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RESEARCH ARTICLE

Effects of HIV infection and/or malaria on maternal and neonatal health in a high-prevalence setting

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Abstract

Objective: HIV infection and malaria have been associated with different complications during pregnancy and delivery. HIV-positive pregnant women are at increased risk for all adverse outcomes of malaria during pregnancy. The main objective was to analyse the obstetric and perinatal consequences of malaria, HIV infection and HIV/malaria co-infection in pregnant women and newborns, which has been less well evaluated.

Methods: A cross-sectional study was carried out in the Maternity Service of the Provincial Hospital of Tete Mozambique, involving completion of a structured questionnaire that included demographic data, and information on the current pregnancy, delivery and the newborn. In total, 819 women (13–45 years old) in the immediate postpartum period were enrolled between 1 March and 31 October 2016.

Results: The overall prevalence of HIV and malaria, considered separately, in pregnant women was ~12% (103 women with HIV and 101 with malaria). Only one-fifth of HIV-infected women knew their HIV status before pregnancy. A significantly higher proportion of women with HIV attended four or more antenatal care visits than women without HIV. Caesarean section was less frequent in HIV patients, and peripartum urinary infection was more frequent than in seronegative women (13/103 [12.6%] vs. 34/716 [4.7%]). HIV/malaria co-infection were 17/819 (2%) and was significantly associated with the development of pre-eclampsia when HIV-infected patients received anti-retroviral treatment, and with an increase in urinary tract infections around delivery. With respect to the newborn, co-infection increased the frequency of early neonatal death, as well as neonatal asphyxia and jaundice.

Conclusions: In Mozambique, the prevalence of malaria and HIV infection in women of childbearing age continues to be high and contributes additively to complications during pregnancy and childbirth, and in the newborn. Therefore, integrating HIV, malaria and reproductive health services is essential if maternal and foetal outcomes are to improve.

KEYWORDS
Africa, HIV, malaria, Mozambique, pregnancy

INTRODUCTION

Malaria and HIV remain a major public health threat in sub-Saharan Africa. During pregnancy, both infections can have a significant impact on both the mother and the newborn. Maternal and child health, malaria and HIV infection are priority aspects of Sustainable Development Goal 3, which aims to reduce maternal mortality and the eradicate malaria by 2030 [1].

Malaria, a protozoan parasitic disease, accounted for 241 million cases and 627, 000 deaths in 2020, with ~95% of cases and deaths occurring in sub-Saharan Africa. Four African countries accounted for just over half of all malaria deaths worldwide: Nigeria (31.9%), the Democratic Republic

Sustainable Development Goal: Good Health and Wellbeing.

of the Congo (13.2%), the United Republic of Tanzania (4.1%) and Mozambique (3.8%) [2], whereas HIV, which is a viral disease, accounted for 37.7 million cases and about 1 million deaths in 2020 [3]. This region of the world has the highest proportion of HIV-positive pregnant women, with 85% of the global burden [4]. Both diseases affect the poorest segment of the population and particularly pregnant women.

Malaria is a major cause of morbidity and mortality among HIV-infected pregnant women in endemic regions of sub-Saharan Africa, where at least 1 million malaria co-infections occur annually among pregnant women [5].

The World Malaria Report estimated that 11.6 million pregnant women in sub-Saharan Africa (35% of pregnancies in that region) in 2020 were infected with *Plasmodium* spp. In East Africa and Southern Africa, the prevalence of malaria exposure during pregnancy was 22% [6].

Focusing on Mozambique, malaria transmission occurs throughout the country, ranging from low, seasonal transmission in the south, to holoendemic in the centre and north of the country [7, 8]. Malaria is the fourth leading cause of mortality in pregnant women (10.1%) [9]. Mozambique is one of the sub-Saharan African countries most affected by the HIV/AIDS epidemic [10], where the two infections coexist, with 2.2 million infected people and an overall prevalence of 12.6% in adults between 15 and 49 years of age, with a clear predominance in women (60%) [11].

