenatal en la ciudad de Armenia durante 2018.

Resultados: Encontramos que antes de la implementación, el 27,3 % de los niños remitidos a la consulta especializada no tenían diagnóstico prenatal; por otra parte, luego del lanzamiento de las guías de práctica clínica, todas las gestantes fueron diagnosticadas. Además, observamos que el tratamiento prenatal se asoció con menos síntomas, lo que mejoró significativamente después de la implementación de las guías. En el centro de atención primaria de salud en 2018, todas las madres fueron diagnosticadas y tratadas, según lo recomendado por las guías nacionales.

Conclusión: Las guías de práctica clínica basadas en la evidencia han tenido un impacto positivo al mejorar el diagnóstico precoz y el tratamiento de la toxoplasmosis prenatal y la reducción de las formas graves, como se observó en el centro de referencia.

Financiamiento: Ministerio de Ciencia de Colombia

Palabras claves: toxoplasmosis; el embarazo; tratamiento; diagnóstico; guías.

1. Introduction

Toxoplasmosis, a disease caused by the obligate intracellular protozoan *Toxoplasma gondii*, represents an emerging global public health threat[1]. The parasite may cross the placenta of an infected pregnant woman and can infect the foetus congenitally[2]. Congenital toxoplasmosis results mainly from primary maternal infection during pregnancy but can occasionally result from preconceptional infection or reactivation of latent infection in immunodeficient pregnant women[2–4]. Congenital toxoplasmosis is a significant public health problem in Colombia and other countries in South America[5]. Studies in different regions in Colombia reported between 0.5% and 2.8% of women with a primary infection during pregnancy[6–10]. The consequences for Colombian neonates of this infection were described at the First Multicentric Newborn Screening program in 15,000 children from seven capital cities with a rate of one congenital infection per 1,000 neonates, 25% mortality of those untreated, and an estimate of over 500 children infected annually[11].

The Systematic Review on Congenital Toxoplasmosis (SYROCOT) international collaborative study found that mothers from South America have a greater risk of transmission[12] and a comparative study of the consequences through follow up of the infected children showed that they were more symptomatic when compared with a European cohort[13]. It is now well established that the higher clinical severity of human toxoplasmosis in South America correlated with strains possessing virulent genotypes of ROP proteins interacting with particular host genetic traits and giving rise to modifications of the cytokine immune response[14–20]. The South American strains pass over a genetic bottleneck and clonal structure, as occurred in strains from the northern hemisphere[21,22].

Diagnosis of gestational toxoplasmosis is based on detecting IgG and IgM antibodies[23]. Absence of IgG indicates susceptibility to infection and follow up is conducted with monthly IgM[24]. Positive IgM can indicate an acute infection; a test is also available to detect avidity in IgG antibodies, acute infection shows prevalence of low avidity, in contrast with chronic infection that shows a high avidity test[25]. It is recommended that women with suspected toxoplasmosis receive control and follow up with monthly foetal ultrasound[26]. Echography findings that can indicate or suggest foetal infection are unilateral or bilateral dilation of the ventricles, intracranial or intrahepatic calcifications, hepatomegaly and splenomegaly[27]. In neonates, the diagnosis criteria include persistence of anti-*Toxoplasma* IgG antibodies beyond 1 year of age or the presence of specific anti-*T. gondii* IgM or IgA after the 10^{th} day of life [28,29]. Aside from these, the presence of clinical manifestations and other laboratory findings at birth can also be helpful for diagnosis[30].

Starting active treatment during pregnancy reduces the risk of foetal loss and early neonatal death, as well as the systemic manifestations[24,31,32]. The treatment regimen is based on spiramycin, 3 g per day, from diagnosis to the end of pregnancy; if confirmation of transmission to the foetus is made, the treatment regimen should be changed to pyrimethamine + sulfadiazine + folinic acid [2,31].

In Colombia, the frequency of congenital toxoplasmosis varied significantly among cities according to mean annual rainfall: the cities with low mean annual rainfall (48 - 806 mm^3/year) had low frequency of congenital toxoplasmosis (0.5% - 0.7% of newborns with congenital toxoplasmosis) and cities with high mean annual rainfall (3,840 - 2,500 mm^3/year) showed high frequency of congenital toxoplasmosis (6% - 3% of newborns with congenital toxoplasmosis [33]. This is explained because survival of sporulated *T. gondii* oocysts is greater in soil with high humidity[34–36]. The department of Quindío, a region with high rain precipitation index and high frequency of congenital toxoplasmosis[33], since 1998 pioneered the implementation of control programs and was the first region in Colombia with an official public regional policy for gestational toxoplasmosis (Resolution No. 336 of 1986 by the Quindío Health Secretary). The development and results led to conducting numerous clinical and epidemiological reports based on the program's experience[7,37,38]. Additional reports in other regions provide additional support to justify the development of national evidenced-based guidelines[10,39]. The Colombian evidence-based clinical guidelines to diagnose and treat toxoplasmosis during pregnancy were launched officially in 2013 [26]. These guidelines are unique given that they were the first in the world to conduct a GRADE evaluation of evidence for recommen-

