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Low IgG avidity for *Toxoplasma gondii* in consecutive pregnancies

Baixa avidez de IgG para *Toxoplasma gondii* em gestações consecutivas

Baja avididad de IgG para *Toxoplasma gondii* en embarazos consecutivos

Cynthia Dantas de Macedo Lins[1], Cristiana Menechini Winkler[1], Ana Vitória Soares de Deus Mota de Macedo[1], Frutuoso Lins Cavalcante Neto[2], Vera Lucia Pereira-Chioccola[3], Cristina da Silva Meira Strejevitch[3], Fabiana Nakashima[1], Ana Iara Costa Ferreira[1], Maria Regina Reis Amendoeira[4].

ABSTRACT

Objective: To present a clinical case of a pregnant woman who consistently showed low avidity IgG test results for *Toxoplasma gondii* in two consecutive pregnancies. **Case details:** G5P2A2, 41 years old, followed up in the High-Risk Prenatal Care due to serologies for *T. gondii* with IgM+/IgG+ and avidity test performed at 11 weeks of gestation, showing 49% avidity. She brought exams from the previous pregnancy that also showed serologies for *T. gondii* with IgM+/IgG+ and low IgG avidity (42%). The fetus was evaluated at the Fetal Medicine outpatient clinic and showed no ultrasonographic abnormalities. The pregnancy progressed to spontaneous vaginal delivery at 38 weeks, resulting in a healthy newborn. **Final considerations:** The importance of the avidity test in managing gestational toxoplasmosis and the diagnostic limitations when low avidity is present in isolation is noted. It is suggested to standardize effective medical records across health services to allow tracking the serological history of pregnant women, in addition to training professionals in clinical protocols, such as the Technical Note (NT) Nº 100/2022 do Ministry of Health, to avoid unnecessary treatments.

Keywords: *Toxoplasma gondii,* Gestational toxoplasmosis, Prenatal care, Medical records.

RESUMO

Objetivo: Apresentar um caso clínico de uma gestante que permaneceu com teste de avidez baixa para *Toxoplasma gondii* em duas gestações consecutivas. **Detalhamento do caso:** G5P2A2, 41 anos, acompanhada no Pré-Natal de Alto Risco devido sorologias para *T. gondii* com IgM+/IgG+ e teste de avidez realizado com 11 semanas, exibindo 49% de avidez. Trouxe exames da gestação anterior que também mostraram sorologias para *T. gondii* com IgM+/IgG+ e avidez de IgG baixa (42%). O feto foi avaliado no ambulatório de Medicina Fetal, onde não demonstrou alterações ultrassonográficas. Durante o estudo, testes adicionais foram realizados na paciente, incluindo *Enzyme Linked Immuno Sorbent Assay* confirmatório, avidez de IgG (59%) e Reação em Cadeia da Polimerase em Tempo Real, com resultado negativo. Evoluiu para parto vaginal espontâneo com 38 semanas, com um recém-nascido saudável. **Considerações finais:** Observa-se a

[1] Federal University of Roraima (UFRR), Boa Vista – RO.
[2] Women's Health Reference Center (CRSM), Boa Vista – RO.
[3] Adolfo Lutz Institute (IAL), São Paulo – SP.
[4] Oswaldo Cruz Foundation (FIOCRUZ), Rio de Janeiro – RJ.

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importância do teste de avidez no manejo da toxoplasmose gestacional e a limitação diagnóstica quando da presença da baixa avidez, sugerindo-se a padronização de prontuários eficazes entre os serviços de saúde com histórico sorológico das gestantes, além da capacitação dos profissionais em protocolos clínicos, como a Nota Técnica (NT) Nº 100/2022 do Ministério da Saúde, a fim de evitar tratamentos desnecessários.

Palavra clave: *Toxoplasma gondii*, Toxoplasmose gestacional, Cuidado pré-natal, Prontuário médico.