Interactions between pregnancy, HIV infection and malaria are multiple. HIV infection has been associated with a number of complications during pregnancy and delivery [12, 13, 14, 15], including: (i) increased incidence of anaemia, especially severe anaemia in pregnancy; (ii) increased antepartum bleeding; (iii) increased prevalence of hypertensive disorders of pregnancy; (iv) increased puerperal sepsis and endometritis; (v) pre-term delivery; (vi) low birth weight (LBW); and (vii) stillbirth. However, the results of several individual studies and meta-analyses are inconsistent and even contradictory, depending, among other factors, on the study site or the use of anti-retroviral treatment. At the same time, malaria also has multiple negative consequences in pregnancy, such as maternal anaemia, LBW, foetal growth retardation, preterm delivery, spontaneous abortion, stillbirth, neonatal and maternal death [16]. Finally, a number of interactions between HIV infection and malaria have been described, so that the coexistence of both infections 'increases the frequency of clinical parasitemia and severe malaria, with increased viral and parasite load and impaired immunity to malaria' [17, 18].

The role of HIV/malaria co-infection in pregnancy, childbirth and the newborn has been less well evaluated [19, 20, 21]. The main objective of this study was to analyse the obstetric and perinatal consequences of both malaria, HIV infection and HIV/malaria co-infection among women giving birth in the maternity unit of a tertiary hospital in Tete Province, Mozambique.

POPULATION AND METHODS

Study site

The study was conducted in the Maternity Services Unit of Tete Provincial Hospital (HPT). The province of Tete is located in the central region of Mozambique, bordering on Zambia to the north and Zimbabwe to the east (Figure 1); Mozambique is one of the least developed countries in the world [22]. The province has an area of 100,724 km^2 and average temperatures range between 23.4°C and 32.9°C. Tete province is the third most populated province in the country and has a population of 2,829,594 inhabitants, 1,442,880 of whom are women [23]. In recent years, Tete has experienced a boom in mineral resources, which has led to major socioeconomic changes and considerable population growth due to national and international immigration. Despite this, the local economy is still based primarily on subsistence agriculture, and levels of poverty and inequality are high. Literacy levels are low, especially among women, and access to safe water and sanitation or improved housing is scarce [22]. The average fertility rate is 4.7 births per woman [24]. It has a limited health system with a shortage of trained health personnel, especially in rural areas. The number of physicians is ~0.1 physicians per 1000 inhabitants [25]. The specific data of the hospital are shown in Table 1.

Study population

Between 1 March and 31 October 2016, the women in the study were recruited during labour and/or the immediate postpartum period. For sample selection, the primary criterion was to recruit women only when investigators were present at the time of delivery.

During the study period, 2906 deliveries were recorded. Investigators were present at the time of delivery in 1162 (40%) cases. In total, 215 women refused to participate for different reasons resulting in a sample of 947 (33%) women. Data were only completed in 819 (28%) cases, this being the final number of women included in the study. The flow chart of selection is shown in Figure 2.

Procedures

A cross-sectional study was conducted by completing a structured questionnaire that included demographic data and information about the current pregnancy, delivery and the newborn. The interviews were conducted by the researchers with the help of medical students from Zambeze University who were in the Maternity Services and acted as translators. Each interview lasted between 10 and 15 min. In addition, to complete the questionnaire data, the pregnancy record of the National Health Service of the Republic of Mozambique and the clinical history of childbirth of all women in the study were reviewed.