dations and to have socioeconomic analysis of its implementation [40–42]. One of the most important recommendations was the monthly screening with IgM for sero-negative women[26]. While in France a maternal screening program has existed since 1978 and serological monthly follow up of pregnant women is performed in the majority of mothers[24], in Colombia there was no mandatory serological follow up during pregnancy and less than 47% had diagnosis during pregnancy when clinical records of prenatal care were analysed in 2002 [43]. Then, during the National Newborn Screening in 2009-2010, 70% of mothers had toxoplasmosis tests during pregnancy; however, most had only one test without confirmation or additional follow up [33]. Some benefits related with the publication and implementation of the Colombian clinical practice guidelines have been found, such as reduction of severe cases of hydranencephaly [44]. However, after seven years of implementation, there is no evaluation of its implementation in prenatal care and of its impact after guidelines became official by the Ministry of Health. Herein, we describe the prenatal diagnosis and management of mothers of children with congenital toxoplasmosis that were referred to specialized consultation in the Health Centre at Universidad del Quindío before (2001-2012) and after (2013-2019) implementing the guideline and management of prenatal toxoplasmosis in a primary public health care centre in Armenia for one year (2018). We chose this city because it is the place where this program was initiated, the frequency of congenital infection is high, and the medical community and public health program are well familiarized with this medical condition. The present work does not seek to be representative of the performance of the program in other cities or regions of Colombia, but can demonstrate the benefits of well-implemented guidelines and their impact on reducing neurological and ocular sequelae in children.

2. Materials and Methods

2.1. Source of information

This is an observational retrospective study of two cohorts: the first were the children with confirmed toxoplasmosis referred at the Centre at Universidad del Quindío during 2001-2019, based on the history of management during the gestational period. The second cohort were the pregnant woman who attended the prenatal control at Red Salud-Armenia. The analysis was based, for the first cohort, on clinical chart records in the health care centre at Universidad del Quindío where specialized consultation exists in tropical medicine and parasitology. We analysed data about diagnosis criteria, results of the follow-up examination, and management during an 18-year period (2001-2019).

For the second cohort, we analysed management at the primary care level of pregnant women based on the records of prenatal controls of mothers with diagnosis for acquired toxoplasmosis during pregnancy at the primary health care centre "Red Salud" in Armenia during 2018. Red Salud is the public health service that covers 36% of the city's population (~110,000 inhabitants).

2.2. Inclusion criteria of confirmed congenital toxoplasmosis cases and estimation of the date of infection during pregnancy

The criteria for diagnosis of congenital toxoplasmosis used at the referral centre were presence of specific new-born antibodies, as shown by Western blot, persistence of specific IgG for more than a year of follow up, positive blood PCR or symptoms suggestive of congenital toxoplasmosis, and presence of IgM in the mother's serum. Eye examination and imaging evaluation (CT or brain ultrasound) were requested for all children at the beginning of the follow up. Data were analysed for the effect of treatment for children with at least one year of follow up.

Values of gestational age at maternal seroconversion were entered by using all the serological information available to us. Given that there were no women with seroconversion data (date between the last negative and first positive IgM tests) in the first cohort, the study assumed, from the first date of IgG positive, the risk of infection to be four weeks prior. This was used previously as a manner of estimating the date of infection, on the understanding that it is imprecise, but as the only way for groups of mothers with lack of serological follow up during pregnancy[38].

2.3. Data analysis

We collected from clinical charts the diagnostic criteria applied during pregnancy in the child and if prenatal treatment was set up. Diagnosis, follow up, and management were also evaluated.

In mothers seen at Red Salud, the number of cases with serological test, diagnostic method and criteria for diagnosis, prenatal treatment performed, ultrasound findings, and foetal outcomes associated with the disease were included in the analysis. Data were accessed through institutional informed consent and were recorded in Excel® spreadsheet by using codes to protect patients' identities.

2.4. Statistical methods

Results were expressed as the median [min-max range] for continuous variables and N (%) for categorical variables. Epi-Info was used to perform Mantel Haenszel for stratified analysis and odds ratio calculation with 95%CI. GraphPad Prism was 8.0.1 used to elaborate the graphs.

Role of the funding source

The funding organization had no role in the design and study course; nor in the collection, management, analysis, and interpretation of the data or in the final preparation, review, or approval of the manuscript.

3. Results

3.1. Analysis of prenatal management of referred cases of congenital toxoplasmosis (2001-2019) in Quindío

From the 170 children referred with suspected congenital toxoplasmosis to the reference centre in toxoplasmosis at Universidad del Quindío from 2001 to 2019, 99 of these (58.2%) met the diagnostic criteria and follow-up time; 72.7% (72/99) of the mothers were tested for toxoplasmosis during pregnancy, most during the period after 2013, coinciding with the implementation of the clinical practice guidelines that allowed detecting seven cases of sero-conversion through monitoring with IgM during pregnancy, as well.

Additionally, 27.3% (27/99) of the mothers had not been diagnosed during pregnancy. Figure 1 shows the evolution in the implementation of diagnostic tests used as criteria for treatment during pregnancy over time (2001-2019).