RESUMEN

Objetivo: Presentar un caso clínico de una gestante que mostró consistentemente resultados de pruebas de avidez baja de IgG para *Toxoplasma gondii* en dos embarazos consecutivos. **Detalles del caso:** G5P2A2, 41 años, seguida en el Prenatal de Alto Riesgo debido a serologías para *T. gondii* con IgM+/IgG+ y prueba de avidez realizada a las 11 semanas de gestación, mostrando una avidez del 49%. Trajo exámenes del embarazo anterior que también mostraron serologías para *T. gondii* con IgM+/IgG+ y avidez baja de IgG (42%). El feto fue evaluado en el consultorio de Medicina Fetal, donde no mostró alteraciones ecográficas. El embarazo progresó a un parto vaginal espontáneo a las 38 semanas, resultando en un recién nacido sano. **Consideraciones finales:** Se observa la importancia de la prueba de avidez en el manejo de la toxoplasmosis gestacional y las limitaciones diagnósticas cuando se presenta baja avidez de manera aislada. Se sugiere estandarizar historiales médicos efectivos en los servicios de salud para permitir el seguimiento del historial serológico de las gestantes, además de capacitar a los profesionales en protocolos clínicos, como la Nota Técnica (NT) Nº 100/2022 do Ministerio da Salud (MS), para evitar tratamientos innecesarios.

Palabras claves: *Toxoplasma gondii*, Toxoplasmose gestacional, Cuidado pré-natal, Prontuário médico.

INTRODUCTION

Gestational toxoplasmosis is na infection caused by the obligate intracellular protozoan Toxoplasma gondii that can be transmitted transplacentally to the embryo orfetus during pregnancy. Although its epidemiology varies geographically, toxoplasmosis remains a common infection worldwide (GUNDESLIOGLU OO, et al., 2024).

Early diagnosisis essentiall to prevent fetal complications, making serologic screening an essential component of prenatal care (Zhou Y, et al., 2024). Diagnostic methods include the detection of specific IgM and IgG antibodies and IgG avidity testing, the latter being particularly useful in estimating the timing of maternal infection. It is recommended that avidity testing be performed before 16 weeks' gestation in cases with positive IgM and IgG results (BRASIL, 2022; DUBEY JP, 2021; TEIMOURI A, et al., 2020).

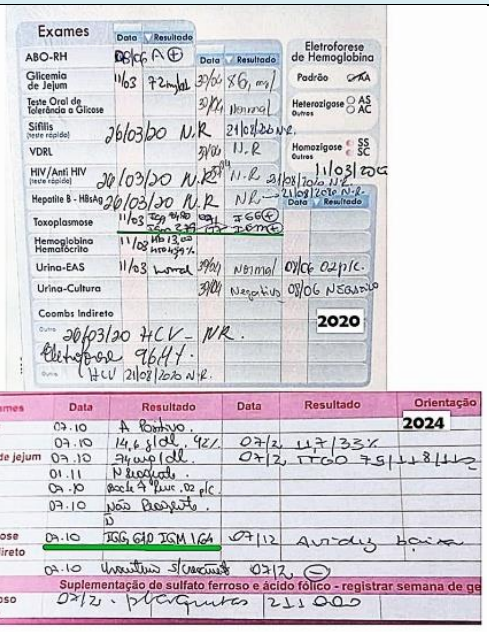
Anavidity test result indicating high avidity before 16 weeks suggests preconceptional infection, where as low avidity may indicate recent infection during pregnancy, which is associated with a higher risk of vertical transmission and the need for therapeutic intervention (BRAZIL, 2022; DUBEY JP, 2021; TEIMOURI A, et al., 2020). In Brazil, clinical management guidelines are outlined in Technical Note No. 100/2022 of the Ministry of Health, which provides national diagnostic and treatment protocols for gestational and congenital toxoplasmosis (BRASIL, 2022).

Accurate interpretation of diagnostic tests is essential for appropriate clinical decision making, avoiding both overtreatment and missed opportunities for essential interventions. The aim of the present study is to report a case of a pregnant woman with persistently low IgG avidity for T. gondii during two consecutive pregnancies, with an interpregnancy interval of three years. This study was approved by the National Research Ethics Committee (CONEP), CAAE: 59249722.2.0000.5302, and by the Ethics Committee of the Adolfo Lutz Institute, CAAE: 59249722.2.3001.0059.

CASE REPORT

The patient, hereafter referred to as CGS, was a 41-year-old, 5 pregnancies, 2 deliveries and 2 abortus, married, of mixed ethnicity, and a postgraduate student residing in Boa Vista, Roraima. She started prenatal care at 8 weeks' gestation in a primary health unit and was referred to the high-risk prenatal care service after a serologic screening in October 2023, which showed positive IgM and IgG for T. gondii. An avidity test performed at 11 weeks showed low avidity (49%). Upon review of her obstetric history, CGS presented records from a previous pregnancy three years prior that showed persistent positive serologies for T. gondii (IgM+/IgG+) and low IgG avidity, with values of 54% in the first trimester and 42% in the third trimester (**Table 1**).

