Duazary / Vol. 20, No. 2 – 2023 / 127 - 138
DOI: https://doi.org/10.21676/2389783X.5375

Article of scientific and technological research

Obstetrical complications and immunological parameters in VIH serum-positive pregnant women

Complicaciones obstétricas y parámetros inmunológicos en gestantes seropositivas al VIH

José Ramón Urdaneta-Machado [1], Isabel Breuker-Mata [2]

1. Universidad Austral de Chile. Valdivia, Chile. Correo: jose.urdaneta@uach.cl - https://orcid.org/0000-0002-6972-1522
2. Universidad del Zulia. Maracaibo, Venezuela. Correo: issabelbreuker@hotmail.com - https://orcid.org/0000-0002-7226-5572

How to cite this article: Urdaneta JR, Breuker I. Complicaciones obstétricas y parámetros inmunológicos en gestantes seropositivas al VIH. Duazary. 2023; 20 (2): 127-138. https://doi.org/10.21676/2389783X.5375

Received on February 01, 2023
Accepted on June 29, 2023
Posted online June 30, 2023

ABSTRACT

Introduction: HIV-positive pregnant women could present different pregnancy complications related to both their immunological status and retroviral therapy. **Objective:** To relate the immunological parameters with the obstetric complications presented by pregnant women seropositive to the Human Immunodeficiency Virus (HIV) attended in a Venezuelan maternity hospital. **Method:** A retrospective correlational study, where a sample of 161 HIV-positive pregnant women was studied; analyzing obstetric complications, CD4+ count and viral load. **Results:** The most common maternal pathologies were anemia (57.76%); while fetal and ovular complications prevailed low birth weight (13.04%) and premature rupture of membranes (13.04%), respectively. A higher and significant frequency of morbidities was evidenced in women with CD4+= 200-499 cells/ml and viral load >1,000 copies/ml for most pathologies; a lower CD4+ count was associated with a highly significant risk of presenting pathologies such as anemia (OR= 14.44; 95%CI 05.94-35.08), low birth weight (OR= 5.94; 95%CI 02 0.05-17.20) and urinary tract infection (OR= 3.38; 95% CI 1.74-6.55). Viral load was not associated with increased risk of obstetric complications. **Conclusions:** HIV infection is associated with a higher risk of obstetric complications in relation to immunological status.

Keywords: Pregnancy; Pregnancy Complications; CD4 Lymphocyte Count; Viral Loud; Human Immunodeficiency Virus.

RESUMEN

Introducción: las gestantes seropositivas al HIV pudiesen presentar diferentes complicaciones en el embarazo relacionadas tanto con su estado inmunológico como con la terapia retroviral. **Objetivo**: relacionar los parámetros inmunológicos con las complicaciones obstétricas presentadas por gestantes seropositivas al Virus de la Inmunodeficiencia Humana (VIH) atendidas en una maternidad venezolana. **Método:** estudio correlacionar retrospectivo, donde se estudió una muestra de 161 gestantes seropositivas al VIH; analizándose complicaciones obstétricas, contaje de CD4+ y carga viral. **Resultados:** las patologías maternas más frecuentes fueron: anemia (57,76%); mientras que de las complicaciones fetales y ovulares prevalecieron el bajo peso al nacer (13,04%) y rotura prematura de membranas (13,04%), respectivamente. Se evidenció una mayor y significativa frecuencia de morbilidades en las mujeres con CD4+= 200-499 células/ml y carga viral >1.000 copias/ml para la mayoría de las patologías; un contaje de CD4+ más bajo se asociaba con un riesgo altamente significativo de presentar patologías como anemia (OR= 14,44; IC95% 05,94-35,08), bajo peso al nacer (OR= 5,94; IC95% 02,05-17,20) e infección urinaria (OR= 3,38; IC95% 1,74-6,55). La carga viral no se asoció a mayor riesgo de complicaciones obstétricas.

Palabras clave: embarazo; complicaciones del embarazo; recuento de linfocitos cd4; carga viral; virus de la inmunodeficiencia humana.

Conclusiones: la infección por el VIH se asocia a un mayor riesgo de complicaciones obstétricas en relación al estado inmunológico.

INTRODUCTION

Since the appearance of the first documented cases in the eighties, the management of Human Immunodeficiency Virus (HIV) infection has changed thanks to advances in antiretroviral therapy (ART) and its diagnosis[1]. More than 37 million people worldwide are infected by this virus, without differences by age or sex[2].

In Venezuela, HIV is facing a concentrated epidemic, with a rising trend in the number of infected women and a vertical transmission rate of 21.8%, estimated for 2013[3]. Although the studies of infected Venezuelan women are limited, a national investigation in different areas showed that the majority were in the range of 21-30 years (36.6%)[4]. Even though there are no official data on prevalence in pregnant women, from 2004 to 2016, 3,930 infected pregnant women have been treated, with a progressive increase in cases since 2005[5].

From a treatment perspective, pregnant women are a unique population, mainly due to the opportunity to prevent mother-to-child transmission with ART and the need to consider the safety of the women and their offspring[6]. Fortunately, pregnancy does not seem to alter the natural history of HIV infection, since although it is true that a decrease in the CD4+ cell count has been described during pregnancy, these return to their baseline after delivery; although, there could be a rapid progression in those women who are in advanced stages[7].