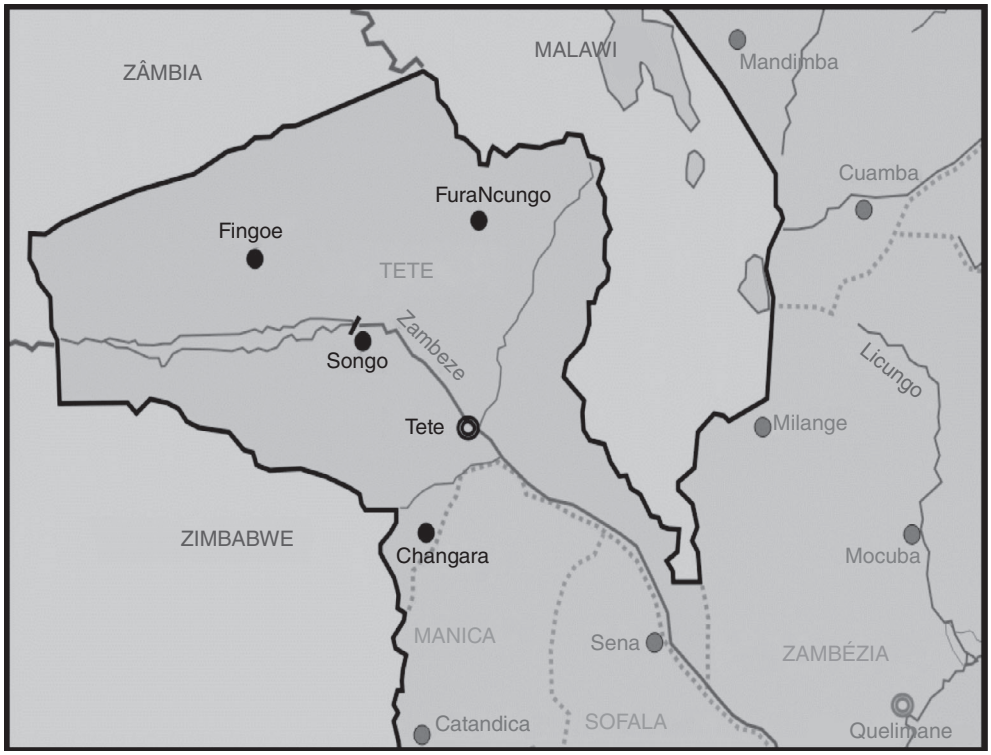

FIGURE 1 Political map of Tete (Mozambique).

HIV serostatus was assessed using a rapid test (Determine, Abbot Laboratories, USA) and positive results were confirmed using the Uni-gold rapid test (TM HIV, Trinity Biotech, Ireland). Test were performed during pregnancy control visits and/or delivery. The diagnosis of malaria was made from peripheral blood samples using the SD BIOLINE Malaria Ag P.f/Pan test (Abbott®). In suspected cases, malaria was also diagnosed using Giemsa-stained thick blood films for microscopic observation of plasmodium parasites. Proteins in urine were measured with the Multistix® 10 SG reagent strip.

Definitions

Several types of data were evaluated:

i. *Demographic* data, including age and residence (urban: Ciudad de Tete and Moatize), semiurban (Changara) and rural (Chifunde, Chiuta, Maravia, Mutarara, Zumbu, Macanga, Angonia, Cahora-Bassa and Tsangano),
ii. *Pregnancy data*, including pregnancy number (first, second or later); previous abortion history, defined as the expulsion of the conceptus before 28 weeks of gestation, or before the foetus weighs 500 g; expected date of delivery as calculated by midwives by adding 9 months and 7 days to the last menstrual period; symphysis fundal height (SFH) measured taking as a reference that the umbilical scar is normally reached at 20 weeks; pregnancy follow-up assessments based on completing at least four or more antenatal care (ANC) visits (≥4); complications during pregnancy. Complications evaluated were antepartum haemorrhage (including placenta previa and placental abruption) and hypertensive disorders induced by pregnancy (pre-eclampsia and eclampsia). For the diagnosis of preeclampsia, current criteria [26, 27] were used, which included (a) the presence of arterial hypertension (systolic blood pressure equal to or over 140 mm Hg and/or diastolic blood pressure equal to or over 90 mm Hg), determined on two occasions at least 4 h apart; (b) onset after the 20th week of pregnancy; and (c) proteinuria>300 mg/24 h and/or adverse conditions that increase the risk of severe complications and/or severe complications that warrant delivery. A diagnosis of eclampsia was made if seizures developed in patients with criteria for pre-eclampsia,
iii. *Infection data*, including HIV and malaria status. HIV patients were subdivided into two groups, according to whether or not they were on HAART (highly active anti-retroviral therapy) during pregnancy. Patients diagnosed with malaria were also subdivided into two groups, depending on whether the infection was diagnosed during pregnancy or at delivery (malaria in pregnancy [MiP] and no malaria in pregnancy [no MiP]).
iv. *Delivery data*, included type of delivery (vaginal or caesarean section), use of episiotomy, complications, such as urinary tract infection, maternal fever and uterine rupture. When available, haemocytometer parameters were recorded.
v. *Neonatal characteristics*, including: gestational age (*pre-term* was defined as occurring before week