Table 1 - Results of Toxoplasmosis avidity tests performed and GA (gestational age) of the delivery in weeks, with images of the exams recorded on each prenatal card.

Year of gestation	Serology for Toxoplasmosis	Toxoplasmosis avidity test	GA of childbirth	Prenatal card (registered tests)
2020	IgG+/IgM+	42%	33	
2024	IgG+/IgM+	49%	37	

Source: Lins CDM, et al., 2025.

Her personal and obstetric history included previous infections with cytomegalovirus, rubella, and varicella. The patient had two early spontaneous miscarriages (before seven weeks' gestation) and two vaginal deliveries. The first delivery was preterm, at 37 weeks and 1 day of gestation, with a newborn weighing 2,360 grams. The second delivery, in 2020, was preterm, at 33 weeks and 2 days, with a newborn weighing 2,300 grams. During this latter pregnancy in 2020, the patient presented with Toxoplasma gondii infection with low IgG avidity and was treated with spiramycin until delivery. Both children are currently alive and well.

When asked about her lifestyle and living conditions, the patient reported that she occasionally handled soil during her occupational activities without the proper use of personal protective equipment. She also noted the presence of flies during the rainy season. She denied any contact with cats or consumption of raw meat, stating that she consumed properly sanitized vegetables and mineral water.

General and obstetric physical examinations were unremarkable at the initial high-risk prenatal care visit. Follow-up visits to the Fetal Medicine Outpatient Clinic revealed no fetal ultrasound abnormalities. Throughout the pregnancy, the patient attended ten prenatal visits and was started on spiramycin therapy at 12 weeks'

gestation, which was discontinued at 30 weeks' gestation due to the development of generalized pruritus despite normal transaminase levels. She progressed to spontaneous vaginal delivery at 38 weeks, giving birth to a newborn weighing 3,090 grams with Apgar scores of 9 and 10 at 1 and 5 minutes, respectively.

The newborn underwent serologic testing for toxoplasmosis at 24 hours of life, which was positive for IgG with a titer of 91.4 IU/mL and nonreactive for IgM. In addition, transfontanellar ultrasonography and fundoscopic examination were performed, both with normal findings. Serologic testing was repeated at 48 days of age and confirmed a positive IgG titer of 35.2 IU/mL and nonreactive IgM, with testing performed in different laboratories. The chemiluminescence method was used for both evaluations. At 21 weeks' gestation, the patient consented to participate in a research study on toxoplasmosis in pregnant women in the state of Roraima, approved by the National Research Ethics Commission (CAAE: 59249722.2.0000.5302). As study participants, their clinical and epidemiological data were collected through interview and review of their medical records from the high-risk prenatal care program.

During the study, laboratory tests were performed following the collection of a peripheral blood sample at 21 weeks' gestation, including an enzyme-linked immunosorbent assay (ELISA) for serologic confirmation (IgM+/IgG+), an avidity test (59% - moderate), and detection of T. gondii genetic material by real-time polymerase chain reaction (qPCR), which was negative. After delivery, cord blood was collected for qPCR analysis, which was also negative. Samples were initially processed at the Molecular Biology Laboratory of the Health Sciences Center of the Federal University of Roraima (UFRR), and aliquots of plasma, extracted DNA, and placental tissue fragments were subsequently sent for further testing at the Molecular Biology Laboratory of Parasites and Fungi of the Parasitology Service of the Adolfo Lutz Institute, São Paulo, Brazil.