In pregnant women with advanced disease, a higher frequency of anemia, sexually transmitted diseases, chorioamnionitis, and premature rupture of membranes have been described; Caesarean section in these patients increases the risk of postpartum endometritis, maternal sepsis, pneumonia, increased hospital stay, need for blood transfusion, need for intensive care unit (ICU) and need for antibiotic therapy. Similarly, in patients receiving ART, the risk of preterm delivery, intrauterine growth restriction, hypertensive disorders, stillbirth, and gestational diabetes may be increased, although the reported results are contradictory and cannot fully establish a causal relationship[8].

The determination of the viral load and the CD4 lymphocyte count help to establish the stage of the disease, establishing that the value of the viral load must be less than or equal to 1000 copies/mL and the CD4 lymphocyte count greater than 200 cells./mm^3 to reduce the risk of vertical transmission; In addition, the useful viral load should be considered to determine both the prognosis and response to treatment, as well as the route and time of delivery to avoid complications[9]. Given this scenario, it was proposed to relate immunological parameters (CD4+ lymphocyte count and plasma viral load) with obstetric complications presented by HIV-seropositive pregnant women treated in a maternity hospital in Maracaibo, Venezuela.

METHOD

Design of investigation

Correlational research with a non-experimental and retrospective design.

Participants

A population of 270 HIV-seropositive pregnant women annually attended a reference maternity hospital in the city of Maracaibo, as recorded in the registry of pregnant women attended in the National AIDS/STI Program of the Ministry of People's Power for Health carried out in said institution, we proceeded to select a probabilistic sample with a confidence level of 95% made up of 161 patients. A representative sample of seropositive pregnant women was selected, given the difficulties in storing medical records in Venezuelan hospitals, making it impossible to carry out a population census.

The medical records registered under the coding of chapter 15 of the International Code of Diseases (ICD-10) related to "Human immunodeficiency virus (HIV) disease that complicates pregnancy, childbirth, and puerperium" were reviewed, corresponding to codes: O98.711, O98.712, O98.713, O98.719, O98.72 or O98.73. The records of patients whose diagnosis of the infection was made at the time of delivery or postpartum, uncontrolled pregnancies, who had not received ART during pregnancy or who were not included in the AIDS/Sexually Transmitted

Infections program were excluded, as well as those without registration of the immunological tests in their clinical records or with delays in the ART withdrawal date indicated in their respective kardex, as an indirect measure of therapeutic adherence. It should be noted that all the study participants, being included in the sexually transmitted infection program, were given ART free of charge during pregnancy according to the first-choice scheme and an alternative adjusted to the expert's recommendation and the national regulations[10], monitoring compliance by controlled drug delivery and registration in an individual kardex for each user.

Instruments

A documentary observation sheet designed "ad hoc" was prepared according to the purposes of the study, which was validated through the judgment of three experts and was divided into three sections:

(a) General and demographic characteristics: chronological age, menarche, sexarche, number of couples, marital status, educational level, type of dwelling, and family income.

(b) Virological aspects and immunological status: HIV diagnosis, stage of infection, viral load, lymphocyte population (CD4+ count), use of antiretroviral therapy (type of antiretroviral drugs, use prior to pregnancy, gestational age at initiation of therapy, complications or adverse effects).

(c) Morbidity - Mortality: The presence or absence of maternal complications (Anemia, Vaginal Candidiasis, Urinary Infection, Bacterial Vaginosis, Preterm Delivery, Hypertensive Disorders, Gestational Diabetes, Hyperemesis gravidarum, Tuberculosis, Hepatitis B Virus), complications were recorded. Fetal (low birth weight, stillbirth, congenital malformations), ovular complications (premature rupture of membranes, placenta previa), and direct and indirect maternal deaths.

Procedure

The medical records of the selected patients were reviewed, and the clinical and epidemiological data of interest for the study were recorded. To determine the immunological parameters, the results of the determination of the viral load were taken from the files using the RT-CPR polymerase chain reaction technique and the CD4+ count obtained by flow cytometry; for the interpretation of both tests, the cut-off points proposed by the Centers for Disease Control and Prevention (CDC)[11].

Statistical analysis

The collected data were organized in a database, and through the Statistical Package for Social Sciences (SPSS), version 21, a descriptive statistical analysis was performed, expressing the results through absolute and relative frequencies (percentages), measures of central tendency (means) and dispersion (standard deviation). To establish the association between the immunological parameters with maternal morbidity and mortality, 3 x 2 contingency tables were made to relate said parameters with the presence or absence of each morbid condition or maternal death, establishing the risk in odds ratios (OR) with their respective confidence indices of 95% (IC95%). The statistical significance of these tables was determined using the Chi-square test (X^2) with a confidence level of 95% with the significance of $p<0.05$.

Declaration on ethical aspects

The proposed study did not represent risks for them, nor did it violate the ethical norms of the Declaration of Helsinki, with the approval of the bioethics committee of the institution covered by the study (CBE-SAHUM No. 143/2020).

RESULTS

Table 1 presents the quantitative analysis of a sample of 161 HIV-seropositive pregnant patients, evidencing that they were women with an average age of 24 years; meanwhile, with term pregnancies of 37 weeks (range between 26.4 and 39.3 weeks of gestation). Likewise, the average menarche was around 11 years of age, the first sexual relationship in adolescence averaged 16.15 years ± 1.9 years, and the number of couples averaged three people.

Table 1. Characterization of the sample of HIV-seropositive pregnant women: Quantitative analysis.