TABLE 1 Tete provincial hospital structure

	Tete provincial hospital
12 immediate puerperium beds	6 beds and also
12 immediate puerperium beds	2 for intermediate care
12 immediate puerperium beds	4 beds for complicated pregnancies
12 immediate puerperium beds	12 immediate puerperium beds
Childbirths	4350 deliveries in 2016
Staffing rates	Gynaecology and obstetrics service
	5 gynaecologists
	3 senior nurses and 6 nurses during normal hours
	Maternity Service: 8 nurses on duty rotation and 2 morning nurses
Services available	3 operating rooms (general, gynaecology and obstetrics and emergencies), Neonatology Service (6 beds and 6 for neonatal ICU)
	Gynaecology and Obstetrics Service Internal Medicine
	Paediatric
	Legal Medicine
	Traumatology
	Surgery
	Emergency
	Radiology
	Urology

37, *at-term* as between weeks 37 and 42, and *post-term* from 42 weeks of gestation), anthropometric measurements (sex, weight [kg]) and complications: stillbirth, LBW, Apgar score <7 at 1 min [28], respiratory distress (> 60/min), neonatal fever (T > 38.0°C) and neonatal jaundice (clinical assessment of conjunctiva/sclera). Stillbirth was defined as occurring after 28 complete weeks of gestation, and LBW as weighing <2500 g at birth.

Specifically, the variables that were collected from medical or antenatal records were pregnancy number, previous abortion history, SFH, ANC, HIV infection diagnosed before delivery, HAART before delivery and malaria during pregnancy. The rest of the variables were collected through the questionnaire carried out by the researchers.

Statistical analysis

Categorical variables are summarised as frequencies and percentages, and continuous variables as means and standard deviation (SD). Categorical data were analysed for associations using the Chi-square test or Fisher's exact test. Means of continuous variables were compared using Student's *t*-test (2 groups) or ANOVA (>2 groups) when the data followed a normal distribution, and the Mann–Whitney *U* test (2 groups) or Kruskal–Wallis (>2 groups) for non-normally distributed data. Multivariate analyses were performed on adverse maternal and neonatal outcomes found in univariate analysis to be associated with gestational malaria and/or HIV. Logistic regressions were performed for binary outcomes (i.e., peripartum urinary tract infection, intrapartum maternal fever, neonatal death, respiratory distress, and neonatal jaundice) and linear regression for continuous outcomes (i.e., neonatal weight). The multivariate models controlled for maternal age, number of previous pregnancies, and gestational age at delivery. For each model, odds ratios and p-values are shown. Statistical significance was set at $p < 0.05$. Data were analysed using Stata version 15 (StataCorp®).

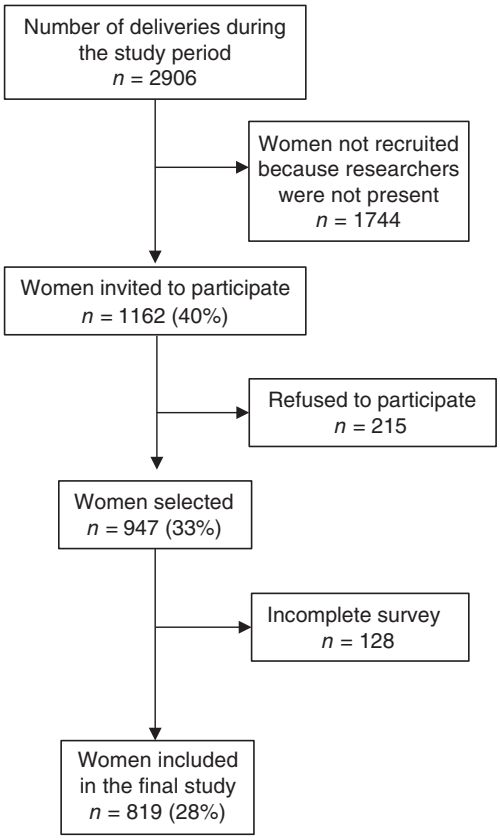

FIGURE 2 Flowchart for selecting the women in the study.

Ethics approval and consent to participate

Study protocols and informed consent forms for trials were reviewed and approved by the National Ethics Review Committee in Mozambique 432/CNBS/16. The study was conducted under the provisions of the Declaration of Helsinki and in accordance with Good Clinical Practice guidelines set up by the WHO and the International Conference on Harmonisation. Participation in the

study was completely voluntary. All the study participants were informed about the purpose of the study and written informed consent was obtained from each study participant. The consent was signed by parent/guardian if the participant was under 18 years of age. Illiterate women were read and explained the consent and the information sheet for the patient and those who verbally agreed to participate in the study signed the consent form with their finger.