Regarding treatment during pregnancy, 52.5% (52/99) of the mothers received management against *T. gondii* infection, the average duration was three months (1 - 7 range); 44 mothers were treated with spiramycin since the diagnosis until the end of the pregnancy, and three underwent changes to sulfadoxine/pyrimethamine after positive PCR results in amniotic fluid. In

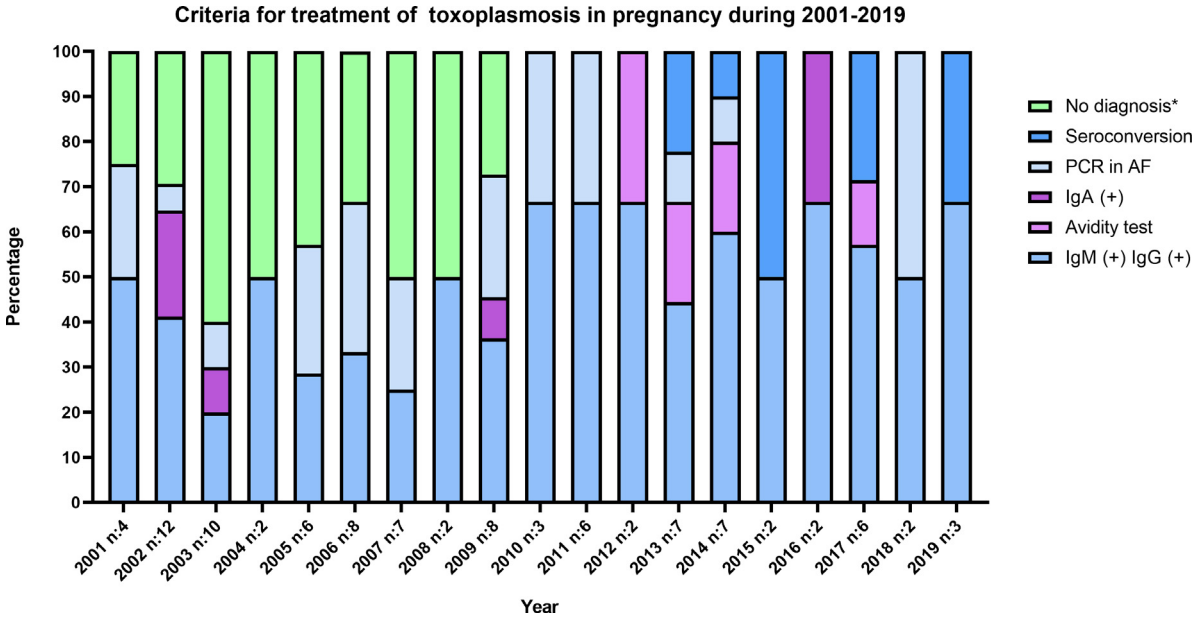

Figure 1. Diagnostic process from 2001 to 2019 during gestational period of patients diagnosed with Congenital Toxoplasmosis. The diagnostic method and percentage of yearly tests is shown. (*) Mothers with undiagnosed toxoplasmosis during pregnancy were included *n: number of patients per year. PCR-AF: PCR in amniotic fluid.

Table 1
Outcomes in children with congenital toxoplasmosis according to prenatal treatment at first year of life.

Prenatal treatment	Chorioretinitis	Neurological compromise	Ocular and neurological compromise	Hepatosplenomegaly	Total of symptomatic children*	Mortality
Yes						
2001 – 2012	0	0	3/29 (10.35%)	1/29 (3.45%)	4/29 (13.79%)	0
2013 – 2019	0	0	2/23 (8.7%)	0	2/23 (8.6%)	0
Total					6/52 (11.5%)	0/52
No						
2001 – 2012	11/40 (27.5%)	8/40 (20%)	5/40 (12.5%)	3/40 (7.5%)	27/40 (67.5%)	4/40 (10%)
2013 – 2019	2/7 (20.57%)	0/7 (0%)	2/7 (28.57%)	0/7 (0%)	4/7 (57.14%)	0/7 (0%)
Total					31/47 (67.39%)	4/47(8.5%)

* Adjusted OR for the effect of treatment on symptoms after one year of life in children whose mothers had an estimated infection date (n: 45 of 99 mothers) = 0.14 (95%CI= 0.02 – 0.78)

eight, the mothers' treatment was with sulfadoxine/pyrimethamine since the diagnosis of the infection. The criteria for treatment with sulfadoxine/pyrimethamine were PCR positive in amniotic fluid in 8/11 cases (72.7%%), ultrasound findings of hydrocephaly in 1/11(9%), and IgA positive in 1/11(9%). In the group of children, where management during pregnancy was reported, 6/52 symptomatic cases (11.5%) occurred, four of these from 2000 to 2012, and two cases between 2013 and 2019. There was no mortality during the first year of follow up.

Furthermore, 47.5% (47/99) of the cases of congenital toxoplasmosis did not receive prenatal treatment; of these, 83% (39/47) did not have a diagnosis during pregnancy; 40 of the 47 untreated (85.1%) cases correspond to the period from 2001 to 2012, while only seven (14.9%) of the untreated cases were found as of 2013, a period that coincides with the implementation of the clinical practice guidelines (Figure 2).

In 31 of the 47 (66%) children not treated during the gestational period, there were events related with ocular compromise, ocular and neurological compromise, and hepatosplenomegaly, in addition to four cases of mortality during the first year of follow up (Table 1).

In 45 mothers of children with congenital infection, the approximate date was calculated of infection during the gestational period. After a stratified analysis, controlling for the estimated trimester of infection, we found an adjusted OR of 0.14 of confirmed congenital infection in offspring for those who received treatment (95%CI 0.0278 - 0.7802).