Clinical features	Mean ± SD	Range
Age (years)	24.21±5.5	15 - 44
Gestational age (weeks)	36.70±4.4	26.4 - 39.3
Menarche (years)	11.80±1.5	9 - 17
Sexarchy (years)	16.15±1.9	10 - 21
number of couples	02.90±2.9	1 - 13

Similarly, Table 2 shows other characteristics of the evaluated sample, appreciating that most seropositive pregnant women correspond to adult women, with 1 to 4 deliveries. Regarding prenatal control, there is a significant number of patients with adequate control for their high-risk pregnancy, while, regarding the use of ART, in most of the patients, it was indicated during the first weeks of the second trimester of pregnancy. Likewise, it was found that the majority were single or in free union, of mestizo and indigenous race, of a socioeconomic level corresponding to the working class or lower middle class, of urban origin, with low educational levels, and unemployed.

Table 3 shows the morbidity registered in these pregnant women; it is essential to note that of the 161 patients included, all presented some maternal complication, ranging from an additional pathology to HIV infection to a maximum of 5 pathologies (average 2 ± 0.9 pathologies), being the most frequently observed correspond to anemia and urogenital infections (candidiasis, urinary infection, and bacterial vaginosis); pathologies typical of pregnancy such as preterm delivery, hypertensive disorders associated with pregnancy and gestational diabetes occurred in a lower proportion. Regarding fetal complications, they were present in 27.33% (n= 44/161) patients, predominantly low birth weight, while ovular complications occurred in 14.91% of the cases (n= 24/161), prevailing premature rupture of membranes. It should be noted that no maternal deaths were associated with this infection during the study period.

Table 2. Characterization of the sample of HIV-positive pregnant women: Qualitative analysis.

Characteristics	Af*	%
Age		
Teenagers	56	34.78
adults	105	65.22
Parity		
nulliparous	47	29.19
I-IV	69	42.86
multiparous	Four. Five	27.95
birth control		
Appropriate	131	81.34
Inappropriate	27	16.77
not controlled	3	01.86
Initiation of antiviral therapy in pregnancy		
Yeah	105	65.22
No	56	34.78
Civil status		
Single woman	86	53.41
Free Union	61	37.89
married	14	08.70
Race		
mestizo	90	55.90
Indigenous	47	29.19
White	16	09.94
Afro-descendants	8	04.97
Socioeconomic level		
Graffar 2 (High Medium)	2	01.24
Graffar 3 (Low average)	45	27.95
Graffar 4 (Working class)	97	60.25
Graffar 5 (Marginal)	17	11.56
Origin		
Rural	43	26.71
Urban	118	73.29
Scholarship		
illiterate	5	03.11
Primary	61	37.88
Bachelor	81	50.31
Technique	6	03.73
academic	8	04.97
employment status		
unemployed	114	70.81
casual employee	32	19.88
formal employee	15	09.31

Af: Absolute frequency

Table 3. Morbidity in HIV-positive pregnant women.

Morbidities	Af*	%**
Maternal complications***	161	100.00
• Anemia	93	57.76
• Vaginal yeast infection	68	42.23
• Urinary infection	64	39.75
• bacterial vaginosis	60	37.27
• preterm labor	42	26.08
• Hypertensive Disorders	24	14.91
• Gestational diabetes	11	06.83
• hyperemesis gravidarum	06	03.73
• Tuberculosis	03	01.86
• Hepatitis B virus	02	01.24
Fetal complications***	44	27.33
• low birth weight	21	13.04
• Congenital malformations	06	03.73
• Stillbirth	08	04.97
Ovular complications***	24	14.91
• Premature rupture of membranes	21	13.04
• Previous placenta	03	01.86

*Absolute frequency.
**Estimated percentages for each pathology concerning the total sample (n= 161).
***Estimated percentages according to the number of patients with one or more morbidities.

Regarding the immunological parameters (Table 4), the CD4+ lymphocyte count was, on average, 565.07±188.14 cells/ml, with a range between 208 and 1,097 cells/ml, with CD4+ values >500 cells/ml standing out in 59.63%; while the viral load had an average of 2632.98 ± 4734.16 copies/ml, with a range between 20 and 4809 copies/ml, presenting most values less than <1000 copies/ml and the rest between 1000 and 5000 copies. /ml. It should be noted that all the patients were in clinical stage A.

When relating the presence of complications in these pregnant women with the sub-population of CD4+ lymphocytes (Table 5), greater and more significant morbidity was evidenced in pregnant women with a lower concentration of CD4+ lymphocytes (200-499 cells/ml), with statistically significant differences. Significant complications include anemia, vaginal candidiasis, urinary infection, bacterial vaginosis, preterm delivery, and low birth weight ($p<0.05$). Likewise, it was shown that pregnant women with fewer CD4+ counts showed significant risks for presenting these complications, being the greatest risks of presenting anemia (OR = 14.44; 95%CI 5.94-35.08) and low birth weight (OR= 5.94; 95%CI 2.05-17.20).

Table 4. Immunological parameters in pregnant women seropositive to HIV.

