

Clinical-epidemiological characteristics of pregnant women with HIV/syphilis coinfection: an integrative review

Características clínico-epidemiológicas de gestantes com coinfeção HIV/sífilis: revisão integrativa

Características clínico-epidemiológicas de gestantes con coinfección VIH/sífilis: revisión integrativa

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ABSTRACT

Background and Objectives: HIV/syphilis coinfection is an important problem to be considered during pregnancy due to the various negative outcomes such as abortion, stillbirth, prematurity and congenital infections. The study is justified by the need to identify scientific evidence of clinical-epidemiological characteristics and vulnerabilities related to infections, factors that influence the prevalence, and if there are related health problems. The objective was to synthesize scientific evidence about sociodemographic characteristics and clinical manifestations of associated cases of syphilis and HIV. **Content:** this is an integrative literature review, searching the PubMed, MEDLINE, CINAHL, LILACS, BDNF and MedCarib databases, using the descriptors "HIV", "Syphilis", "Epidemiology", "Coinfection" and "Pregnant woman", combined by Boolean operators "AND" and "OR", guided by the question: what is the scientific evidence related to the clinical-epidemiological characteristics of pregnant women co-infected with HIV/syphilis? It was held from June to September 2022, including articles published in the last eight years. Nine primary articles published between 2015 and 2020 were selected. The association of infections was present in pregnant women of young adult age, non-white race/color, married, low level of education, housewives, residents of urban areas and belonging to more economically disadvantaged social classes. **Conclusion:** the study highlighted the importance of improving prenatal care, with the aim of reducing the risks of vertical transmission of these diseases, especially with the implementation of public policies aimed at the clinical management of co-infected pregnant women, the allocation of resources and the development of specific intervention protocols.

Keywords: HIV. Syphilis. Pregnant Women. Coinfection. Health Profile.

RESUMO

Justificativa e Objetivos: A coinfeção HIV/sífilis é um problema importante a ser considerado durante a gravidez devido aos diversos desfechos negativos como aborto, natimorto, prematuridade e infecções congênitas. O estudo justifica-se pela necessidade de identificar evidências científicas de características clínico-epidemiológicas e vulnerabilidades relacionadas às infecções, fatores que influenciam a prevalência e se há problemas de saúde relacionados. O objetivo foi sintetizar evidências científicas sobre características sociodemográficas e manifestações clínicas de casos associados de sífilis e HIV. **Conteúdo:** trata-se de uma revisão integrativa da literatura, com busca nas bases de dados PubMed, MEDLINE, CINAHL, LILACS, BDNF e MedCarib, utilizando os descritores "HIV", "Syphilis", "Epidemiology", "Coinfection" e "Pregnant woman", combinados por Operadores booleanos "AND" e "OR", norteados pela questão: quais as evidências científicas relacionadas às características clínico-epidemiológicas de gestantes coinfectadas com HIV/sífilis? Foi realizado de junho a setembro de 2022, incluindo artigos publicados nos últimos oito anos. Foram selecionados nove artigos primários publicados entre 2015 e 2020. A associação das infecções esteve presente em gestantes em idade adulta jovem, raça/cor não branca, casadas, baixa escolaridade, donas de casa, residentes em zona urbana e pertencentes a classes sociais mais desfavorecidas economicamente. **Conclusão:** o estudo destacou a importância da melhoria da assistência pré-natal, com o objetivo de reduzir os riscos de transmissão vertical dessas doenças, especialmente com a implementação de políticas públicas voltadas ao manejo clínico das gestantes coinfectadas, à alocação de recursos e o desenvolvimento de protocolos de intervenção específicos.

Palavras-chave: HIV. Sífilis. Gestantes. Coinfeção. Perfil de Saúde.