DISCUSSION

One of the modes of transmission of *Toxoplasma gondii* is congenital, which occurs when the parasite reaches the embryo or fetus, potentially affecting vital organs such as the brain, resulting in severe manifestations such as hydrocephalus, retinochoroiditis, and microcephaly. Both tachyzoite and bradyzoite forms of the protozoan can be identified in affected tissues (PIRES LB, et al., 2023). The proportion of live births among fetuses exposed to T. gondii infection is directly related to the gestational age at which maternal infection occurred, with vertical transmission rates of approximately 15% in the first trimester, 30% in the second trimester, and 60% in the third trimester. In addition, the severity of fetal infection tends to be less when transmission occurs during the third trimester (BOLLANI L, et al., 2022). In Brazil, analysis of official data on live births (LB), gestational toxoplasmosis (GT), and congenital toxoplasmosis (CT) in 2023 revealed the following incidence rates: 59.0 cases of GT and 25.9 cases of CT per 10,000 live births nationwide. Conversely, in Roraima, the only Brazilian state located in the northern hemisphere and the site of the present study, the incidence rates were 38.9 cases of GT per 10,000 live births (34% lower than the national incidence) and 25.9 cases of CT per 10,000 live births (identical to the national rate). In contrast, in the extreme south of the country, the state of Rio Grande do Sul reported 83.1 cases of GT per 10,000 live births (40% higher than the national incidence) and 21.24 cases of CT per 10,000 live births (18% lower than the national rate) (BRASIL, 2024). These official figures suggest geographic variability in the incidence of GT and CT in Brazil, or possibly regional differences in T. gondii strains, as previously described by Brito RMM, et al. (2023).

In 2022, the Brazilian Ministry of Health issued Technical Note No. 100/2022 in response to an epidemiological scenario in which the prevalence of congenital toxoplasmosis (CT) ranged from 6 to 23 cases per 10,000 live births, with the majority of infected pregnant women being asymptomatic. It was estimated that approximately 90% of infected newborns were asymptomatic at birth. This official document established national flowcharts for the diagnosis and management of this disease, applicable throughout the Brazilian territory (BRAZIL, 2025).

For prenatal screening, serologic testing for *Toxoplasma gondii* IgG and IgM should be performed at the first prenatal visit for all pregnant women. This strategy aims at early detection and treatment, preferably within a maximum of three weeks after infection (AHMED M, et al., 2020). This protocol was followed for patient CGS in both pregnancies. According to the 2020 Technical Note, the first decision box in the diagnostic flowchart for gestational toxoplasmosis before 16 weeks' gestation states: "Review the result of serology for toxoplasmosis performed in a previous pregnancy; if IgG+ and IgM+ or IgM-, do not request new serology; preventive counseling should be provided." Similarly, the Brazilian Ministry of Health's High-Risk Pregnancy Manual states: "A case of gestational toxoplasmosis is excluded if IgG is positive more than three months before conception (residual IgM: infection occurred before pregnancy)" (BRASIL, 2023; BRASIL, 2022). These documents confirm that patient CGS would be classified as having had a previous Toxoplasma gondii infection prior to her current pregnancy based on the described findings, despite a low-avidity IgG test.

In the case of patient CGS, she remained positive for anti-*Toxoplasma gondii* IgM and IgG immunoglobulins two years after her previous pregnancy. The prolonged persistence of positive IgM antibodies has been documented in the literature since the 1980s, with reports describing IgM positivity lasting between 40 and 50 weeks, and in some cases up to 70 weeks. Several explanations have been proposed for this phenomenon, including antigenic variation of the parasite, specificity and sensitivity limitations of serologic assays, and peculiar immunologic responses in pregnant women, who often remain asymptomatic on screening tests, in contrast to adults with acute infections. Robert-Gangneux F and Dardé ML (2012) previously reported that IgM titers for toxoplasmosis can remain positive for up to two years in some pregnant women, even when different diagnostic techniques are used (VARGAS-VILLAVICENCIO JA, et al., 2022; ROBERT-GANGNEUX F and DARDÉ ML, 2012).

Given the persistence of positive IgM results, the importance of IgG avidity testing in prenatal care to exclude active toxoplasmosis during the current pregnancy becomes paramount. In the case of CGS, three years after the previous pregnancy, the avidity test for toxoplasmosis remained low, creating a diagnostic dilemma for the medical team, who ultimately chose to continue spiramycin therapy.

The IgG avidity test technique was first developed by Hedman and Seppälä in 1989. It is based on the interaction between antigens and antibodies through chemical bonds, the strength of which is defined as avidity. High avidity is expected in cases of chronic infection, whereas low avidity is typically associated with recent infections. The method was originally described for the diagnosis of Rubella (HEDMAN K and ROUSSEAU SA, 1989).

In the diagnostic management of gestational toxoplasmosis, the IgG avidity test is used to more accurately distinguish between the acute and chronic phases of the disease, using a methodology originally based on the work of Hedman and Seppälä. However, commercial kits are now widely used. A meta-analysis by Tork M, et al. (2025) concluded that antigen standardization and purification are some of the most challenging aspects of avidity test kit development, highlighting the need for more detailed studies of kit development to effectively differentiate between acute and chronic infections. The authors concluded that the *T. gondii* IgG avidity assay remains a standard test and is highly effective as a complementary tool to serologic testing, assisting in the temporal assessment and differentiation of infection stages (acute versus chronic) during *T. gondii* infection (TORK M, et al., 2025).