Parameter	Af*	%
CD4+ Lymphocyte Count		
• 200-499 cells/ml	65	40.37
• ≥ 500 cells/ml	96	59.63
Viral load		
• <1,000 copies/mL	98	60.87
• 1,000 - 5,000 copies/ml	63	39.13

*Absolute frecuency

On the other hand, when associating the presence of obstetric complications and the viral load (Table 6), it was evidenced that the lower the viral load, the lower the morbidity, with statistically significant differences for complications such as anemia, vaginal candidiasis, urinary infection, bacterial vaginosis, preterm delivery, low birth weight and premature rupture of membranes; except for hypertensive disorders and gestational diabetes that did not show differences. However, the risk analysis did not establish a greater probability of presenting these morbidities with a higher viral load.

DISCUSSION

One of the main findings that stand out in the study carried out was the high prevalence of anemia among HIV-seropositive pregnant women (57.76%) with a high and significant risk of presenting it by reducing the sub-population of CD4+ lymphocytes, coinciding with a Colombian study[8] where anemia was found to be the second most frequent maternal complication in this group of patients with a prevalence of 18%. For his part, Ikpim *et al*[12] reported that the frequency of anemia in Nigerian HIV-positive pregnant women was 8.1%, while, in another African research, the rates of anemia between 32 and 34 weeks of gestation reached 61.8%[13]. The etiology of anemia among HIV-positive pregnant women is multifactorial and can be attributed to iron deficiency or anemia due to HIV inflammation, opportunistic infections, or other infections, for instance, malaria or hookworm infection[14].

For their part, genital infections such as vulvovaginal candidiasis and bacterial vaginosis ranked second and fourth among the causes of maternal morbidity in

HIV-infected pregnant women; It is known that these reproductive tract infections, which contribute to the incidence of adverse pregnancy outcomes, occur more frequently in seropositive pregnant women due to immunosuppression[15]. Vulvovaginal candidiasis is one of the most common fungal infections in HIV-infected women, who present vaginal infections more frequently, and when chronic or recurrent, it constitutes one of the first clinical manifestations of HIV infection in women[16].

Table 5. Morbidity in HIV-seropositive pregnant women according to CD4+ lymphocyte subpopulation.

Morbidities	**CD4+ 200-499 (cells/ml)**		**CD4+ ≥500 (cells/ml)**		**OR**	**95%CI**	**p******
	Af	**% ***	**Af**	**% ****			
Maternal complications							
• Anemia	58	89.23	35	36.46	14.44	05.94-35.08	0.0001
• Vaginal yeast infection	36	55.38	32	33.33	02.48	01.30-04.74	0.0089
• Urinary infection	37	56.92	27	28.13	03.38	01.74-06.55	0.0005
• bacterial vaginosis	3. 4	52.31	26	27.08	02.95	01.52-05.73	0.0021
• preterm labor	26	40.00	16	16.67	03.33	01.60-06.92	0.0018
• Hypertensive Disorders	eleven	16.92	13	13.54	01.30	00.54-03.11	0.7140
• Gestational diabetes	05	07.69	06	06.25	01.25	00.37-04.28	0.9700
Fetal complications							
• low birth weight	16	24.62	05	05.21	05.94	02.05-17.20	0.0008
Ovular complications							
• Premature rupture of membranes	eleven	16.92	10	10.41	01.75	00.70-04.40	0.3349

*Estimated percentages for each pathology for the total sub-sample with CD4+ 200-499 cells/ml (n= 65)
**Estimated percentages for each pathology concerning the total sub-sample with CD4+ ≥ 500 cells/ml (n= 96)
*** Chi-square test (X^2) with statistical significance of $p < 0.05$.

Table 6. Morbidity in HIV-positive pregnant women according to viral load.

M**orbidities**	**Viral load < 1000 (copies/ml)**		**Viral load 1000-5000 (copies/ml)**		**OR**	**95%CI**	**P******
	Fa	**% ***	**Fa**	**% ****			
Maternal complications							
• Anemia	32	32.65	61	62.24	0.02	0.004-0.07	0.0001
• Vaginal yeast infection	33	33.67	35	35.71	0.41	0.21-0.78	0.0099
• Urinary infection	17	17.35	47	47.96	0.07	1.26-4.94	0.0001
• bacterial vaginosis	25	25.51	35	35.71	0.27	0.14-0.54	0.0002
• preterm labor	19	19.39	23	23.47	0.42	0.20-0.86	0.0257
• Hypertensive Disorders	08	08.16	16	16.33	0.26	0.10-0.65	0.7304
• Gestational diabetes	06	06.12	05	05.10	0.76	0.22-2.59	0.9003
fetal complications							
• low birth weight	08	08.16	13	13.27	0.34	0.13-0.88	0.0400
ovular complications							
• Premature rupture of membranes	08	08.16	13	13.27	0.34	0.13-0.88	0.0400

*Estimated percentages for each pathology concerning the total sub-sample with viral load <1,000 copies/ml (n= 98)
**Estimated percentages for each pathology for the total sub-sample with viral load 1,000 - 5,000 copies/ml (n= 63)
***Chi square test (X^2) with statistical significance of $p < 0.05$.

Bacterial vaginosis represents the most frequent vaginal infection among HIV-infected women, associated with changes in the diversity of the genital microbiota[17]. It has been reported that seropositive pregnant women have a higher risk of contracting bacterial vaginosis than seronegative women, while antiretroviral drugs are associated with a lower prevalence of the same[18]. In this regard, Foessleitner *et al*[19] recommend screening and treatment of asymptomatic infections as part of routine prenatal

care in HIV-positive pregnant women since these vaginal microbiota imbalances can lead to preterm delivery.