RESUMEN

Antecedentes y objetivos: La coinfección VIH/sífilis es un problema importante a considerar durante el embarazo debido a los diversos resultados negativos como aborto, muerte fetal, prematuridad e infecciones congénitas. El estudio se justifica por la necesidad de identificar evidencia científica de características clínico-epidemiológicas y vulnerabilidades relacionadas con las infecciones, factores que influyen en la prevalencia y si existen problemas de salud relacionados. El objetivo fue sintetizar evidencia científica sobre las características sociodemográficas y manifestaciones clínicas de los casos asociados de sífilis y VIH. **Contenido:** se trata de una revisión integradora de la literatura, buscando en las bases de datos PubMed, MEDLINE, CINAHL, LILACS, BDNF y MedCarib, utilizando los descriptores "VIH", "Sífilis", "Epidemiología", "Coinfección" y "Mujer embarazada", combinados por Operadores booleanos "Y" y "O", guiados por la pregunta: ¿cuál es la evidencia científica relacionada con las características clínico-epidemiológicas de las gestantes coinfectadas con VIH/sífilis? Se realizó de junio a septiembre de 2022, incluyendo artículos publicados en los últimos ocho años. Se seleccionaron nueve artículos primarios publicados entre 2015 y 2020. La asociación de infecciones estuvo presente en mujeres embarazadas de edad adulta joven, de raza/color no blanca, casadas, de bajo nivel educativo, amas de casa, residentes de áreas urbanas y pertenecientes a clases sociales más desfavorecidas económicamente. **Conclusión:** el estudio destacó la importancia de mejorar la atención prenatal, con el objetivo de reducir los riesgos de transmisión vertical de estas enfermedades, especialmente con la implementación de políticas públicas orientadas al manejo clínico de las gestantes coinfectadas, la asignación de recursos y el desarrollo de protocolos de intervención específicos.

Palabras clave: VIH. Sífilis. Mujeres embarazadas. Coinfección. Perfil de Salud.

INTRODUCTION

Sexually Transmitted Infections (STIs) are considered a public health problem and are part of the most common communicable pathologies, directly influencing the epidemiological scenario due to the negative consequences for individuals' health and lives worldwide.¹

Syphilis is an infectious, systemic disease, exclusive to humans, and transmitted mainly through sexual and vertical routes. Its association with the Human Immunodeficiency Virus (HIV) occurs frequently, since both are influenced synergistically: increased HIV transmissibility, transient increase in viral load, decreased number of TCD4+ lymphocytes, or even changes in the natural evolution of treponemal infection, with exacerbation of clinical manifestations, in addition to changes in diagnosis and decreased response to treatment.²⁻³ Furthermore,

both STIs affect similar vulnerable groups, such as homeless people, low education, multiple sexual partners and the young-adult age group.^{1,2,3}

HIV and syphilis are diseases that must be notified to the Epidemiological Surveillance. However, many professionals do not include it in their routines, which can harm the planning of actions to prevent and control these infections and vertical transmission. From this perspective, HIV notification has occurred more effectively than syphilis.⁴

In Brazil, in 2020, 61,441 cases of syphilis in pregnant women were reported in the Notifiable Diseases Information System (SINAN - *Sistema de Informação de Agravos de Notificação*), with a detection rate of 21.6/1,000 live births. Between 2017 and 2019, there was an increase of 25.7%. In part, this increase can be attributed to the

change in the criterion for defining cases for surveillance purposes, which made it more sensitive.⁵

In the period from 2000 to June 2021, 141,025 pregnant women with HIV were reported, with the highest prevalence in the Southeast. The detection rate of HIV infection has shown a slight upward trend in recent years, mainly due to the increase in rapid tests distributed by Stork Network.⁶

Regarding simultaneous HIV/syphilis infection, both are transmitted mainly through unprotected sex and vertically.¹ These are important problems during pregnancy, due to several negative outcomes, such as spontaneous abortion, fetal or neonatal death, prematurity and congenital infections.⁷

There is difficulty for SINAN in crossing information about HIV/syphilis co-infection, making it impossible to know the prevalence of these diseases in an associated way, as there are no co-infection data in the notification and investigation forms.⁸ Therefore, to obtain this information, it would be necessary to cross-reference databases relating to each problem, using nominal data.

In this way, in isolation, the clinical-epidemiological characteristics of the diseases⁸ of interest for this work are known. However, identifying scientific evidence that reports pregnant women who acquired HIV/syphilis co-infection is necessary to understand the factors, whether clinical, social and/or epidemiological, that can influence the prevalence of these STIs.

From this perspective, the objective was to synthesize scientific evidence about the clinical-epidemiological characteristics of pregnant women with HIV/syphilis co-infection globally.

METHOD

This is an integrative review, organized in the following stages: guiding question elaboration, literature search, data collection or extraction, study critical analysis, interpretation and presentation of results.⁹

The research question was prepared using the PICO strategy,¹⁰ in which P (Population): pregnant women, I (Phenomenon of interest): clinical-epidemiological characteristics and Co (Context): HIV/syphilis co-infection, resulting in the following question: What is the scientific evidence related to the clinical-epidemiological characteristics of pregnant women with HIV/syphilis co-infection?