3.2. Analysis of prenatal management in a primary public health care centre in Armenia Quindío during 2018

Moreover, during 2018, 1,809 pregnant women were seen for prenatal controls at Red Salud in Armenia. We found that according to the clinical records, anti-*Toxoplasma* IgG and IgM antibodies were requested from all the mothers at the first prenatal control they attended. The median of weeks of pregnancy when request for the tests were performed was 11.9 (range: 7-27). However, results of tests were delivered at nineteen weeks of pregnancy (range: 8.5 -32.4), representing a delay of 7 weeks between the test request and the delivery of the results.

Among the 1809 pregnant women that attended during 2018, we found that 26 had diagnosis of gestational toxoplasmosis (1.43%, 95%CI 1.15-1.71). The mean age of the pregnant women with toxoplasmosis disease was 22 years (SD 6.8). These mothers attended an average of seven prenatal controls (range: 2-13).

Overall, in 6/26 (23%), the diagnosis was made during the first 16 weeks of gestation. Avidity test was requested for all these patients and three of the six patients (50%) reported a result of high avidity ≥30%. In 15/26 (57.7%), the diagnosis was made after week 16. Anti-*T. gondii* IgA test was requested in all these pregnant women, but only three were reported: two were negative and one positive. In all cases, treatment was continued. The mean levels of specific anti-*Toxoplasma* antibodies reported for cases with diagnosis of gestational toxoplasmosis were 354.3 UI/ml (range 30.16 – 1031) for IgG and 10.5 of Index (range: 1.07-40.2) for IgM.

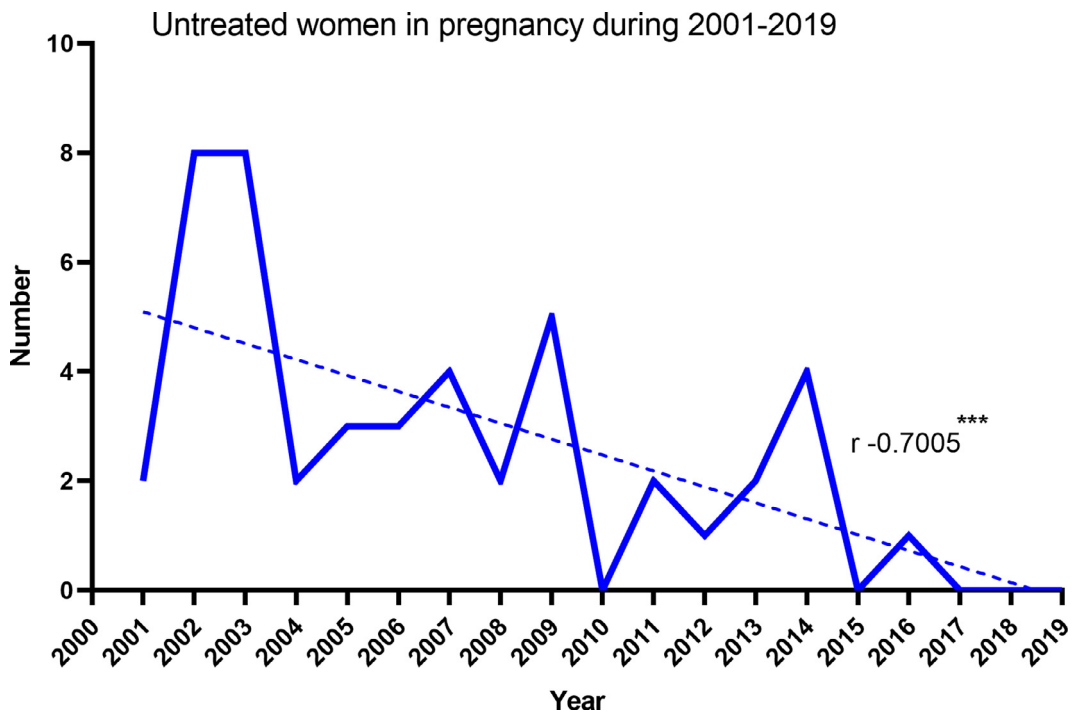

Figure 2. Women untreated during pregnancy during 2001-2019. Spearman's rank correlation coefficient was performed to compare: Untreated vs. Year r: -0.7005 p: 0.0008 (***).

In 5/26 (19.2%), diagnosis was made because there was sero-conversion during the monthly follow up. The range of specific anti-*T. gondii* antibodies before diagnosis were 3 – 5 UI/mL for IgG and 0.3 – 0.6 UI/mL for IgM. These mothers were between weeks 12 and 24 at the moment of sero-conversion (Figure 3). For comparison, in previous reports, no diagnosis of gestational toxoplasmosis was made through sero-conversion criteria. Three amniocenteses for PCR were performed, all with negative results.

The treatment of choice was spiramycin at a dosage of 3 M.U.I, one tablet every 8 h, established from the moment of diagnosis. In three patients, the drug was suspended due to the avidity test for high IgG.