RESULTS

In total, 81.5% (947/1162) of the 40% (1162/2906) of eligible women agreed to participate (Figure 2). A total of 819 women (13–45 years) were recruited during delivery and/or in the immediate postpartum period. 103/819 (12.6%) women had HIV infection. Infection was diagnosed during gestation in 67/103 (65.0%) cases, at delivery in 15/103 (14.6%) and before gestation in 21/103 (20.3%). 96/103 (93.2%) of HIV-positive pregnant women were in Stage I of the disease (asymptomatic, one case had persistent lymphadenopathy), 6/103 (5.9%) in Stage II (recurrent infections) and 1/103 (0.9%) in Stage III (weight loss >10%). A total of 86/103 (83.4%) women received anti-retroviral treatment during pregnancy, and the most commonly used regimen was tenofovir disoproxil, lamivudine and efavirenz in 65/86 (75.5%) of cases.

In our study, the frequency of malaria during pregnancy and/or delivery was 101/819 (12.4%): 93 (11.5%) during pregnancy, and 8 (0.9%) at delivery. Malaria and HIV co-infection was found in 17/819 (2%) of pregnant women. 17/103 (16.7%) of women with HIV had an episode of malaria during pregnancy, higher than the incidence of 84/716 (11.7%) in pregnant women without HIV, although with no significant differences ($p = 0.158$) between the two groups.

No significant differences were observed when different obstetric complications (previous abortions, antepartum haemorrhage and pre-eclampsia/eclampsia) were compared (Table 2). However, mean age was significantly higher in HIV-negative women without malaria and lower in HIV-uninfected women with gestational malaria (Table 2). Significant differences were also found when comparing the number of pregnancies, being higher in multiparous HIV-infected women without malaria and in HIV-uninfected women with gestational malaria (Table 2). A larger proportion of HIV-infected women had ≥4 ANC visits than HIV-uninfected women.

When the characteristics of delivery were compared in the different groups and subgroups, significant differences were observed between HIV-infected and non-HIV-infected women, with fewer Caesarean births in infected patients (Table 3). Significant differences were also observed in delivery complications, with urinary tract infection being more frequent in HIV-infected patients, and intrapartum fever in HIV-uninfected women with gestational malaria (Table 3). Regarding newborn characteristics, birth weight was lower in the presence of gestational malaria (both in HIV-infected and uninfected women; Table 4). It was statistically significantly ($p = 0.020$) more likely that newborns would have some of these complications if during pregnancy the mother was co-infected with HIV and malaria (Table 4).

HIV/malaria co-infection was significantly associated with a higher number of stillbirths ($p = 0.02$), asphyxia

TABLE 2 Demographic and obstetric characteristics of pregnant women.

	HIV-infected ($n = 103$)			Non-HIV infected patients ($n = 716$)			Overall	
Variable, by class	A MiP ($n = 17$)	B No MiP ($n = 86$)	p	C MiP ($n = 84$)	D No MiP ($n = 632$)	p	p^*	p^{**}
Age, median years (range)	24.4 (5.0)	26.6 (6.4)	0.186	22.4 (5.6)	23.3 (6.2)	0.237	**<0.001**	**<0.001**
Residence, n (%)			0.497			**0.047**	0.091	0.091
Urban	15/15 (100)	74/81 (91.3)		61/75 (81.3)	516/576 (89.6)			
Semi-urban	0	5/81 (6.2)		7/75 (9.3)	21/576 (3.6)			
Rural	0	2/81 (2.5)		7/75 (9.3)	39/576 (6.8)			
Number of pregnancies, n (%)			0.239			**0.053**	**<0.001**	**<0.001**
1	5/17 (29.4)	11/83 (13.3)		42/81 (51.8)	232/613 (37.8)			
2	5/17 (29.4)	26/83 (31.3)		17/81 (21)	164/613 (26.8)			
≥3	7/17 (41.1)	46/83 (55.4)		22/81 (27.2)	217/613 (35.4)			
Antenatal care visits, n (%)	6/10 (60)	43/62 (69.3)	0.556	27/58 (46.5)	268/478 (56.0)	0.169	0.086	**0.036**
Previous abortions, n (%)	4/17 (23.5)	20/86 (23.3)	0.981	8/84 (9.5)	103/631 (16.3)	0.106	0.724	1.000
Antepartum haemorrhage, n (%)	1/17 (5.9)	3/86 (3.5)	0.641	2/84 (2.4)	28/632 (4.5)	0.368	0.207	0.657
Pre-eclampsia/eclampsia, n (%)	5/17 (29.4)	12/86 (13.9)	0.117	16/84 (19)	89/632 (14.1)	0.227	0.199	0.733