The survey of studies was carried out from June to September 2022 in the U.S. National Library of Medicine (PubMed), Cumulative Index to Nursing and Allied Health Literature (CINAHL Latin American Literature in Health Sciences (LILACS), Medical Literature and Retrieval System Online (MEDLINE) and Nursing Database (BDENF) databases. The controlled terms in Portuguese and their respective English counterparts were used, such as "HIV", "Syphilis", "Epidemiology", "Coinfection" and "Pregnant", with the help of the Boolean operators "AND" and "OR".

Full articles on the topic, available online and free of

charge, published in Portuguese, English and/or Spanish and published between 2012 and 2022, were included. Duplicate articles and articles that did not answer the guiding question were excluded.

As for the time frame of the study, it is justified by the establishment of Ordinance 77 of January 12, 2012, which provided for rapid tests to be carried out in Primary Care to detect HIV and syphilis.¹¹

To report the process of identification, screening, eligibility and inclusion of studies, the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) was used.¹² Duplication detection and article selection were carried out by two independent reviewers, using the Rayyan Systems Inc and EndNote (TM) platforms.

Data extraction and analysis were carried out using an adapted instrument, but validated by Ursi (2005), using the variables on identification, country and/or institution hosting the study, publication journal and methodological characteristics.¹³ The interpretative analysis of included references was presented and organized in a descriptive way.

The methodological quality of studies was assessed in accordance with a tool modified by Machotka *et al.*, (2009), consisting of 12 criteria that represent key elements to assess the methodological quality of the studies. Each item marked affirmatively was assigned a score=1, with the total score on this scale (maximum 12 points) being converted into a percentage (0-100%). The higher this result, the better the methodological quality of the study, with a score of 8.0 being considered acceptable.¹⁴

As this is an integrative literature review, this work did not require authorization from the Research Ethics Committee, in accordance with Resolutions 466/2012 and 510/2016, which deal with research carried out exclusively with scientific texts to review scientific literature.

RESULTS AND DISCUSSION

Based on the criteria established for the integrative review, 8 studies were selected, published between 2015 and 2020. The results found in the search are displayed in the flowchart (Figure 1) adapted from PRISMA.¹²

The articles were published between 2015 and 2020. The majority were in English, and one of them was in Portuguese. The methodological quality assessment scale¹⁴ found that the majority of studies (87.5%) reached an acceptable score.

In Chart 1, the studies, authors and year of publication, country of publication, study design and a summary of the content of studies are presented, focusing on the main results, clinical-epidemiological characteristics and conclusions.

Regarding study setting, it was observed that the studies were carried out in America, Asia and Africa. Regarding the research design, there was a predominance of cross-sectional studies, and two used secondary analysis of data from randomized clinical trials (Chart 1).