Robert-Gangneux F, et al. (2012) described that an avidity test showing high IgG avidity indicates that infection occurred more than 16 weeks previously. This definition, which recommends that the avidity test be performed up to 16 weeks of gestation, is adopted in the Brazilian Technical Note (NT) No. 100/2022 and in the High-Risk Pregnancy Manual 2022 (BRASIL, 2022). However, if the avidity test shows low or intermediate avidity for toxoplasmosis, the interpretation becomes ambivalent, meaning that it cannot definitively confirm or exclude that the infection occurred within the previous 16 weeks (BRASIL, 2022). According to the 2022 High-

Risk Pregnancy Manual, approximately 15% of patients with a previous infection may continue to have low IgG avidity for up to one year (KODYM P, et al., 2023; BRASIL, 2022; ROBERT-GANGNEUX F and DARDÉ ML, 2012).

Kodym P, et al. (2023) analyzed 442 specimens from patients with suspected toxoplasmosis collected at a national reference laboratory in Prague (including pregnant women, non-pregnant women, men and women). In light of this scenario, it is emphasized that the avidity test is a valuable tool in the management of gestational toxoplasmosis, especially when performed before 16 weeks of gestation, where its high negative predictive value allows the exclusion of acute toxoplasmosis. However, not all pregnant women with low IgG avidity necessarily have an acute infection, underscoring the importance of reviewing previous serologic results for toxoplasmosis. This need is highlighted in the diagnostic flowchart of the Brazilian Technical Note 2022, which emphasizes the importance of obtaining serologic records prior to the current pregnancy or from previous pregnancies (BRASIL, 2023; KODYM P, et al., 2023; BRASIL, 2022).

The clinical case of patient CGS reinforces key aspects of health care protocols for pregnant women with low IgG avidity for *Toxoplasma gondii*. High IgG avidity testing performed prior to 16 weeks' gestation serves as a useful diagnostic adjunct to effectively rule out acute infection. Although low avidity testing also contributes to the diagnosis of acute toxoplasmosis, its sensitivity and specificity are lower - 77.8% and 81.5%, respectively - compared with detection by amniotic fluid analysis. Therefore, avidity testing should be interpreted in conjunction with other diagnostic tools, including the patient's serologic history, to support a presumptive diagnosis (BRASIL, 2023; KODYM P, et al., 2023).

It is evident that the previous serologic tests for toxoplasmosis, especially in the case of CGS, were of great value in clinical decision-making, as outlined in the toxoplasmosis management protocol based on the Brazilian Technical Note 2022 (BRASIL, 2022). This approach helped avoid invasive procedures such as PCR testing of amniotic fluid by amniocentesis, a procedure associated with a risk of fetal loss of 0.1% to 1% and, also, avoided unnecessary treatments that are not free of potential adverse effects (MANDELBROT L, et al., 2021; MOSHONOV R, et al., 2021).

It is concluded that the clinical case of CGS identified a multiparous patient with a high-risk pregnancy due to a previous preterm delivery, with a false positive IgM for Toxoplasmosis and low avidity test three years ago, having had contact with *Toxoplasma gondii*, possibly during the previous pregnancy, and progressing to a full-term delivery, with an appropriate weight and Apgar score for the fetus and no clinical or laboratory signs of toxoplasmosis in the newborn from the last pregnancy.

Management discussions should be encouraged to promote the standardization of effective medical record systems across health services in Brazil, thereby improving communication between primary, secondary, and tertiary care levels (Bednorz, A et al., 2023). Such measures could facilitate health professionals' access to patients' obstetric histories. Another important strategy is to optimize toxoplasmosis avidity testing, which is performed on the same specimen collected for initial IgM testing, especially in regions with limited diagnostic access, such as the Legal Amazon (MARGONATO FB, et al., 2007). In addition, continuous education and training of health care teams, pregnant women, and communities about toxoplasmosis is essential to improve preventive measures, ensure early treatment when indicated, and avoid unnecessary interventions, always respecting the principle of primum non nocere (LOVE JS, et al., 2020).

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