Note: Percentages expressed data of the column. Bold indicates statistically significant value.
Abbreviations: MiP, malaria in pregnancy; No MiP, no malaria in pregnancy.
*All groups (A, B, C, D).
**HIV infected (A + B) versus Non-HIV infected (C + D).

TABLE 3 Delivery characteristics. Clinical complications

Variable, by class	HIV-infected ($n = 103$)			Non-HIV infected patients ($n = 716$)			Overall	
	A MiP ($n = 17$)	B No MiP ($n = 86$)	p	C MiP ($n = 84$)	D No MiP ($n = 632$)	p	p^*	p^{**}
Type of delivery, n (%)			0.790			0.666	0.215	**0.045**
Vaginal	14/17 (82.3)	66/83 (79.2)		57/84 (67.8)	442/630 (70.1)			
Caesarean	3/17 (17.6)	17/83 (20.5)		27/84 (32.1)	188/630 (29.9)			
Clinical complications, n (%)								
Peripartum urinary infection	3/17 (17.6)	11/86 (12.8)	0.593	6/84 (7.1)	28/632 (4.4)	0.223	**0.003**	**0.001**
Intrapartum maternal fever	1/17 (5.8)	3/86 (3.5)	0.641	13/84 (15.5)	16/632 (2.5)	**<0.001**	**<0.001**	1.000

Note: Percentages expressed data of the column. Bold indicates statistically significant value.
Abbreviations: MiP, malaria in pregnancy; No MiP, no malaria in pregnancy.
*All groups (A, B, C, D).
**HIV infected (A + B) versus Non-HIV infected (C + D).

TABLE 4 Neonatal characteristics

Variable, by class	HIV infected ($n = 103$)			Non-HIV-infected patients ($n = 716$)			Overall	
	A MiP ($n = 17$)	B No MiP ($n = 86$)	p	C MiP ($n = 84$)	D No MiP ($n = 631$)	p	p^*	p^{**}
Gestational age, n (%)			0.588			0.931	0.724	0.498
Term delivery	14/17 (82.3)	75/86 (87.2)		71/84 (84.5)	543/621 (86.0)			
Pre-term	3/17 (17.6)	9/86 (10.5)		12/84 (14.3)	81/621 (13.0)			
Post-term	0/17 (0)	2/86 (2.3)		1/84 (1.2)	6/621 (1)			
Neonatal sex, n (%)			0.487			0.256	0.628	0.902
Male	5 (55.5)	29/67 (43.3)		30/59 (50.8)	188/437 (43.0)			
Female	4 (44.4)	38/67 (56.7)		29/59 (49.1)	249/437 (57.0)			
Anthropometrics measures, n (%)								
Neonatal weight (g)	2803.1 (757.7)	3096.6 (483.2)	**0.047**	2806.8 (638.1)	2952.4 (558.2)	**0.032**	**0.008**	**0.063**
Neonatal complications	9/17 (53)	18/86 (20.1)	**0.006**	32/84 (38.1)	231/632 (33.7)	0.425	**0.020**	0.107
Stillbirth	3/17 (17.6)	3/86 (3.5)	**0.023**	6/84 (7.1)	47/632 (7.4)	0.923	0.185	0.563
Apgar <7	5/17 (29.4)	9/84 (10.7)	**0.042**	16/77 (20.8)	114/611 (18.7)	0.654	0.171	0.221
Neonatal jaundice	1/14 (7.1%)	0/84 (0.0%)	0.014	2/84 (2.4%)	4/571 (0.7%)	0.113	**0.025**	0.893

Note: Percentages expressed data of the column; Neonatal complications include stillbirth, low birth weight, Apgar <7, respiratory distress, neonatal fever and neonatal jaundice. Bold indicates statistically significant value.
Abbreviations: MiP, malaria in pregnancy; No MiP, no malaria in pregnancy.
*All groups (A, B, C, D).
**HIV infected (A + B) versus Non-HIV infected (C + D).

