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Research Article

# Analysis of prenatal care for mothers of children from a congenital syphilis cohort based on serological test requests

## Análise do pré-natal das mães de crianças de uma coorte de sífilis congênita baseada nas solicitações dos exames sorológicos

## *Análisis de la atención prenatal de madres de niños de una cohorte de sífilis congénita a partir de la solicitud de pruebas serológicas*

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## Abstract

**Introduction:** The identification of serological status during prenatal care is essential to prevent infections in pregnant women, as well as to diagnose and treat both the mother and the fetus. However, test requests must follow scientific recommendations based on cost-effectiveness studies. **Objectives:** Describe the request for prenatal serological tests in a congenital syphilis cohort and evaluate the relevance of the requests and conducts adopted according to the results. **Methods:** A descriptive and retrospective study with an analysis of prenatal data from mothers with gestational syphilis, whose children were part of a prospective cohort of infants infected or exposed to *Treponema pallidum* during pregnancy. To compare the median of continuous variables, the Mann Whitney test was used, while for categorical variables, the Fisher's exact test was used, with a significance level of 0.05%. **Results:** Prenatal care was done in 94.5% of the women, with 6 or more visits in 75% of mothers. The first VDRL was done in 90% of the women, but repeated in 51%; the second HIV test done in only 26% of the cases. Only 9% of susceptible pregnant women repeated toxoplasmosis serology testing. Although there was no recommendation, serology for rubella was performed in 66% and for cytomegalovirus in 58% of cases. The screening for HIV, syphilis, hepatitis and HTLV was not performed at the recommended frequency. **Conclusions:** In this cohort, some misconceptions were observed in serologies requested and the conduct adopted according to the results. This highlights the importance of training health professionals, as well as improving laboratory network structure for the adequate care of pregnant women.

**Keywords:** Serology; Prenatal care; Infectious disease transmission, vertical; Syphilis, congenital; Disease prevention.

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## Resumo

**Introdução:** A identificação do status sorológico no pré-natal é fundamental para prevenir infecções na gestante, diagnosticar e tratar a mãe e concepto. Entretanto, as solicitações devem seguir as recomendações científicas, baseadas em estudos de custo-efetividade. **Objetivos:** Descrever a requisição de testes sorológicos no pré-natal de uma coorte de sífilis congênita e avaliar a pertinência das solicitações e das condutas diante dos resultados. **Métodos:** Estudo descritivo e retrospectivo com análise de dados do pré-natal de mães com sífilis gestacional, cujos filhos fizeram parte de uma coorte prospectiva de crianças infectadas ou expostas ao *Treponema pallidum* na gestação. Para comparação da mediana de variáveis contínuas, foi aplicado o teste de Mann-Whitney e, para variáveis categóricas, o teste exato de Fisher, sendo o nível de significância de 0,05%. **Resultados:** O pré-natal foi realizado em 94,5%, com seis ou mais consultas em 75% das mães. O primeiro VDRL foi realizado em 90% das mulheres, porém repetido em 51%. O segundo anti-HIV foi realizado em apenas 26% dos casos. Somente 9% das gestantes suscetíveis repetiram a sorologia para toxoplasmose. Apesar de não recomendadas, a sorologia para rubéola foi realizada em 66 %, e para citomegalovírus (CMV) em 58% dos casos. A triagem para HIV, sífilis, hepatites e HTLV não foi realizada com a frequência recomendada. **Conclusões:** Observam-se alguns equívocos na solicitação das sorologias e na condução de seus resultados nessa coorte. É importante a capacitação dos profissionais de saúde, assim como a estruturação da rede laboratorial para o atendimento adequado das gestantes.


**Palavras-chave:** Sorologia; Cuidado pré-natal; Transmissão vertical de doenças infecciosas; Sífilis congênita; Prevenção de doenças.