4. Discussion

Although exceptional cases exist of reinfection with subsequent transmission of congenital infection in siblings[3], *T. gondii* sero-negative women is the primary target of screening programs during pregnancy[24,45,46]. These pregnant women are susceptible to infection and must have serological follow-up to detect their acquisition [24,45,46]. *T. gondii* infection during pregnancy exposes the foetus to risks of congenital infection and sequelae that depend heavily on gestational age at the time of infection[47,48]; thereby, early diagnosis is required. Health programs to detect toxoplasmosis during pregnancy reduce neonatal mortality, neurological and ophthalmological sequelae, which require complying with evidence-based recommendations[24,26,46]. Notwithstanding this knowledge, previous limited data existed in the literature about the evolution of the care, diagnosis, management, and monitoring of toxoplasmosis during pregnancy in Colombia. In 2000, Gómez *et al*., found in an analysis of medical records from a health centre in the city of Bogotá that only 47% of the pregnant women received IgG antibodies and none of the sero-negative patients were followed up[49]. Thereafter, in 2011, a multicentre study revealed that 70% of the patients received IgG antibodies upon admission to prenatal control[33]. The current work found that pregnant women were monitored every four weeks with timely initiation of treatment in the public health service. This is crucial, given that the SYROCOT study showed decreased risk of congenital infection related with the time in which treatment was begun after sero-conversion: in the first four weeks OR for transmission was reduced to 0.48 (95%CI 0.28 - 0.80) versus a risk of 0.6 (95%CI 0.4 - 1.0) if treatment was begun after week four of sero-conversion[12].

This observational descriptive study shows the importance of strategies implemented in an early detection program for gestational toxoplasmosis in a public health centre in Armenia, Quindío within the prenatal controls and with regular follow up of pregnant women. We show that health professionals followed the algorithm for diagnosis and management of toxoplasmosis during pregnancy; no adverse foetal outcomes were found. The program in Red Salud included telephone follow up to track and contact patients. It is now important to extent the analysis of the implementation of guidelines to other regions in Colombia.

Likewise, in the referral centre, after implementing the national guidelines, it was observed that all the mothers of children with congenital toxoplasmosis had timely diagnosis and establishment of treatment; a reduction in the number of referred cases was observed, possibly associated with improved implementation of evidence-based recommendations. Also, an important reduction of the frequency of the severe forms was seen at the referral centre. It is necessary to perform long-term follow up of the infants to determine possible subsequent sequelae. However, the correct application of the latest clinical practice guidelines in the post-implementation period is highlighted. No reports exist of the establishment and analysis of the impact of similar guidelines. A search was carried out in Pubmed with the terms "Guideline" [Publication Type] AND "Toxoplasmosis"[Mesh], “toxoplasmosis guidelines evidence based”, “impact evaluation toxoplasmosis guidelines”, finding five publications of guidelines for toxoplasmosis with GRADE evaluation, but without analysis of socioeconomic or impact evaluation; additionally, in the SIGN website (https://