($p = 0.042$) and jaundice ($p = 0.02$) (Table 4). Antiretroviral treatment did not influence obstetric morbidity except in women who also had malaria, in whom an increased risk of hypertensive disorder was observed (Table 5).

In multivariate analyses on adverse maternal and neonatal outcomes found in the univariate analyses associated with gestational malaria and/or HIV, we found results very similar to those shown by the univariate analysis. However, with regard to neonatal asphyxia and jaundice as well as HIV infection in women undergoing treatment for pre-eclampsia, statistical significance disappeared. HIV increased the risk of urinary tract infection, while malaria increased the risk of intrapartum maternal fever and was associated with lower neonatal weight, and HIV / malaria co-infection increased the risk of early neonatal death.

DISCUSSION

In low-income and middle-income countries, malaria and HIV are the main causes of indirect maternal mortality [29]. In our series, the overall prevalence of each infection considered separately was ~12% in pregnant women. These figures are lower than those published for *Plasmodium falciparum* infection (24%) in Mozambique [30] and similar to those reported for HIV infection [14]. In our study, it was also observed that pregnant women with malaria were younger and usually primiparous, unlike those infected with HIV, as already described in the literature [14, 16].

In general, *HIV infection* is asymptomatic, and its diagnosis depends on women agreeing to undergo offered and recommended screening tests during pregnancy and delivery. Between 60% and 70% of HIV-infected women in our series had adequate pregnancy control, which was

TABLE 5 The impact HIV, malaria and HIV/malaria co-infection on maternal and neonatal morbidity and neonatal mortality

	Multivariate[a]		
	OR	**95% CI**	***p*-value**
Peripartum urinary infection			
HIV	**3.31**	**1.49–7.33**	**0.003**
Malaria	1.60	0.64–4.03	0.317
HIV/Malaria	0.91	0.17–4.93	0.911
Intrapartum maternal fever			
HIV	1.67	0.45–6.11	0.441
Malaria	**5.83**	**2.47–13.76**	**0.000**
HIV/Malaria	0.29	0.24–3.55	0.335
Neonatal death			
HIV	0.31	0.72–1.31	0.111
Malaria	0.75	0.25–2.17	0.595
HIV/Malaria	**11.62**	**1.33–101.24**	**0.026**
Neonatal respiratory distress			
HIV	0.50	0.12–2.17	0.358
Malaria	1.81	0.83–3.96	0.137
HIV/Malaria	3.13	0.34–28.47	0.312
Neonatal jaundice			
HIV	_		0.999
Malaria	3.50	0.61–19.98	0.159
HIV/Malaria	_		0.998
	Marginal effect	95% CI	p-value
Neonatal weight (g)			
HIV	94.10	−30.67 to 218.81	0.139
Malaria	−150.14	**−275.44 to − 24.85**	**0.019**
HIV/Malaria	−81.89	−389.10 to 225.29	0.601

Note: Bold indicates statistically significant value.
[a]Models control for mother's age, number of previous pregnancies and gestational age at delivery.

significantly more than in HIV-uninfected pregnant women. Furthermore, approximately two-thirds of HIV infections were diagnosed during a gestational check-up or at the time of delivery, and only 20% before pregnancy. These data are similar to those reported in some studies conducted in Mozambique, which indicated that 72.5% of HIV infection cases were diagnosed during pregnancy [31] and that 7% of women attending ANC were HIV-infected [32]. However, other publications have observed that only 52% of HIV-positive women of childbearing age are aware of the presence of the infection [33]. In this context, the data suggest on the one hand that HIV screening offered to pregnant women is widely accepted, and on the other hand, that screening for HIV infection increases gestational control. In our study, 84% of HIV-infected pregnant women received anti-retroviral treatment, being the regimen of choice recommended by WHO in 2016 (tenofovir, lamivudine and efavirenz) [34], but they recently switched from efavirenz to dolutegravir [35] although in another series of pregnant women studied in Mozambique, the percentage of HIV-positive pregnant women on treatment was markedly lower, ranging between 56% [31] and 61% [32]. Another important aspect, which however was not evaluated in our study, is low adherence to anti-retroviral treatment; in some series, only 37% have an undetectable viral load [33]. Consequently, it cannot be automatically assumed that a prescription for treatment indicates adherence.