## Resumen

**Introducción:** La identificación del estado serológico en el control prenatal es fundamental para prevenir infecciones en la gestante, así como para diagnosticar y tratar tanto a la madre como al concepto. Sin embargo, las solicitudes deben seguir las recomendaciones científicas basadas em estúdios de costo-efectividad. **Objetivos:** Describir la solicitud de pruebas serológicas del control prenatal de una cohorte de sífilis congénita y evaluar la pertinencia de las solicitudes y de las conductas ante los resultados. **Métodos:** Estudio descriptivo y retrospectivo de los datos del control prenatal de una cohorte de niños expuestos a la sífilis o infectados durante la gestación. Se incluyeron datos del control prenatal de 256 madres entre 2016 y 2021. Para la comparación de la mediana de variables continuas se aplicó la prueba de Mann Whitney y para variables categóricas, la prueba exacta de Fisher, con un nivel de significancia del 0,05%. **Resultados:** El control prenatal se realizó en el 94,5%, con 6 o más consultas en el 75% de las madres. La primera prueba de VDRL se realizó en el 90% de las mujeres, pero se repitió en el 51%, al igual que la segunda prueba de VIH, que se realizó solo en el 26% de los casos. Solo el 9% de las gestantes susceptibles repitió la serología para toxoplasmosis. Aunque no se recomendaba, la serología para rubéola se realizó en el 66% y para citomegalovirus (CMV) en el 58% de los casos. La detección de HIV, sífilis, hepatitis y HTLV no se realizó con la frecuencia recomendada. **Conclusiones:** Se observan algunos errores en la solicitud de serologías y en la gestión de sus resultados en esta cohorte. Es importante la capacitación de los profesionales de salud, así como la estructuración de la red de laboratorios para la atención adecuada de las gestantes.


**Palabras clave:** Serología; Atención prenatal; Transmisión vertical de enfermedad infecciosa; Sífilis congénita; Prevención de enfermedades.

# INTRODUCTION

Inadequate prenatal care is frequently cited in the literature as a significant risk factor for adverse pregnancy outcomes.[1] The primary objectives of prenatal care include the prevention, diagnosis, treatment, or mitigation of the consequences of congenital infections. Therefore, missed opportunities for the diagnosis and treatment of such conditions are considered unacceptable.

Among congenital infections, syphilis remains a significant public health concern in Brazil. When undiagnosed and untreated during pregnancy, syphilis can lead to miscarriage, stillbirth, or the birth of infants who are symptomatic at birth or who develop late-onset sequelae.[2] However, when appropriate treatment is initiated before 18 to 20 weeks of gestation, it is nearly 100% effective in preventing fetal infection by *Treponema pallidum*.[3]

Congenital toxoplasmosis is classified as a neglected disease both in Brazil and globally. Primary maternal infection during pregnancy can result in severe fetal complications, primarily affecting the central nervous system and the retinal macula.[4] It is one of the leading congenital causes of visual impairment or blindness. Testing and counseling for pregnant women, particularly those identified

as susceptible, are essential health education strategies for preventing maternal infection and, consequently, fetal transmission.[5]

Although Brazil currently has a low overall prevalence of hepatitis B,[6] with rates ranging from 1 to 8%,[7] certain regions, particularly the Amazon and parts of the states of Paraná and Santa Catarina, continue to exhibit high concentrations of the disease.[6] Mother-to-child transmission accounts for approximately 40% of new hepatitis B cases,[7] and the risk of progression to chronic infection in children exceeds 90%.[8]

Determining the mother's serological status during prenatal care enables not only appropriate maternal treatment but also the administration of the hepatitis B vaccine and specific immunoglobulin to the newborn in the maternity ward, ideally within the first 12 hours of life, resulting in approximately 95% prevention of vertical transmission.[8]

According to data from the Ministry of Health (*Ministério da Saúde* – MS), the detection rate of pregnant women with Human Immunodeficiency Virus (HIV) increased from 2.4 to 3.3 cases per 1,000 live births between 2013 and 2023.[9] In the absence of any intervention during pregnancy, vertical transmission rates range from 20 to 40%.[10] However, with the implementation of appropriate preventive measures, these rates can be reduced to between 0 and 2%.[11]

Accordingly, the Ministry of Health recommends prenatal serological screening for syphilis, HIV types I/II, toxoplasmosis, hepatitis B, hepatitis C,[11] and Human T-Cell Lymphotropic Virus (HTLV) types I/II.[12] In certain cases, testing for Chagas disease is also advised.[13] Globally, there is no consensus regarding the standard serological tests to be requested during prenatal care.[14] Factors such as disease incidence and prevalence, treatment availability and efficacy, and the cost-effectiveness of screening inform this ongoing debate.[14] For instance, the prevalence of cytomegalovirus (CMV) infection at birth in low- and middle-income countries (0.7 to 5.4%)[15] raises questions about the routine inclusion of prenatal CMV screening in these settings. Moreover, different protocols exist for syphilis screening during pregnancy. In women with an initial negative result, repeat testing during the third trimester is recommended in populations with high disease prevalence.[11] These considerations underscore the importance of evaluating the relevance of serological testing and, more critically, the appropriate clinical response to test results.