Regarding urinary infections, these were the third most frequent cause of morbidity in the pregnant women studied, occurring in almost 40% of them; about it Arab *et al*[20] published that seropositive pregnant women have a three times greater risk of presenting urinary infections compared to pregnant women free of this infection (OR= 3.01, 95%CI 2.4-3.79). In this investigation, the risk of presenting urinary tract infections tripled when the CD4+ T lymphocyte count decreased; other investigators [21] have concluded that these infections are more frequent when the CD4+ count falls below 500/ µL or when protease inhibitors are used, which are associated with nephrolithiasis. Likewise, a Nigerian study[22] determined that asymptomatic bacteriuria was present in 31.3% of pregnant women with HIV; having a low CD4 cell count had a significant association with a higher prevalence of asymptomatic bacteriuria among HIV-seropositive pregnant women.

Regarding the rate of preterm deliveries, this was much lower than the 36.5% reported in the Frankfurt-HIV cohort by Reitter *et al*[21], although higher than the prevalence of prematurity in a Spanish study where it was 20.6%[23]. In this regard, a Chinese investigation[24] determined a slight increase in the presentation of preterm labor that was associated with the use of antiretrovirals during the first (OR=1.86, 95%CI 1.261-2,75) and second trimester (OR=1.71, 95%CI 1,20-2,45). Various studies associate prematurity mainly with the use of protease inhibitors[23,25]. However, in a recent Spanish study, although the prematurity rate was much higher than the rate in the general population and most of the infected pregnant women received protease inhibitors, no association could be demonstrated with the therapy used[26].

Conversely, Ikpim *et al*[12] found that preterm births in HIV-positive pregnant women who did not receive ART were more frequent than in HIV-negative women (16.9% vs. 3.9%); ART seems to reduce the risk of preterm births. Although in a meta-analysis found a slight and significant increase in the risk of presenting preterm delivery among HIV-infected mothers (OR=1.56, 95%CI 1.49-1.63, p<0.001), the use of antiretroviral drugs did not significantly change the association between prematurity and maternal exposure to HIV[27].

Coinciding with another study[28], which determined an association between childbirth and maternal immune status deterioration (CD4+<500 cells/mm^3), significant differences were found in the presence of preterm birth about the sub-population of CD4+ lymphocytes and the viral load, showing women with a lower CD4+ count a three times greater risk of having presented a premature birth. In this regard, another investigation[29] determined that HIV-positive pregnant women with concomitant sexually transmitted infections had double the risk of presenting spontaneous preterm birth, which persisted after adjusting for maternal age, history of preterm birth, and low CD4+ count at initiation of prenatal care.

Regarding its pathogenesis, a recent study demonstrated unique macroscopic and histological anatomical findings that indicated placental damage that could be associated with preterm delivery, finding that in HIV-positive pregnant women, the placentas were thinner and had an unusually high insertion rate. Marginal cord, thrombosis, and infarction; although all the samples studied came from women on ART, it was impossible to determine if the observed placental pathologies were associated with HIV infection, treatment, or both[30]. On the other hand, preterm delivery is a risk factor for perinatal transmission of the virus; It has been reported that a maternal viral load of less than 400 copies/ml, but in a delivery that occurred before 34 weeks, is associated with an eight-fold increase in the risk of vertical transmission compared to delivery at term[31].

The results presented in this research demonstrate how most of the morbidities registered in HIV-seropositive pregnant women were related to immunological parameters of infection surveillance and control, such as viral load and CD4+ lymphocyte sub-population, evidencing that at a lower load viral and higher concentration of CD4+ fewer complications presented by these pregnant women; however, this finding is inconsistent with what was reported in a Colombian study[8], which concluded that although pregnant women with HIV infection had a slight increase in maternal and perinatal complications, no association was found between viral load and CD4+ count with maternal or perinatal morbidity.

In the study, gestational diabetes and hypertensive disorders of pregnancy presented a low incidence. They were not shown in the risk analysis to be related

to CD4+ lymphocyte concentrations or viral load, similar to what was reported in a Canadian investigation that established low rates of hypertension and gestational diabetes[32] or in another American study where seropositive pregnant women did not have a higher risk of presenting these complications[29].

Conversely, other researchers[22] have reported gestational diabetes as the second most frequent complication in HIV-seropositive pregnant women (11.4%); protease inhibitors are associated with increased incidence[33]. However, there has been much controversy about the possible association between treatment with these and the increased risk of gestational diabetes. In fact, about new generation drugs such as darunavir and atazanavir, this association does not seem so clear[29].

Regarding hypertensive disorders of pregnancy, it had been suggested that HIV infection or highly active antiretroviral therapy were associated with a greater risk of presenting them[31]. A meta-analysis showed no significant association between HIV positivity and the presence of pregnancy-induced hypertension, preeclampsia, or eclampsia[34]. It is believed that HIV infection causes hemostatic abnormalities, such as hematological disorders and deregulation of the hematopoiesis and coagulation processes that would result in hypertensive disorders of pregnancy[35].

Regarding other infections, such as Tuberculosis (TB) or hepatitis B, these were of low frequency in the research carried out. Although it has been reported that the risk of TB is approximately ten times higher in HIV-infected pregnant women than in seronegative women.[36] Likewise, this infection has been associated with hypertensive disorders of pregnancy and adverse fetal outcomes, which are higher in women diagnosed with TB mono-infection and even higher in women with TB/HIV coinfection; however, more research is needed to understand the link between these two entities[37]. On the other hand, it is known that, among HIV-seropositive pregnant women, Hepatitis B occurs more frequently in those with a high viral load and a low CD4+ lymphocyte count[38]. Therefore, since the patients studied were in clinical stage A, this could explain its low prevalence.