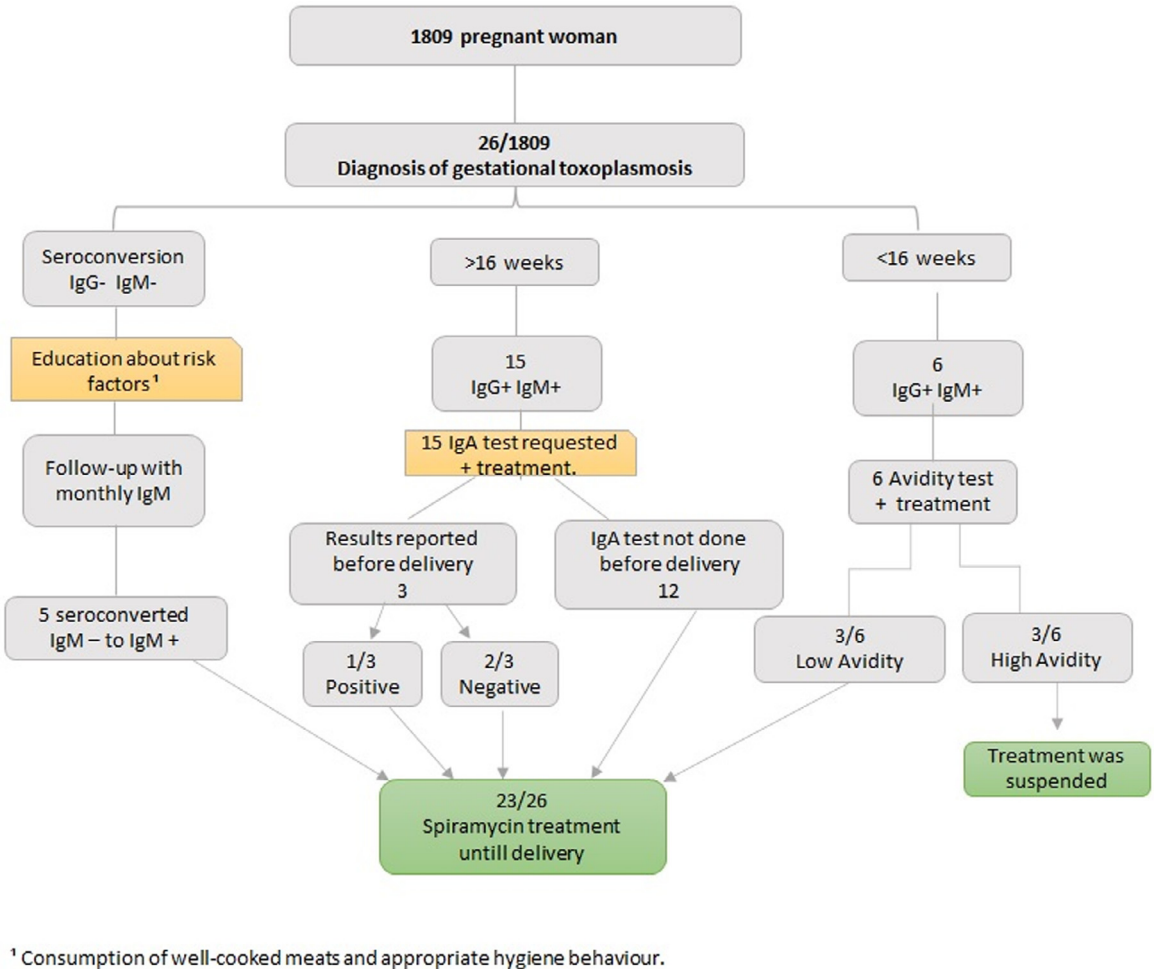

Figure 3. Flowchart of diagnosis and management of toxoplasmosis in 1,809 pregnant women at the public health system in Armenia (Colombia) during 2018.

guidelines.ebmportal.com/) a search with the term "toxoplasmosis" did not find any guideline. Indeed, the Colombian guidelines are the first globally to accomplish the entire process to be adopted officially by the social security system, which means that all public and private health services can base on its recommendations medical interventions for prenatal and congenital toxoplasmosis[40]. The economic impact of congenital toxoplasmosis has been evaluated by many authors and it is significant for any human society[42,45,50,51]. The conclusions of all the economic impact of this condition are clear to show that a benefit exists if early diagnosis and treatment are performed[42,52]. The most significant problem is the availability of resources; for the Colombian guidelines, cost-benefit analysis showed that for a willingness to pay above $407 million Colombian pesos (~USD $107,000) the cost-effective strategy is monthly monitoring[42].

In France, significant risk reduction was achieved since 1992 when monthly screening was introduced, reporting 59.4% vs. 46.6% at 26 weeks of gestational age in a retrospective and transversal study conducted in Lyon, France and providing data from pregnant women diagnosed with *Toxoplasma* infection and assessing how the risks of congenital toxoplasmosis was analysed [24]. It was found that among 2,048 mother-infant pairs, 93.2% of the mothers received prenatal treatment and 513 (24.7%) foetuses were infected [24]. Significant reduction was observed in the risk of clinical signs of congenital toxoplasmosis in infected children born from mothers diagnosed after 1995 when polymerase chain reaction testing on amniotic fluid was initiated [24]. This study indicated that introducing monthly prenatal screening and improving antenatal diagnosis were associated with reduced rates of congenital infection and better outcomes in infected children[24].

In Colombia, after the release of the national guidelines, there was no updated data until now to determine the implementation regarding the diagnosis, monitoring, and management of the disease. The present study identified such implementation in a cohort of pregnant patients, with favourable results. It was opportune to perform this type of study in an area where *Toxoplasma gondii* infection is highly prevalent to determine the implementation of the gestational toxoplasmosis guidelines issued by the Colombian Ministry of Health in 2013.

In conclusion, we found that an early detection program for gestational toxoplasmosis implemented in prenatal control in a public health centre in Armenia, Quindío, based on recommendations from evidence-based guidelines, was properly implemented. Requests for diagnostic tests were timely. In addition, adequate follow up was performed in sero-negative patients and treatment was instituted upon diagnosis. No adverse outcomes were reported.

It is striking to note that there were untreated mothers before implementing the guidelines and this was not the case for mothers diagnosed after said implementation. Also, the children referred to the referral health centre during the period prior to the guidelines showed a significant proportion of ocular and neurological sequelae that reduced after that implementation. Something to highlight is that some IgA results were not reported. No case with negative IgG and positive IgM was registered. Furthermore, it was observed that the frequency of infection has not diminished when compared with previous studies.

Contributors

Manuela Mejia-Oquendo: Methodology, Formal analysis, Investigation, Data curation. Writing - review.

Elizabeth Marulanda: Methodology, Formal analysis, Investigation.

Jorge Enrique Gómez-Marín: Conceptualization, Methodology, Formal analysis, Resources, Data curation, Writing - review & editing, Supervision.

Declaration of interests

The authors declare no competing interests.

Availability of data and material

Data are available upon request to the authors.

Funding

Manuela Mejia is a young researcher beneficiary of the Colombian Ministry of Science, Grant number CT 773-2018.