## METHODS

This descriptive, retrospective study analyzed prenatal data from mothers diagnosed with gestational syphilis whose children were enrolled in a prospective cohort of infants infected with or exposed to *Treponema pallidum* in utero. These children were referred by maternity hospitals for follow-up at the Sexually Transmitted Infections (STI/HIV) outpatient clinic of Hospital Geral de Nova Iguaçu (HGNI), located in the state of Rio de Janeiro. The cohort evaluated guardian adherence to the Ministry of Health's protocol between 2016 and 2021. Maternal demographic and prenatal data (obtained from prenatal care cards and laboratory test results presented by the mothers during the postpartum period) as well as delivery summaries from the maternity hospitals were collected during the child's first clinic visit. The study did not rely on official databases. It is noted that the use of secondary data may introduce inherent biases, such as recording errors or underreporting due to incomplete documentation. All collected data were compiled into a database and analyzed using the Statistical Package for the Social Sciences (SPSS®), version 21.0 (2012) for Windows.

Demographic characteristics were compared between pregnant women classified as immune (those with reactive IgG) and those considered susceptible (with non-reactive IgM and IgG) to toxoplasmosis and CMV. Continuous variables were summarized using medians and interquartile ranges, while categorical variables were presented as absolute numbers and percentages. The Mann-Whitney test was used to compare medians of continuous variables, and Fisher's exact test was applied to categorical variables. A significance level of 0.05% was adopted.

The use of nonparametric statistical tests was chosen due to their more conservative nature and reduced reliance on assumptions regarding data distribution. This approach aimed to minimize the likelihood of random results, even if it may lead to a reduction in statistical power. The study was approved by the Research Ethics Committee of HGNI, under opinion number 77 073017.0.3002.8044.

## RESULTS

A total of 256 infants and their mothers were enrolled in the study. Notably, 94.5% (242/256) of the mothers received prenatal care. Among those with available data, 54.7% (129/236) initiated care in the first trimester, while 4.7% (11/236) began in the third trimester. In 75% (136/234) of cases, the number of prenatal visits was six or more. The median maternal age was 23 years, with a range of 13 to 44 years. Regarding educational attainment, 70.5% (177/251) of the mothers had nine or more years of schooling, with a median of 10 years and an interquartile range (IQR) of 8 to 12 years. Family income was up to one minimum wage in 58% (148/254) of cases, and only 16.4% (42/256) of the mothers reported formal employment.

With regard to serological testing, screening for toxoplasmosis was conducted in 82% of cases (median gestational age-GA of 17 weeks; IQR: 12-23). Among these, 57% presented a susceptibility pattern (non-reactive IgM and IgG). Current guidelines recommend that serological testing be repeated each trimester for susceptible pregnant women to confirm or rule out maternal and fetal infection and to guide treatment decisions. However, only 9% (10/109) underwent repeat testing in accordance with MS recommendations (Table 1).

Although not routinely included in prenatal care, rubella screening was performed in 66% of cases (median of 18 weeks; IQR: 11.7-25), and CMV screening was conducted in 57.9% of cases. The serological status for hepatitis B was unknown in 20% of the pregnant women, and for hepatitis C, in 42%. HTLV serology was requested in only one case.

All test results for HIV, hepatitis C, and hepatitis B were non-reactive. A low frequency of reported rapid test results for syphilis was noted (67%), and the serological status for hepatitis B and C remained unknown in a subset of the women (Table 1).

In the comparison between pregnant women who were immune to CMV (reactive IgG) and those who were susceptible (non-reactive IgM and IgG), no statistically significant differences were observed. However, for toxoplasmosis, women classified as immune had a higher median age and a greater number of children compared to susceptible women, with statistically significant differences ($p<0.05$) (Table 2).

Although the cohort consisted of fetuses treated for syphilis, the first Venereal Disease Research Laboratory (VDRL) test was performed in 89.8% (211/235) of the women and was repeated in only 51% (119/235). Initial HIV screening was requested in 92% of cases (median GA of 17 weeks; IQR: 23-11), but repeat testing was conducted in only 26% of the women. Table 3 presents the VDRL and anti-HIV testing data by gestational trimester.