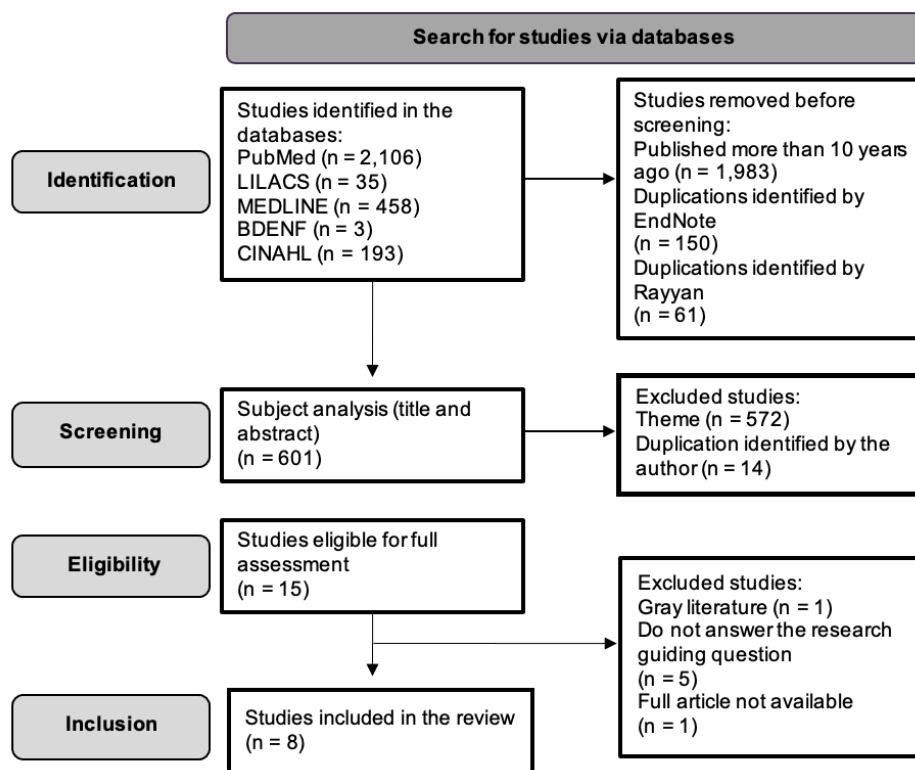


Figure 1. Study selection flowchart adapted from the PRISMA methodology (2021).

The pregnant women who were part of the study sample had similar sociodemographic characteristics that place them in a situation of greater vulnerability to contracting STIs, such as age range between 20 and 49 years old, black race/color, single, low level of education, housewives and early late prenatal care.

The diversity in the epidemiological scenario of HIV/syphilis co-infection indicated prevalence rates that varied from 0.05% to 10.2%.¹⁵⁻¹⁷ The different prevalence shows the heterogeneous distribution of syphilis, and may also be related to the diagnostic criteria adopted by services.^{17,18}

Other factors attributed to variation in prevalence may be related to the laboratory diagnosis method used, sociocultural diversity, socioeconomic status, prevention and control strategies, social risk factors, level of knowledge about prevention and, finally, access to health units to carry out prenatal care.¹⁹

In general, younger women are at greater risk of acquiring an STI.²⁰⁻²¹ However, in the case of pregnant women with HIV/syphilis co-infection, the prevalence was higher among those aged 25 or older, increasing with each change in age group, a finding also observed among the selected studies.^{16-18,23-24} The finding may be attributed to the increased risk of exposure to STIs over time, making women more vulnerable to engaging in sexual activities without using barrier methods.²⁵

Regarding the race/color variable, co-infection was more common in non-white women, and they are twice as affected as white women.^{15,17,24} However, two studies,

one in the city of Salvador (BA) and another carried out in 17 locations in Brazil, South Africa, Argentina and the USA, found different results, in which 89% of pregnant women with HIV/syphilis co-infection were white.^{24,26}

Regarding marital status, four studies considered this variable.^{16,23,27,28} Studies on HIV infection have shown that married pregnant women are the most exposed to the HIV virus, with a 3.29 greater chance of being infected with HIV when compared to single women, especially when partners have multiple partnerships.^{17,20,23,29,30}

Considering that pregnant women and partners who participated in the studies had fewer years of study, it is possible to infer that formal education can be decisive in accessing health information and, consequently, in understanding the importance of prenatal care and adherence to treatment.^{17,27-30}

The occurrence of STIs may be associated with income, as the most economically disadvantaged social stratum results in less access to preventive information and health care, greater use of sex for economic purposes and as a psychosocial coping mechanism, and housing in rural areas, characterized by compromised socioeconomic indicators, which impose difficulties in accessing specialized care.¹⁵⁻¹⁸

Two of the studies reported a higher prevalence of HIV/syphilis coinfection in pregnant women living in urban areas. Possible reasons are the presence of sex workers and the high prevalence of HIV in the urbanized population.^{23,28}

It is also important to highlight the vulnerable situ-

Chart 1. General characterization of included studies, authors and year, countries, study design, in addition to a summary of the content of studies focusing on the main results, clinical-epidemiological characteristics and conclusions of selected studies.