In our series, HIV infection in pregnant women was not globally associated with maternal morbidity, according to the presence and number of previous abortions, antepartum haemorrhage or pre-eclampsia/eclampsia, although there was a trend towards a higher frequency of previous abortions in patients with HIV infection ($p = 0.064$). The design of our study did not allow us to evaluate other causes of maternal morbidity, such as severe anaemia or urinary tract infection, which in some studies are more frequent in HIV-infected pregnant women [12–16, 36].

With regard to *delivery*, we observed two significant differences between HIV-infected and HIV-uninfected pregnant women. First, caesarean sections were less frequent in infected patients. In some situations, this procedure is recommended for prevention of mother-to- child transmission of HIV [36], both in Mozambique and in neighbouring countries. Due to the high cost of caesarean section, required infrastructure, and health care workers' concerns about the risk of occupational transmission of HIV and the possible complications of the procedure, caesarean section was not indicated, as has been pointed out in other studies [13, 37]. Secondly, pregnant women with HIV infection more frequently presented peripartum urinary tract infection than seronegative women (12.6% vs. 4.5%), as reported in other publications [38, 39]. Considering that the prevalence of asymptomatic bacteriuria is similar in women with or without HIV infection [40], it is likely that the smaller number of Caesarean sections plays a role in the higher incidence of peripartum urinary tract infections. In our series, HIV infection did not appear to influence newborn morbidity and mortality, also reflected in another study [31].

Globally, it has been estimated that 1 million pregnant women per year suffer from *malaria and HIV* [14, 18] in sub-Saharan Africa. In our series, this co-infection accounted for 2% of pregnant women, similar to the proportion described in East Africa (0.94% in Ethiopia) and much less than in West Africa (37% in Nigeria) [18].

With regard to pregnancy, co-infection was not observed to increase complications, although HIV/malaria co-infection was significantly associated with the development of preeclampsia when HIV-infected patients receiving anti-retroviral treatment were evaluated separately. However, this association is not found in multivariate analysis. The effect between HIV infection on treatment and an increased risk of the onset of preeclampsia has been widely reported in the literature [12, 15, 41]. The data are controversial, and malaria infection has the potential to be an important factor for hypertensive disorders, but it has not been confirmed as such as the studies on this has poor design and marked biases [42, 43].

However, HIV/malaria co-infection was significantly associated with an increase in urinary tract infections around delivery compared with the rest of the groups in our series. This observation is similar to that published in the literature, where the authors also showed a greater variety of bacterial species and a higher prevalence of resistant strains [38].

Finally, with respect to the newborn, HIV/malaria co-infection in our series significantly increased the frequency of stillbirths. In this sense, the results are similar to those described in the literature [44, 45] and can be explained as placental involvement in both infections.

Limitations

This study has several limitations, such as: (i) the omission of including women from rural areas where deliveries are carried out in health centres or at home, as this study was performed in the main urban hospital in the province; (ii) limited documentation in the patient's medical records because record-keeping is poor during ANC and, less so, during admissions; (iii) underestimation of malaria diagnosis, since diagnostic tests were only performed in the presence of clinical manifestations; (iv) difficulty in accessing information on pregnancy in women without malaria or HIV infection, (v) lack of diagnostic resources in the hospital, which prevented the collection of laboratory values (blood count, CD4 and HIV viral load) in a significant number of pregnant women as well as urine culture in women with suspected urinary tract infection for confirmation and (vi) lack of human resources to offer the survey to all women who gave birth during the study period.

CONCLUSIONS

In summary, in HPT, Mozambique, the prevalence of malaria and HIV infection among women of childbearing age remains high and further contributes to complications during pregnancy, childbirth and increases the frequency of stillbirths. HIV screening should be a priority among women of reproductive age, as only one-fifth of HIV-infected women know their HIV status before pregnancy. An improved approach to quality of care has the potential to find significant benefits for all mothers and newborns at Tete Provincial Hospital.

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DATA AVAILABILITY STATEMENT

All relevant data related to the study were included in the article. The data will not be publicly shared to protect the anonymity of participants. Anonymised data used for analysis are available from the corresponding author on reasonable request.

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