Regarding fetal complications, the most prevalent was low birth weight (13.04%); Coincidentally, in other investigations[8,15] it was found that this was the most frequent perinatal morbidity observed in HIV-seropositive pregnant women, in both with a frequency of 21.7%. In this regard, a meta-analysis[27] determined a significant association between maternal HIV infection and low birth weight. On the other hand, it was established that there was a greater risk of presenting it by having a smaller sub-population of CD4+ lymphocytes. Low birth weight could be related to immunosuppression, and the reduction of CD4+ T cells, with a higher risk of low birth weight infants being found in women with CD4+ cell counts below 350 cells/mm[3(39)].

Regarding stillbirth, present in 4.9% of the sample, a South African study found a doubling of the risk of pregnancy loss, whether abortion or stillbirth, in women who had high viral loads before pregnancy, which could be associated with problems in the registration or retention of pregnant women in antiretroviral therapy programs, lack of therapeutic adherence or non-compliance with the guidelines for prenatal monitoring of viral load[40]. Regarding congenital disabilities, these were low frequency (3.7%) in the analyzed sample; other studies have established their low prevalence during prenatal genetic screening[32].

Regarding premature rupture of membranes, a higher frequency was found than that reported in the Frankfurt-HIV cohort[22]. This was observed mainly in pregnant women with a higher viral load ($p<0.05$), contrary to what was reported in another study[26] where bag rupture was unrelated to viral load but to the ART used since almost all patients received a protease inhibitor.

On the other hand, studies that compare the prevalence of complications between seropositive and seronegative pregnant women report that among seropositive women, both their incidence and the risk of presenting them were significantly higher[20]; however, a recent Spanish study[26] indicates that only certain complications are more frequent in HIV-infected pregnant women, such as low birth weight, prematurity, preterm premature rupture of membranes, and proteinuria. Finally, regarding maternal mortality among HIV-seropositive pregnant women, no maternal deaths were recorded during the study period; This result is similar to that found in a Colombian investigation[8], although other studies[20,40] revealed that the risk of maternal death among seropositive pregnant women was between six and

ten times that of pregnant women without this condition.

One of the strengths of this study is that it reports a representative and well-characterized sample of HIV-infected women, in which data on pregnant women who received prenatal care in the same hospital, which represents the reference center, were identified for the care of HIV-positive pregnant women in the region and neighboring states. Likewise, it presents a risk analysis of the parameters of surveillance and immunological control of the infection to know the probability of presenting different morbidities that can occur in patients living with HIV/AIDS, which allows not only to know the epidemiological behavior of this infection but also to take measures to prevent such complications and minimize their consequences.

However, this research presents some limitations due to its retrospective nature, such as the omission of data of interest in some clinical records, which had to be excluded, so that a population census could not be carried out to know more precisely the patient's situation. HIV in pregnant women; likewise, the possibility that the association with recorded morbidity was not only related to HIV status but also secondary to other factors such as maternal nutritional deficiencies, drug use, smoking, or other risk factors cannot be ruled out. Similarly, the association between maternal HIV infection and morbimortality could not be established after controlling for the different clinical stages of HIV infection in these patients due to the lack of such information in their medical records, nor could the rates of vertical transmission or the presence of perinatal complications in newborns be analyzed, due to limitations in access to the newborn's records and their follow-up after birth. Also, there may be an underreporting of some puerperium complications since there is evidence of low coverage in postnatal maternal care in the institution covered by the study.

Finally, it was possible to conclude that maternal HIV infection is associated with more significant maternal morbidity by increasing the frequency of both maternal and fetal and ovular complications in seropositive pregnant women. Likewise, most of the recorded complications demonstrated a significant association with having a higher viral load or a lower CD4+ lymphocyte count; pregnant women with fewer CD4+ counts showed significant risks for presenting these complications, especially anemia and low birth weight.

DECLARATION ON CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest and are independent of the financing and support institutions and that during the execution of the work or the writing of the manuscript, no interests or values other than those usually found in the investigation have been affected. Its content and purpose were made for scientific dissemination.

AUTHORS' CONTRIBUTION

First author: Conception of the work, methodological design, statistical analysis, and manuscript writing.
Second author: Literature review, data collection, fieldwork.

REFERENCES

1. Mejía JV, Bastos TR, Freire D, da Costa AM, Marques S, Abrão FM. Representaciones sociales del VIH construidas por jóvenes embarazadas atendidas en un hospital universitario de Recife-Brasil. Index Enferm. 2021; 30 (3): 209-213.

2. Gámez A, López MA. Resultados del embarazo en mujeres con infección por virus de la inmunodeficiencia humana. Actual Med. 2020; 105: (810): 96-102 http://dx.doi.org/10.15568/am.2020.810.or03

3. Carvajal AC, Rísquez A, Oletta JF, Godoy O. Epidemiología del VIH en Venezuela desde 1983 a 2016. Med Interna. 2019; 35 (2): 79- 93

4. Carvajal A, Castrillo M, Miguel M, Francia M, Castrillo S, Morillo M, et al. Características epidemiológicas y otros indicadores en mujeres infectadas con el Virus de Inmunodeficiencia Humana (VIH) en Venezuela. Trabajo colaborativo. Gac Med Caracas. 2016; 124 (2): 138-148.