Author / Year	Country	Study design	Results	Main clinical-epidemiological characteristics	Conclusions
Endris et al., 2015	Ethiopia	Cross-sectional	Of 385 pregnant women, reactive syphilis was observed in 2.9%, and HIV seroprevalence was 11.2%. The prevalence of syphilis and HIV co-infection was 0.5%.	A high rate of syphilis was observed among women over 30 years of age, housewives, with a history of miscarriage and stillbirth. As for HIV, there were women between 21-29 years old, married and traders.	Syphilis and HIV are still important public health problems. Screening during prenatal care and strengthening health education was recommended.
Moura et al., 2015	Brazil	Cross-sectional	Of the total of 54,813 pregnant women, the prevalence of syphilis and HIV infections were 2.8% and 0.3%, respectively. Coinfection occurred in 0.05%, with a potential risk of HIV-infected pregnant women being coinfecting by <i>T. pallidum</i> (5.71 times).	The average age was 23.3 years old, with 31.5% being adolescents; and 68.3% declared themselves to be of non-white race/color/ethnicity.	Syphilis was twice as prevalent among pregnant women in Maceió, compared to the national average, and coinfections with syphilis/HIV and HTLV/HBV were significantly associated.
Acosta et al., 2016	Brazil	Analytical retrospective cross-sectional	Of 1,500 positive pregnant women, the HIV/syphilis co-infection rate was 10.2%. The greatest vulnerability factors were late HIV diagnosis and lack of prenatal care. An association between vertical transmission of HIV and the presence of HIV/syphilis co-infection was identified.	The majority were young adults (25-34 years old), of black race/color/ethnicity and with less than eight years of education.	The group of pregnant women with HIV/syphilis was more vulnerable. Improving access to qualified health care will have a positive impact on reducing congenital syphilis and eliminating vertical transmission of HIV.
Yeganeh et al., 2016	Brazil, South Africa, Argentine and USA	Secondary analysis of randomized controlled clinical trial	Approximately 10% of 1,664 pregnant women enrolled had serological evidence of syphilis without documented adequate treatment, and 1.4% of infants were dually infected with HIV and syphilis.	Women with co-infection were significantly more likely to self-identify as non-white and consume alcohol, with 88% of HIV infections being acquired in utero.	Syphilis remains a common co-infection in HIV-infected women, and can facilitate intrauterine transmission. Most babies were asymptomatic at birth, but those with symptoms have high mortality rates.
Kinikar et al., 2017	India	Secondary analysis of randomized controlled clinical trial	Of the total of 658 HIV-infected mothers, 5% of mothers were also infected with <i>T. pallidum</i> , and 100% received penicillin. Syphilis diagnosis occurred a median of 29 days before birth.	Mothers with co-infection were more likely to have a low level of education, be housewives and less likely to have received antibiotic therapy.	The analysis showed a high rate of maternal syphilis associated with a greater risk of vertical transmission of HIV.
Mutagoma et al., 2017	Africa	Cross-sectional	Of the 55,432 pregnant women analyzed, HIV/syphilis co-infection was present in rural and urban areas. However, it was more likely in women living in urban areas, but less frequent in women with secondary education.	They occurred in pregnant women aged between 25 and 49 years who lived in urban areas and women with secondary education or higher, being less likely to be screened positive for syphilis.	Syphilis increased in HIV-positive pregnant women and decreased in HIV-negative women. HIV seropositivity and young age were associated risks for syphilis. HIV/syphilis co-infection was associated with a lower level of education and urban residence.
Biadgo et al., 2019	Ethiopia	Retrospective	Of the total of 3,504 pregnant women analyzed, the seroprevalence of HIV and syphilis was 4.1% and 1.9%, respectively. And 0.66% women had co-infection.	Age group 20-29 years and age group ≥30 years, compared with age <20 years and HIV infection, were significantly associated with syphilis infection.	Syphilis and HIV remain critical public health concerns among pregnant women. Screening for all pregnant women and studies on risk factors are recommended.
Kengne-Nde et al., 2020	Cameroon	Cross-sectional	Of the total of 3,901 pregnant women tested for syphilis, almost half (47.9%) were from urban areas and were under 25 years old. While the HIV epidemic was declining, a significant increase in the prevalence of syphilis was observed. Pregnant women residing in rural areas were more likely to be infected with syphilis than those in urban areas.	Single pregnant women were three times more likely to have HIV/syphilis co-infection than those who were married, in a stable relationship, widowed or divorced.	The epidemiological dynamics of syphilis suggest an increasing burden of infection among the general population of Cameroon. In addition to strategies to combat HIV, great efforts must also be made to prevent and combat syphilis, especially among HIV-positive women.

ation in which these pregnant women find themselves, as most of them were housewives, financially dependent on their partners, financially fragile and unable to negotiate the use of condoms.^{17, 23, 28}