**Table 1.** Frequencies of prenatal serologies of mothers from a congenital syphilis cohort at the STI outpatient clinic of HGNI (2016–2021).

| Screening | N | (%) |
|---|---|---|
| | **242** | **100** |
| **Cytomegalovirus** | 235 | 97 |
| Performed | 136 | 58 |
| IgG+ | 99 | 73 |
| IgM/IgG- | 25 | 18 |
| IgM- | 12 | 9 |
| **Toxoplasmosis** | 233 | 96 |
| Performed | 190 | 82 |
| IgG+ | 70 | 37 |
| IgM/IgG- | 109 | 57 |
| IgM- | 11 | 6 |
| **Rubella** | 235 | 97 |
| Performed | 154 | 66 |
| IgG+ | 129 | 84 |
| IgM/IgG- | 18 | 12 |
| IgM- | 7 | 4 |
| **Treponemal test** | 234 | 96.7 |
| Performed | 156 | 67 |
| Negative | 17 | 11 |
| Positive | 139 | 89 |
| **1$^{st}$VDRL** | 235 | 97 |
| Performed | 211 | 89.8 |
| Negative | 50 | 24 |
| Positive | 161 | 76 |
| **1$^{st}$HIV** | 234 | 96.7 |
| Performed | 216 | 92 |
| **Hepatitis B (HBsAg)** | 233 | 96 |
| Performed | 186 | 80 |
| **Hepatitis C** | 234 | 96.7 |
| Performed | 135 | 58 |

# DISCUSSION

## Cytomegalovirus

Cytomegalovirus (CMV) is a common cause of congenital infection, affecting approximately 1% of fetuses. Despite being the leading cause of non-hereditary sensorineural hearing loss, in addition to malformations, prematurity, and various neurological impairments,[16] congenital CMV infection remains relatively unfamiliar to many healthcare professionals.

**Table 2.** Comparative analysis of demographic variables from the prenatal care of women susceptible or immune to Cytomegalovirus and *T. gondii*, whose children were part of a congenital syphilis cohort at the STI outpatient clinic of HGNI (2016–2021).

| Characteristics | Toxoplasmosis | | p-value |
|---|---|---|---|
| | Immune | Non-immune | |
| | N=70 (37%) | N=109 (57%) | |
| Maternal age (years)-median | 25 | 21 | <0.05 |
| IQR | 20–28.25 | 18.5–25 | |
| Previous parity | 2 | 1 | <0.05 |
| IQR | 1–3 | 1–2 | |
| Years of education | 10.5 | 11 | 0.51 |
| IQR | 8–12 | 8–12 | |
| Wage in Brazilian currency (reais – R$) | 936 | 970 | <0.05 |
| IQR | 936–1,100 | 936–1,832 | |
| | **Cytomegalovirus** | | |
| | **Immune** | **Non-immune** | **p-value** |
| | **N=99 (73%)** | **N=25 (18%)** | |
| Maternal age (years)-median | 21 | 23 | 0.28 |
| IQR | 19–26 | 20.5–25.5 | |
| Previous parity | 2 | 2 | 0.82 |
| IQR | 1–2 | 1–2.5 | |
| Years of education | 10 | 11 | 0.59 |
| IQR | 8–12 | 8.5–12 | |
| Wage in Brazilian currency (reais – R$) | 936 | 936 | 0.6 |
| IQR | 936–1,500 | 936–1,159 | |

IQR: Interquartile range.

**Table 3.** Frequency of first and second VDRL and anti-HIV tests by prenatal trimester in mothers from a congenital syphilis cohort. (HGNI: 2016-2021).

| Gestational age | 1st VDRL | 2ndVDRL | 1st HIV | 2nd HIV |
|---|---|---|---|---|
| | N[a] (%) | N[a] (%) | N[a] (%) | N[a] (%) |
| Total tests performed | 211/235 (90) | 119/235 (51) | 216/234 (92) | 61/232 (26) |
| N[b] | 210 | 119 | 213 | 61 |
| **First trimester** | | | | |
| Up to 13 weeks | 70 (33) | 2 (2) | 80 (38) | 6 (10) |
| **Second trimester** | | | | |
| 14-26 weeks | 105 (50) | 48 (40) | 101 (47) | 19 (31) |
| **Third trimester** | | | | |
| 27-40/41 weeks | 35 (17) | 69 (58) | 32 (15) | (59) |

[a]Total tests performed (numerator). Tests performed and not performed (denominator); [b]Number of tests reported by trimester.