References

[1] Rodriguez-Morales AJ, Paniz-Mondolfi AE, Faccini-Martínez ÁA, et al. The Constant Threat of Zoonotic and Vector-Borne Emerging Tropical Diseases: Living on the Edge. Front Trop Dis 2021;2. doi:10.3389/fitd.2021.676905.
[2] Petersen E, Ajzenberg D, Mandelbrot L, Gomez-Marin JE. Protozoan Diseases: Toxoplasmosis. In: International Encyclopedia of Public Health. Amsterdan: Elsevier; 2017. p. 114–32.
[3] Elbez-Rubinstein A, Ajzenberg D, Dardé M-L, et al. Congenital Toxoplasmosis and Reinfection during Pregnancy: Case Report, Strain Characterization, Experimental Model of Reinfection, and Review. J Infect Dis 2009;199:280–5.
[4] Maldonado YA, Read JS. Diagnosis, Treatment, and Prevention of Congenital Toxoplasmosis in the United States. Pediatrics 2017;139:e20163860.
[5] Gómez-Marín JE. Congenital toxoplasmosis in South American children. Sci Med (Porto Alegre) 2010;20:103–7.
[6] Rosso F, Agudelo A, Montoya G. Toxoplasmosis congénita: aspectos clínicos y epidemiológicos de la infección durante el embarazo. Colomb medica (Cali, Colomb 2007;38:316–37.
[7] Gomez-Marin JE, Montoya-de-Londono MT, Castano-Osorio JC. A maternal screening program for congenital toxoplasmosis in Quindio, Colombia and application of mathematical models to estimate incidences using age-stratified data. Am J Trop Med Hyg 1997;57:180–6.
[8] Ángel Muller E, Hougton MP, Eslava C, Riaño J, Rey GE, Gómez Marín JE. Gestational and congenital toxoplasmosis in two hospitals in Bogota, Colombia. Rev la Fac Med 2014;62:179–85.
[9] Barrera AM, Castiblanco P, Jorge E, et al. Acquired toxoplasmosis during pregnancy at the instituto materno-infantil, bogota. Rev Salud Pública 2002;4:286–93.
[10] Rosso F, Les JT, Agudelo A, et al. Prevalence of infection with Toxoplasma gondii among pregnant women in Cali, Colombia, South America. Am J Trop Med Hyg 2008;78:504–8.
[11] Gómez-Marin JE, De-la-Torre A, Angel-Muller E, et al. First Colombian Multicentric Newborn Screening for Congenital Toxoplasmosis. PLoS Negl Trop Dis 2011;5:e1195.
[12] SYROCOTEffectiveness of prenatal treatment for congenital toxoplasmosis: a meta-analysis of individual patients' data. Lancet 2007;369:115–22.
[13] Gilbert RE, Freeman K, Lago EG, et al. Ocular Sequelae of Congenital Toxoplasmosis in Brazil Compared with Europe. PLoS Negl Trop Dis 2008;2:e277.
[14] Alvarez C, De-la-Torre A, Vargas MM, et al. Striking Divergence in Toxoplasma ROP16 Nucleotide Sequences From Human and Meat Samples. J Infect Dis 2015;211:2006–13.
[15] de-la-Torre A, Pfaff AW, Grigg ME, et al. Ocular cytokinome is linked to clinical characteristics in ocular toxoplasmosis. Cytokine 2014;68:23–31.
[16] de-la-Torre A, Sauer A, Pfaff AWAW, et al. Severe South American ocular toxoplasmosis is associated with decreased Ifn-γ/Il-17a and increased Il-6/Il-13 intraocular levels. PLoS Negl Trop Dis 2013;7:e2541.
[17] Hernández-de-los-Ríos A, Murillo-Leon M, Mantilla-Muriel LE, et al. Influence of Two Major Toxoplasma Gondii Virulence Factors (ROP16 and ROP18) on the Immune Response of Peripheral Blood Mononuclear Cells to Human Toxoplasmosis Infection. Front Cell Infect Microbiol 2019;9:413.
[18] Mantilla-Muriel LE, Hernández-de-los-Ríos A, Rincón M, et al. Serotyping, host genes and cytokines response in human ocular toxoplasmosis. Microb Pathog 2020;148:104465.
[19] Sánchez V, De-la-Torre A, Gómez-Marín JE. Characterization of ROP18 alleles in human toxoplasmosis. Parasitol Int 2014;63:463–9.
[20] Torres-Morales E, Taborda L, Cardona N, et al. Th1 and Th2 immune response to P30 and ROP18 peptides in human toxoplasmosis. Med Microbiol Immunol 2014;203:315–22.
[21] Khan A, Böhme U, Kelly KA, et al. Common inheritance of chromosome Ia associated with clonal expansion of Toxoplasma gondii. Genome Res 2006;16:1119–25.
[22] Bertranpetit E, Jombart T, Paradis E, et al. Phylogeography of Toxoplasma gondii points to a South American origin. Infect Genet Evol 2017;48:150–5.
[23] Roberts A, Hedman K, Luyasu V, et al. Multicenter evaluation of strategies for serodiagnosis of primary infection with Toxoplasma gondii. Eur J Clin Microbiol Infect Dis 2001;20:467–74.
[24] Wallon M, Peyron F, Cornu C, et al. Congenital Toxoplasma Infection: Monthly Prenatal Screening Decreases Transmission Rate and Improves Clinical Outcome at Age 3 Years. Clin Infect Dis 2013;56:1223–31.
[25] Torres-Morales E, Gómez-Marín JE. Evaluacion de una prueba ELISA IgG De Avidez para toxoplasma para el diagnostico en el embarazo y correlacion con IgM e IgA en el laboratorio del centro de investigaciones biomidicas de la Universidad del quindio, 2008/Evaluating a toxoplasma IgG avidity. Rev Colomb Obstet Ginecol 2008;59:199–206.