5. Programa Conjunto de las Naciones Unidas sobre el VIH/SIDA/Organización Panamericana de la Salud – Organización Mundial de la Salud Venezuela: Plan maestro para el fortalecimiento de la respuesta al VIH, la tuberculosis y la malaria en la República Bolivariana de

Venezuela desde una perspectiva de salud pública; 2018.

6. Rincón S, Uriel M, Rodríguez LM, Romero Infante XC. Preventive measures to avoid vertical transmission in untreated pregnant women with HIV/AIDS. BMJ Case Rep. 2020 Mar 25;13 (3): e233426. http://dx.doi.org/10.1136/bcr-2019-233426

7. Bailey H, Zash R, Rasi V, Thorne C. HIV treatment in pregnancy. Lancet HIV. 2018; 5 (8): e457– e467. http://dx.doi.org/10.1016/S2352-3018(18)30059-6

8. Valdés E, Sepúlveda A, Candia P, Sepúlveda C, Lattes K. VIH/SIDA: Comportamiento epidemiológico de la transmisión vertical en el contexto general de la infección en Chile. Rev Chil Obstet Ginecol. 2011; 76 (1): 52-57. http://dx.doi.org/10.4067/S0717-75262011000100011

9. Gómez AC, Carrillo ME, Rodríguez JA. Morbimortalidad materno-perinatal en pacientes con infección por VIH, Hospital Simón Bolívar, 2003-2011, Bogotá (Colombia). Rev Colomb Obstet Ginecol. 2014; 65 (4): 308-316. http://dx.doi.org/10.18597/rcog.34

10. Ministerio del Poder Popular para la Salud. Guía de Tratamiento Antirretroviral de las personas que viven con el VIH/Sida en Venezuela. Programa Nacional de SIDA/ITS del Ministerio del Poder Popular para la Salud (2014-2016). 5ta. Ed. Caracas: Ministerio del Poder Popular para la Salud; 2014.

11. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antirretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services; 2011.

12. Ikpim EM, Edet UA, Bassey AU, Asuquo OA, Inyang EE. HIV infection in pregnancy: maternal and perinatal outcomes in a tertiary care hospital in Calabar, Nigeria. Trop Doct. 2016; 46 (2): 78-86. http://dx.doi.org/10.1177/0049475515605003

13. Odhiambo C, Zeh C, Angira F, Opollo V, Akinyi B, Masaba R, et al. Anaemia in HIV-infected pregnant women receiving triple antiretroviral combination therapy for prevention of mother-to-child transmission: a secondary analysis of the Kisumu breastfeeding study (KiBS). Trop Med Int Health. 2016; 21 (3): 373-384. http://dx.doi.org/10.1111/tmi.12662

14. Finkelstein JL, Herman HS, Plenty A, Mehta S, Natureeba P, Clark TD, et al. Anemia and Micronutrient Status during Pregnancy, and Their Associations with Obstetric and Infant Outcomes among HIV-Infected Ugandan Women Receiving Antiretroviral Therapy. Curr Dev Nutr. 2020; 4 (5): nzaa075. http://dx.doi.org/10.1093/cdn/nzaa075

15. Tanton C, Weiss HA, Le Goff J. Correlates of HIV-1 genital shedding in Tanzanian women. PLoS ONE. 2011; 6 (3): e17480. http://dx.doi.org/10.1371/journal.pone.0017480

16. Ray A, Ray S, George AT, Swaminathan N. Interventions for prevention and treatment of vulvovaginal candidiasis in women with HIV infection. Cochrane Database of Syst Rev. 2011; 8: CD008739. http://dx.doi.org/10.1002/14651858.CD008739.pub2

17. Lamont RF, Sobel JD, Akins RA, Hassan SS, Chaiworapongsa T, Kusanovic JP, et al. The vaginal microbiome: New information about genital tract flora using molecular based techniques. BJOG. 2011; 118 (5): 533-549. http://dx.doi.org/10.1111/j.1471-0528.2010.02840.x

18. Vallone C, Rigon G, Lucantoni V, Putignani L, Signore F. Pregnancy in HIV-positive patients: Effects on vaginal flora. Infect Dis Obstet Gynecol. 2012; 2012: 287849 http://dx.doi.org/10.1155/2012/287849

19. Foessleitner P, Petricevic L, Boerger I, Steiner I, Kiss H, Rieger A, et al. HIV infection as a risk factor for vaginal dysbiosis, bacterial vaginosis, and candidosis in pregnancy: A matched case-control study. Birth. 2021; 48 (1): 139-146. http://dx.doi.org/10.1111/birt.12526

20. Arab K, Czuzoj-Shulman N, Spence A, Abenhaim HA. Obstetrical outcomes of patients with hiv in pregnancy, a population based cohort. Arch Gynecol Obstet. 2017; 295(3): 599-606. http://dx.doi.org/10.1007/s00404-016-4271-y

21. Reitter A, Stücker AU, Linde R, Königs C, Knecht G, Herrmann E, et al. Pregnancy complications in HIV-positive women: 11-year data from the Frankfurt HIV cohort. HIV Med. 2014; 15(9): 525–536. http://dx.doi.org/10.1111/hiv.12142

22. Akadri AA, Odelola OI. Determinants of asymptomatic bacteriuria in HIV-positive and negative pregnant women in Sagamu, South-west Nigeria. West Afr J Med. 2020; 37 (1): 1-6.