Factors such as low socioeconomic status, advanced maternal age, and a higher number of children have been associated with increased seroprevalence among pregnant women.[16] However, this study was not able to assess the relationship between these factors and immune versus susceptible maternal status.

Serological testing for CMV is not currently recommended in Brazil or in many other countries.[15] However, advances in therapeutic options for infected pregnant women (such as the use of Valacyclovir during primary infections in the first trimester) have prompted renewed discussion on the potential value of prenatal screening.[15] One argument against universal screening is that most pregnant women in developing countries are already immune (*i.e.*, have positive IgG or reactive IgM and IgG with high IgG avidity in the first trimester), suggesting past infection and presumed fetal protection via maternal antibodies.[15,17] However, it is now known that congenital CMV is most commonly caused by non-primary maternal infections, which account for more than 95% of cases in Brazil.[17] Additionally, there are reports of maternal stress resulting from a diagnosis of primary infection, sometimes leading to pregnancy termination, even in the absence of fetal infection or significant impairment, in countries where abortion is legally permitted.[15] Furthermore, the efficacy of available treatments in preventing fetal sequelae remains a subject of ongoing investigation.[15] In light of these considerations, any move toward universal CMV screening during pregnancy would necessitate the development of a comprehensive, multidisciplinary program. Such a program should include continuing education for healthcare professionals, counseling for pregnant women, referral pathways to high-risk pregnancy services, diagnostic confirmation using molecular methods, imaging technologies such as magnetic resonance imaging to detect fetal complications, access to anti-CMV therapies, and systematic monitoring of both maternal and child outcomes.[15]

In this study, 58% of pregnant women underwent CMV serological testing. Among them, 18% were found to be susceptible to CMV, a proportion consistent with findings from a study conducted in Mato Grosso do Sul, which reported 17.9% susceptibility among pregnant women.[18]

Mother-to-child transmission of CMV can occur via transplacental passage, during childbirth through contact with cervicovaginal secretions, or through breastfeeding.[16] The vertical transmission rate can reach up to 50% in cases of primary maternal infection and approximately 2% in cases of recurrent infection. The most common sources of infection for pregnant women include direct contact with young children attending daycare (where the virus may be present in saliva, urine, or on toys contaminated by these fluids) as well as transmission through sexual contact.[16]

Revello et al.[19] demonstrated that hygiene education and guidance provided to susceptible pregnant women significantly reduced the rate of seroconversion. The preventive measures outlined below should be incorporated into the prenatal care of all pregnant women to reduce the risk of both primary and recurrent CMV infections:[15] Wash hands with soap and water for 15 to 20 seconds, particularly after changing diapers, feeding young children, or handling secretions and toys. Do not share personal items such as utensils, plates, cups, toothbrushes, or towels. Avoid contact with saliva when kissing young children. Clean and disinfect toys and surfaces that come into contact with children's secretions, as the virus can survive on these surfaces for several hours.

## Toxoplasmosis

Toxoplasmosis is a significant endemic disease in Brazil, caused by the protozoan *Toxoplasma gondii*, whose sexual forms develop in the intestinal epithelium of felines. Oocysts are shed in the feces of infected cats for up to 14 days following infection. Human contamination can occur through the ingestion of water or food contaminated with sporulated oocysts, or by consuming raw or undercooked meat containing tissue cysts.[20]

The estimated seroprevalence among pregnant women in Brazil varies by region, ranging from 36 to 92%.[21] In the present study, 37% of pregnant women tested positive for IgG, indicating prior exposure. Consequently, 63% were classified as susceptible and at risk of acquiring the infection during pregnancy.

Factors such as educational level, socioeconomic status, and age have been associated with the risk of acquiring toxoplasmosis.[22] In this study, pregnant women classified as immune were, on average, older and had a greater number of children compared to those in the susceptible group.

Cultural, climatic, and socioeconomic factors may contribute to regional differences in the seroprevalence of toxoplasmosis. Therefore, understanding the specific risk factors associated with disease acquisition in each location is essential for developing effective strategies to prevent both gestational and congenital toxoplasmosis.[23] In Rio de Janeiro, consumption of untreated water is a significant risk factor for infection.[24] Additional contributing factors include lack of basic sanitation, consumption of undercooked meat (a common practice in the southern region of the country),[25] ingestion of poorly washed vegetables, occupational exposure involving soil contaminated with oocysts, and the tropical climate.[23,25] These elements present important cultural and regional challenges to adherence with recommended preventive measures during pregnancy.