[26] Cortes JA, Gómez JE, Silva PI, et al. Clinical practice guideline. Integral Care Guidelines for the prevention, early detection and treatment of pregnancy, childbirth and puerperium complications: Section on toxoplasmosis in pregnancy. Infectio 2017;21:102–16.
[27] Codaccioni C, Picone O, Lambert V, et al. Ultrasound features of fetal toxoplasmosis: A contemporary multicenter survey in 88 fetuses. Prenat Diagn 2020;40:1741–52.
[28] Ciardelli L, Meroni V, Avanzini MA, et al. Early and accurate diagnosis of congenital toxoplasmosis. Pediatr Infect Dis J 2008;27:125–9.
[29] Lebech M, Joynson DHM, Seitz HM, et al. Classification system and case definitions of Toxoplasma gondii infection in immunocompetent pregnant women and their congenitally infected offspring. Eur J Clin Microbiol Infect Dis 1996;15:799–805.
[30] Torres E, Rivera R, Cardona N, et al. Evaluation of IgG anti-toxoplasma avidity and polymerase chain reaction in the postnatal diagnosis of congenital toxoplasmosis. Pediatr Infect Dis J 2013;32:693–5.
[31] Peyron F, L'ollivier C, Mandelbrot L, et al. Maternal and Congenital Toxoplasmosis: Diagnosis and Treatment Recommendations of a French Multidisciplinary Working Group. Pathogens 2019;8:24.
[32] Cortina-Borja M, Tan HK, Wallon M, et al. Prenatal Treatment for Serious Neurological Sequelae of Congenital Toxoplasmosis: An Observational Prospective Cohort Study. PLoS Med 2010;7:e1000351.
[33] Gómez-Marin JE, De-la-Torre A, Angel-Muller E, et al. First Colombian Multicentric Newborn Screening for Congenital Toxoplasmosis. PLoS Negl Trop Dis 2011;5:e1195.
[34] Frenkel JK, Ruiz A, Chinchilla M. Soil survival of toxoplasma oocysts in Kansas and Costa Rica. Am J Trop Med Hyg 1975;24:439–43.
[35] Lélu M, Villena I, Dardé M-LL, et al. Quantitative estimation of the viability of Toxoplasma gondii oocysts in soil. Appl Environ Microbiol 2012;78:5127–32.
[36] Dumètre A, Aubert D, Puech P-H, Hohweyer J, Azas N, Villena I. Interaction forces drive the environmental transmission of pathogenic protozoa. Appl Environ Microbiol 2012;78:905–12.
[37] Gómez J, Montoya M, Castaño J, Ríos M, Perez J. Epidemiología de la infección por Toxoplasma gondii en gestantes de Armenia, Quindío, Colombia. Colomb medica (Cali, Colomb 1993;24:14–18.
[38] Gómez JE, Gomez-Marin J. Evaluación del tratamiento de la toxoplasmosis gestacional en una cohorte colombiana. Infectio 2005;9:16–23.
[39] Barrera AM, Castiblanco P, Gómez JE, et al. Toxoplasmosis Adquirida Durante el Embarazo, en el Instituto Materno Infantil en Bogotá; 2002. www.medicina.unal.edu.co/ist/revistasp (accessed Sept 1, 2020).
[40] Gómez M JE. Guías de atención integral para toxoplasmosis basadas en evidencia: una contribución de Colombia para el mundo. Infectio 2012;16:191.
[41] Chicaíza-becerra L, García-Molina M, Oviedo-ariza S, Gómez-Marín JE, Gómez-Sánchez PI. Costo efectividad de diferentes estrategias diagnósticas para detección de toxoplasmosis congénita en el recién nacido. Infectio 2013;17:53–60.
[42] Chicaíza L, García Molina M, Oviedo S, et al. Cost Effectiveness of Diagnostic Strategies for Opportune Detection of Toxoplasma Gondii in Pregnant Women. SSRN Electron. J. 2012 published online July. DOI:. doi:10.2139/ssrn.2194572.
[43] Gómez Marín JE. Toxoplasmosis: un problema de salud pública en Colombia. Rev salud pública 2002;4:7–10.
[44] El Bissati K, Levigne P, Lykins J, et al. Global initiative for congenital toxoplasmosis: an observational and international comparative clinical analysis. Emerg Microbes Infect 2018;7:1–14.
[45] Stillwaggon E, Carrier CS, Sautter M, McLeod R. Maternal Serologic Screening to Prevent Congenital Toxoplasmosis: A Decision-Analytic Economic Model. PLoS Negl Trop Dis 2011;5:e1333.
[46] Hotop A, Hlobil H, Gross U. Efficacy of Rapid Treatment Initiation Following Primary Toxoplasma gondii Infection During Pregnancy. Clin Infect Dis 2012;54:1545–52.
[47] Dunn D, Wallon M, Peyron F, Petersen E, Peckham C, Gilbert R. Mother-to-child transmission of toxoplasmosis: Risk estimates for clinical counselling. Lancet 1999. doi:10.1016/S0140-6736(98)08220-8.
[48] Daffos F, Forestier F, Capella-Pavlovsky M, et al. Prenatal Management of 746 Pregnancies at Risk for Congenital Toxoplasmosis. N Engl J Med 1988. doi:10.1056/NEJM198802043180502.

[49] Toxoplasmosis Gomez J. Un problema de Salud Pública en Colombia. Rev Salud Pública 2002;4:7–10.
[50] Prusa A-R, Kasper DC, Sawers L, Walter E, Hayde M, Stillwaggon E. Congenital toxoplasmosis in Austria: Prenatal screening for prevention is cost-saving. PLoS Negl Trop Dis 2017;11:e0005648.
[51] Binquet C, Lejeune C, Seror V, et al. The cost-effectiveness of neonatal versus prenatal screening for congenital toxoplasmosis. PLoS One 2019;14:e0221709.
[52] Bobić B, Villena I, Stillwaggon E. Prevention and mitigation of congenital toxoplasmosis. Economic costs and benefits in diverse settings. Food Waterborne Parasitol 2019;16:e00058.