23. Soriano A, Noguera A, López M, Soler P, Mur A, Méndez M, et al. El embarazo como una oportunidad de diagnóstico del virus de la inmunodeficiencia humana en mujeres inmigrantes en Catalunya. Enferm Infecc Microbiol Clin. 2018; 36(1): 9–15. http://dx.doi.org/10.1016/j.eimc.2016.07.011

24. Wang A, Wang X, Dou L, Wang F, Wang Q, Qiao Y, et al. Incidence of and related risk factors on preterm delivery among HIV-infected pregnant women in China. Zhonghua Liu Xing Bing Xue Za Zhi. 2015; 36 (4): 349-353.

25. Ehsanipoor RM, Major CA. Herpes simplex and HIV infections and preterm prom. Clin Obstet Gynecol. 2011; 54 (2): 330–360. http://dx.doi.org/10.1097/GRF.0b013e318217d7a6

26. Calvo M, de la Calle M, Montes ML, Escosa L, Elorza MD, González J, et al. Complicaciones obstétricas relacionadas con la terapia antirretroviral en gestantes infectadas por el VIH. Clín Inv Ginecol Obstet. 2022; 49: 100713. http://dx.doi.org/10.1016/j.gine.2021.100713

27. Xiao PL, Zhou YB, Chen Y, Yang MX, Song XX, Shi Y, et al. Association between maternal HIV infection and low birth weight and prematurity: a meta-analysis of cohort studies. BMC Pregnancy Childbirth. 2015; 15: 246. http://dx.doi.org/10.1186/s12884-015-0684-z

28. Mirpuri J, Jain L. Issues of prematurity and HIV infection. Clin Perinatol. 2010; 37(4): 887-905. http://dx.doi.org/10.1016/j.clp.2010.08.012

29. Burnett E, Loucks TL, Lindsay M. Perinatal outcomes in HIV positive pregnant women with concomitant sexually transmitted infections. Infect Dis Obstet Gynecol. 2015: 508482. http://dx.doi.org/10.1155/2015/508482

30. Obimbo MM, Zhou Y, McMaster MT, Cohen CR, Qureshi Z, Ong'ech J, et al. Placental structure in preterm birth among HIV-positive versus HIV-negative women in Kenya. J Acquir Immune Defic Syndr. 2019; 80(1): 94-102. http://dx.doi.org/10.1097/QAI.0000000000001871

31. European Collaborative Study, Boer K, England K, Godfried MH, Thorne C. Mode of delivery in HIV-infected pregnant women and prevention of mother-to-child transmission: Changing practices in Western Europe. HIV Med. 2010; 11(6): 368-378. http://dx.doi.org/10.1111/j.1468-1293.2009.00800.x

32. Yudin MH, Caprara D, MacGillivray SJ, Urquia M, Shah RR. A ten-year review of antenatal complications and pregnancy outcomes among HIV-positive pregnant women. J Obstet Gynaecol Can. 2016; 38 (1): 35- 40. http://dx.doi.org/10.1016/j.jogc.2015.10.013

33. Soepnel LM, Norris SA, Schrier VJ, Browne JL, Rijken MJ, Gray G, et al. The association between HIV, antiretroviral therapy, and gestational diabetes mellitus. AIDS. 2017; 31: 113–125. http://dx.doi.org/10.1097/QAD.0000000000001277

34. Browne JL, Schrier VJ, Grobbee DE, Peters SA, Klipstein K. HIV, antiretroviral therapy, and hypertensive disorders in pregnancy: A systematic review and meta-analysis. J Acquir Immune Defic Syndr. 2015; 70(1): 91-98. http://dx.doi.org/10.1097/QAI.0000000000000686

35. Phoswa WN. the role of HIV infection in the pathophysiology of gestational diabetes mellitus and hypertensive disorders of pregnancy. Front Cardiovasc Med. 2021; 8: 613930. http://dx.doi.org/10.3389/fcvm.2021.613930

36. Organización Panamericana de la Salud. Nuevas generaciones sin la infección por el VIH, la sífilis, la hepatitis B y la enfermedad de Chagas en las Américas 2018: Whashignton, D.C.; 2019.

37. Phoswa WN, Eche S, Khaliq OP. The association of tuberculosis mono-infection and tuberculosis-human immunodeficiency virus (TB-HIV) co-infection in the pathogenesis of hypertensive disorders of pregnancy. Curr Hypertens Rep. 2020; 22 (12): 104. http://dx.doi.org/10.1007/s11906-020-01114-5

38. Juganariu G, Teodor A, Petrovici C, Cristina N, Miftode E. Characteristics of hepatitis B virus coinfection among HIV-infected pregnant women. Rev Med Chir Soc Med Nat Iasi. 2015; 119 (4): 1010 - 1017.

39. Kim HY, Kasonde P, Mwiya M. Pregnancy loss and role of infant HIV status on perinatal mortality among HIV-infected women. BMC Pediatr. 2012; 12: 138. http://dx.doi.org/10.1186/1471-2431-12-138

40. Moodley Y, Tomita A, de Oliveira T, Tanser F. HIV viral load and pregnancy loss: results from a population-based cohort study in rural KwaZulu-Natal, South Africa. AIDS. 2021; 35 (5): 829-833. http://dx.doi.org/10.1097/QAD.0000000000000279