Primary infection during pregnancy can result in fetal death, stillbirth, prematurity, severe birth defects, or late-onset abnormalities in the child.[4] The rate of vertical transmission ranges from 10 to 12% during the first trimester and increases to 60 to 81% in the third trimester.[26]

In this study, 19% of pregnant women did not undergo serological testing for toxoplasmosis. Even in regions with low prevalence, prenatal serology is considered cost-effective due to the severe consequences of congenital infection in children and the potential for prevention and treatment.[26]

The Ministry of Health recommends that susceptible pregnant women undergo at least three serological tests during pregnancy.[27] However, this study found that only 9% of susceptible women completed the recommended repeat testing. In France, susceptible pregnant women receive monthly serological screening to detect seroconversion promptly and initiate treatment (ideally within three weeks of seroconversion) to prevent fetal infection and reduce the risk of sequelae associated with rapid maternal parasitemia.[28]

Due to the high sensitivity of serological tests, IgM antibodies can remain reactive for more than two years (residual IgM) and should not be used alone as a marker of acute infection.[4] When both IgM and IgG are present, an IgG avidity test should be performed before the 16$^{th}$ week of gestation, as high IgG avidity during the first trimester effectively rules out acute infection during pregnancy.[29]

Health education is a low-cost and highly effective strategy. In Belgium, seroconversion rates decreased by 63% following the implementation of a counseling program for pregnant women. The guidelines were provided in written form, communicated clearly, and reinforced at each prenatal visit.[5] These recommendations include:[5,20]

- Avoid eating raw vegetables (cooking at 60°C for 15 minutes or at 90°C for 30 seconds inactivates sporulated oocysts);
- Wear gloves when handling raw meat and thoroughly wash all utensils used in its preparation (knives, cutting boards, surfaces);
- Wash fruits and vegetables under running water. Preferably, consume fruits that can be peeled;
- Drink filtered water (ideally boiled). Chemical methods (chlorine, methanol, liquid ammonia, formalin solution) are not suitable for inactivating sporulated oocysts in water and food due to the high concentrations required, which pose toxicity risks;

- Do not consume raw or undercooked meat (cook to at least 67°C for 10 minutes);
- Do not consume unpasteurized milk and cheese;
- Wash hands with soap and water before eating;
- Do not handle cat feces (if necessary, use gloves, and clean/change the litter box every 24 hours to prevent oocyst sporulation);
- Wear gloves when handling soil or gardening.

## HIV

According to MS, all pregnant women should undergo HIV serological testing at their first prenatal visit (preferably using a rapid test), with repeat screening in the third trimester if the initial result is negative. If the rapid test is reactive, a confirmatory test from a different manufacturer should be performed. When both tests are reactive, the pregnant woman is considered HIV-positive and should begin antiretroviral therapy regardless of symptoms or immunological status.[11]

A significant decrease was observed in the proportion of women who underwent a second anti-HIV test in this sample, with only 26% receiving repeat screening. Similarly, a 2018 study reported that just 29.27% of pregnant women completed a second anti-HIV test.[30] Feitoza et al.[31] found that 23.8% of women were diagnosed with HIV at delivery, underscoring missed opportunities to prevent vertical transmission.

Without intervention during pregnancy, vertical transmission rates of HIV range from 20 to 40%.[10] However, with appropriate preventive measures, these rates can be reduced to between 0 and 2%.[11] In this study, only 36% of women received antiretroviral treatment during the first trimester. The interval between initiation of antiretroviral therapy and delivery is a critical factor in reducing maternal viral load and the risk of vertical transmission.[11]

Key measures to prevent vertical transmission of HIV include: early enrollment of pregnant women during the first trimester; prompt diagnosis and initiation of antiretroviral therapy; appropriate determination of the delivery route, and prophylactic antiretroviral treatment for the newborn.[11]

## Rubella

Since the introduction of universal childhood vaccination and immunization of women of childbearing age, Brazil has experienced a decline in cases of rubella and congenital rubella syndrome (CRS) since 2002.[32]

The gestational age at the time of infection is the most critical factor influencing the severity of fetal compromise. Infections during the first trimester may result in spontaneous abortion, fetal death, stillbirth, or CRS, with cataracts, cardiac defects, and deafness being the most common manifestations. Clinical suspicion of maternal infection is challenging, as 20 to 50% of cases are asymptomatic.[33]