Pregnant women with HIV are more susceptible to developing other STIs, and syphilis is one of the most common co-infections.²¹ When they occur in association, one can affect the natural evolution of the other.^{2,3} Syphilis can increase HIV viral load and decrease CD4 T lymphocyte cells.²¹ HIV, on the other hand, influences the worsening of syphilis symptoms.^{2,3} Furthermore, ulcerative genital lesions caused by syphilis have been associated with increased HIV acquisition and transmission.^{24,27}

In this context, studies show that the prevalence of vertical transmission of HIV is substantially higher among pregnant women with co-infection,^{17,24,27} presenting odds that vary from two to 3.71 times,^{17,24} being explained by placental inflammation caused by *T. pallidum*, which compromises the structural and functional integrity of cells.^{18,27}

It was found that pregnant women with HIV/syphilis co-infection do not adequately adhere to the recommended treatment.^{17,24,27} At the same time, a reduced percentage of partners is treated, which contributes to maintaining prevalence and vertical transmission rates, due to ineffectiveness of treatment and, in the case of syphilis, reinfection.^{17,24,27,32}

Regarding perinatal outcomes, syphilis causes high rates of negative pregnancy outcomes, especially among pregnant women who are not adequately treated.¹⁷ Abortions and perinatal or neonatal deaths occur in 40% of children infected by untreated mothers or those who started prenatal care late, making timely treatment impossible.^{1,15}

Another variable associated with HIV/syphilis co-infection was the consumption of alcohol and illicit drugs during pregnancy.^{17,24} This association occurred with greater prevalence in single pregnant women and is linked to other risk factors, such as low education, low socioeconomic level, unwanted pregnancy, adoption of risky sexual behaviors, in addition to inadequate adherence to prenatal care and treatment.³²⁻³⁴

The fragility of the care provided was pointed out, as the lack of focus on prevention increases the risk of mother-to-child transmission of HIV by up to 30%, and non-adherence to antiretroviral therapy (ART) during pregnancy increases this risk.³¹

Based on the principle of equity of the Brazilian Health System (SUS - *Sistema Único de Saúde*), pregnant women with HIV/syphilis co-infection should be a priority in health care, however indicators of prenatal care quality indicate otherwise.¹⁷

In this sense, the importance of Primary Health Care and its integration with Specialized Care Services (SCS), maternity hospitals and Epidemiological Surveillance stands out, aimed at improving pregnant women's adherence to prenatal care, considering that this is an opportune moment for STI diagnosis, in order to reduce the risk of intrauterine infection.¹⁷ Another issue would be to strengthen the actions that permeate the notification

and monitoring system for mothers and newborns so that, like other countries, syphilis notification is based on data relating to the stage of the disease and monitoring of the main exposures and of HIV co-infection.^{17,31,35-37}

Furthermore, the adoption of records in pregnant women's booklet about the actions adopted and referral to reference services are of great value. In regions that are difficult to access, there is a need to implement an outpatient clinic to monitor infectious diseases instead of adopting separate and disjointed services, especially in areas where the prevalence of diseases remains high. This location will support comprehensive health care, which includes health care, human rights and social participation. It will develop promotion, prevention, diagnosis, treatment and guarantee of clinical and laboratory follow-up of STIs.¹

As limitations of this integrative review, the possibility of underreporting of cases of HIV/syphilis co-infection is cited, as most studies used secondary data, and, in the case of studies carried out in Brazil, notification forms do not have a field to fill in a form. comorbidities. It is also worth highlighting the difficulty in accessing some restricted publications, with only free access texts being included in the study, made available in full.

CONCLUSION

It was found that HIV/syphilis co-infection is more prevalent in pregnant women in the young-adult age group, of non-white race/color, married, with a low level of education, housewives as their occupation, residents of urban areas and belonging to classes most economically disadvantaged social groups.

Additionally, an association was observed between syphilis and the late start of prenatal care with an increased rate of unfavorable pregnancy outcomes, such as miscarriage, stillbirth and prematurity. It has been shown that the natural evolution of diseases can be affected when diseases are associated.

The studies analyzed showed the need to improve prenatal care, in order to ensure assistance, especially in medication administration and diagnostic test provision, with the aim of reducing the risks of vertical transmission by monitoring pregnant women with co-infection, partners and newborns.

Studies of this nature are important so that more effective strategies can be redirected in the implementation of public policies aimed at clinical management of pregnant women with HIV/syphilis co-infection, allocation of resources and development of specific intervention protocols.

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