MS does not recommend routine rubella serological testing during pregnancy, as false-positive IgM results are relatively common. Additionally, in April 2015, Brazil received official verification from the International Committee of Experts confirming the elimination of rubella and CRS in the country, demonstrating the interruption of autochthonous transmission of the virus.[34]

Therefore, requesting rubella serology without a clear clinical indication may lead to the identification of cases that do not meet the criteria for disease definition,[34] causing unnecessary stress for families and placing an additional burden on the healthcare system. Moreover, in cases where mothers present with reactive IgM for

rubella, it is essential to perform follow-up evaluations in newborns. These should include serological testing, viral isolation or molecular diagnostics (such as Polymerase Chain Reaction), as well as expert assessments, hearing evaluations, and imaging studies to detect potential visual, auditory, or cardiac impairments.[32]

The Ministry of Health Manual recommends that rubella serology be performed only in cases of suspected infection or when the pregnant woman has had contact with individuals presenting exanthematous illnesses. In the absence of documented rubella vaccination, only IgG testing should be requested; if the result is non-reactive, the woman should be advised to receive the rubella vaccine after delivery.[34]

## HTLV I/II

HTLV types 1 and 2 (HTLV-1 and HTLV-2) belong to the retrovirus family. One of the primary concerns in infected individuals is the potential progression to adult T-cell leukemia/lymphoma, as well as the development of neurological complications.[35]

In this study, only one pregnant woman had a recorded serological result for HTLV. In Brazil, HTLV screening is not yet universally implemented in prenatal care, despite the country's high absolute number of cases,[36] with the virus being endemic in certain regions. The current MS guidelines recommend serological testing for all pregnant women.[12]

Currently, vertical transmission is the primary route of HTLV spread, occurring in up to 30% of children born to infected mothers.[11] The main mode of vertical transmission is breastfeeding, with risk directly correlated to the duration of breastfeeding.[36] One study reported a transmission rate of 3.9% when breastfeeding lasted less than six months, compared to 20.3% when it exceeded six months.[37] Although approximately 90% of infected individuals remain asymptomatic,[11] the risk of developing adult T-cell leukemia/lymphoma is higher among those infected through vertical transmission.[38] As there is no effective treatment for HTLV, the development of public policies is essential. These should include continuing education for healthcare teams focused on neglected diseases such as HTLV, public awareness campaigns, expanded access to diagnostic services, and the establishment of a formula milk donation program for exposed infants.

## Hepatitis C

According to MS, the estimated prevalence of hepatitis C among pregnant women in Brazil ranges from 0.2 to 1.4%. Since 2020, the Ministry has recommended universal testing for hepatitis C virus (HCV) during prenatal care (ideally in the first trimester) which has contributed to increased detection of the virus in pregnant women.[39]

Transmission of the hepatitis C virus occurs primarily through exposure to blood-contaminated materials, most commonly via injectable drug use and the sharing of equipment for illicit drug consumption.[39]

Notably, 42% of the mothers in this study did not undergo anti-HCV serological testing. Although treatment for hepatitis C is not currently administered during pregnancy, universal prenatal screening is considered cost-effective, as it enables the identification and monitoring of exposed pregnant women and their children.[39] Infected pregnant women are at increased risk for complications such as gestational diabetes, hypertension, and preterm birth.[39] Furthermore, approximately 30% of children infected early through vertical transmission go on to develop active chronic infection.[39]

The risk of vertical transmission of HCV ranges from 6% to 11%, with the peripartum period representing the highest risk for transmission.[40] Risk factors include high maternal viral load, internal fetal monitoring,

prolonged rupture of membranes, exposure to maternal blood, and coinfection with HIV.[41] To date, there is no evidence supporting the use of perinatal prophylactic measures such as elective cesarean section to reduce transmission. Breastfeeding is recommended and should be avoided only in cases of nipple bleeding.

## Hepatitis B

Currently, Brazil has a low overall prevalence of hepatitis B; however, certain regions, particularly in the South and the Amazon, continue to report higher rates of the infection.[6]

The study found that 20% of pregnant women were not tested for hepatitis B surface antigen (HBsAg). MS recommends HBsAg testing during the first trimester or at any gestational age if there is no documented evidence of complete hepatitis B vaccination.[11] This screening is critical for reducing vertical transmission, as this route of infection is the most likely to progress to chronic disease and is responsible for approximately 40% of new hepatitis B cases worldwide.[7]

Pregnant women who test positive for HBsAg should be referred to a specialized healthcare service for hepatitis B treatment. Additionally, it is crucial that delivery takes place in a maternity hospital equipped to administer both hepatitis B-specific human immunoglobulin (HBIG) and the first dose of the hepatitis B vaccine to the newborn, preferably within the first 12 hours of life.[11] The combined administration of the vaccine and HBIG provides between 85 and 95% protection for the child.[8]

Breastfeeding is not contraindicated if the newborn has received appropriate immunoprophylaxis (vaccine and immunoglobulin); however, it should be temporarily avoided in cases of nipple bleeding.[6]

The hepatitis B vaccine is recommended for pregnant women who have not been vaccinated or who have an incomplete vaccination history. The standard schedule consists of three doses: the initial dose (0), followed by a second dose one month later, and a third dose six months after the first. An alternative schedule allows the third dose to be administered four months after the first (0 + 1 + 4 months).[11]

## Syphilis

Between 2012 and 2022, Brazil experienced an increase in adverse pregnancy outcomes associated with syphilis, including deaths from congenital syphilis, miscarriages, and stillbirths.[2]

Most pregnant women with syphilis are asymptomatic. It is therefore recommended that a rapid test be conducted during the first prenatal consultation (following appropriate counseling) for those with no prior history of syphilis. If the test yields a positive result, the partner should also undergo a rapid test, have a VDRL test collected, and both individuals should initiate treatment on the same day. A follow-up visit should be scheduled within seven days for both partners to receive the VDRL results and to evaluate the need for completing the treatment with two additional doses of benzathine penicillin G. In cases of negative test results, rescreening is advised during the third trimester (around the 28$^{th}$ week of gestation).[11] In the present case series, the VDRL test was repeated in only 51% of the pregnant women. A study conducted in the city of Rio de Janeiro reported that 45.8% of pregnant women with syphilis acquired the infection during pregnancy.[3] Repeating the VDRL test in the third trimester is essential for detecting possible seroconversion.

The study indicated that only 33% of pregnant women underwent VDRL testing during the first trimester. When initiated before 18-20 weeks of gestation, appropriate treatment is nearly 100% effective in preventing fetal syphilis.[3]

In cases of reactive VDRL results, monthly testing is recommended to monitor therapeutic response or detect possible reinfection. The most reliable indicator of therapeutic failure is an increase in VDRL titer of at least two dilutions.[11] In the present study, none of the pregnant women underwent monthly VDRL testing, which may indicate non-compliance with MS guidelines.[2]

A common error is to attribute a low VDRL titer to serological scarring without documented evidence of adequate prior treatment and without a history confirming that the pregnant woman was not at risk of reinfection. Proper documentation of treatment and VDRL results on the prenatal card is essential for evaluating the newborn and for the subsequent follow-up of both mother and child.[11]

Since 2011, the use of rapid tests for syphilis in primary care has been expanded. However, in this study, only 67% of pregnant women had documented evidence of testing. The implementation of rapid syphilis testing in primary care has increased diagnostic sensitivity and expedited the initiation of treatment during pregnancy. Nevertheless, this test is not suitable for pregnant women with a previous syphilis diagnosis, as it is a treponemal test and may remain reactive indefinitely.[42]

A limitation of the study is that the data were extracted from the pregnant woman's booklet and the maternity summary. Consequently, the results may be subject to bias due to recording errors or incomplete data entry. Nonetheless, beyond the results, the study facilitated discussion on the investigation and primary management of vertically transmitted infectious diseases during pregnancy.

## CONCLUSION

Although most pregnant women attended a satisfactory number of consultations, errors were identified in the ordering of certain serological tests, such as those for CMV and rubella. Additionally, screening for HIV, syphilis, hepatitis, and HTLV was not performed at the recommended intervals. To strengthen these efforts, investment in continuing education is essential, with particular emphasis on neglected diseases, alongside measures to ensure that trained teams remain in the healthcare units. It is also necessary to organize the health system through streamlined processes that facilitate timely testing and rapid return of results. Furthermore, educational activities for pregnant women should be integrated into routine clinical practice by all members of the healthcare team.

## CONFLICT OF INTERESTS

Nothing to declare

## AUTHORS' CONTRIBUTIONS

MGS: Conceptualization, Data Curation, Formal analysis, Writing – Original Draft. CBH: Conceptualization, Formal Analysis, Writing – Review & Editing.

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