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Treatment dropout after pregnancy: a study of women living with HIV in Rio de Janeiro

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ABSTRACT

Despite the investment in prevention of mother-to-child transmission of HIV, there is still little data about the proportion of women that are retained in treatment after pregnancy in Brazil. Research worldwide shows that a significant proportion of women drop out of treatment after pregnancy. The aim of this study was to identify factors associated with treatment dropout of women that received prenatal care at a federal hospital in Rio de Janeiro between 2016 and 2017 and abandoned treatment after pregnancy. This was a retrospective cohort study using data on prescription refills and hospital medical records. Cross-sectional analysis of data from 454 women showed that 18% were not on cART after pregnancy. Illicit drug use during pregnancy, being less than 35 years old, and being aware of HIV diagnosis before conceiving but not taking cART were factors associated with treatment interruption postpartum. The high prevalence of interruption of HIV treatment after pregnancy suggests that there is a need for better post-natal care to increase adherence in this population.

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Women living with HIV; postpartum retention; mother-to-child transmission

Introduction

The incidence of pregnancy among women living with HIV is high worldwide and in Brazil it is increasing (Brazil, 2018). The current World Health Organization (WHO, 2017) recommendation for HIV treatment is continuous combined antiretroviral therapy (cART) during and after pregnancy. This is a strategy aligned to the 90–90–90 goal for 2020, which aims for 90% of people living with HIV to know the seropositive status, 90% of them to be on cART, and 90% to achieve viral suppression (UNAIDS, 2015).

In Brazil, antiretrovirals are made available free of charge in the public health system, known as the Unified Health System (Portuguese acronym: SUS). All prescriptions and refills in the Unified Health System, including antiretrovirals, are tracked by a database called the System for Logistical Control of Medications (Portuguese acronym: SICLOM). Despite advances in drugs to treat HIV infection and prevent mother-to-child transmission (MTCT), the rate of deaths registered in Brazil is still high. According to the most recent government data, the prevalence of HIV in pregnant women in Brazil is 0.29% (Brazil, 2019) and the national rate of mother-to-child HIV transmission is 2% (Domingues et al., 2018). Similarly, although the rate of MTCT of HIV has been decreasing in recent years in most countries due to cART use during pregnancy, the proportion of women who interrupt treatment after pregnancy worldwide remains high and it represents a challenge to combating the epidemic (Bailey et al., 2014; Kreitchmann et al., 2016; Nachega et al., 2012 Psaros et al., 2015;). In light of this, it is important to identify the principal drivers of treatment interruption.

Brazil's public healthcare system has established reference centers that provide care for women living with HIV during pregnancy, as a strategy to prevent MTCT. There is evidence that some women face multiple barriers to continuing HIV treatment (Bailey et al., 2014; Giuliano et al., 2016; Kreitchmann et al., 2016; Myer & Phillips, 2017; Nachega et al., 2012; Psaros et al., 2015; Sibanda et al., 2013). Nevertheless, literature about barriers to adherence to treatment among women living with HIV either during prenatal care and postpartum remains relatively scarce (Bailey et al., 2014; Kreitchmann et al., 2016; Myer & Phillips, 2017; Nachega et al., 2012; Psaros et al., 2015).

A number of studies have demonstrated an association between the presence of depressive symptoms

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and insufficient adherence and retention to treatment of people living with HIV (Medley et al., 2004; Nachega et al., 2012; Zuniga et al., 2016). There is also evidence that alcohol and drug use are related to suboptimal retention in care (Bardeguez et al., 2008; Nachega et al., 2012). However, there is scant data about treatment dropout after pregnancy in Brazil.

There is evidence that irregular adherence to HIV treatment can have negative consequences such as increased chances of transmission, hospitalization, and cART failure (Giordano, 2011). Another negative consequence for women of childbearing age is the increased risk of MTCT if they have another pregnancy (Stewart et al., 2014). According to a systematic review, the timing of diagnosis influences the risk of treatment dropout insofar as women who were already aware that they were living with HIV at the time of conception are more likely to adhere to antiretrovirals than those diagnosed during pregnancy (Omonaiye et al., 2018). In addition, a multicentric study in Latin America found that older mothers were more likely to adhere to antiretrovirals postpartum than younger mothers (Kreitchmann et al., 2016)..

In Rio de Janeiro, pregnant women living with HIV are referred to a specialized center for the Prevention of Mother-to-Child Transmission (PMTCT). Although PMTCT centers have substantially reduced the rate of MTCT, the proportion of women that continue regular treatment after pregnancy in Rio de Janeiro remains unknown. The aim of this study is to estimate the proportion of women that interrupted treatment after pregnancy and identify factors associated with treatment dropout of women that received prenatal care at a PMTCT center at the Hospital Federal dos Servidores do Estado (HFSE) between 2016 and 2017 and interrupted treatment after pregnancy.

Methods

This was a cross-sectional retrospective study that analyzed data on women living with HIV to identify behavioral risk factors for treatment abandonment. This study was submitted and approved by HFSE Institutional Review Board (protocol number: 000.604)..

The Brazilian Unified Health System adopts a policy of treatment by territories, therefore, after having specialized prenatal and postpartum care, women continue treatment at the primary care clinic closest to their residence.

Participants

Women living with HIV who initiated specialized prenatal care at a PMTCT center at the HFSE between January 2016 and December 2017 were included. By that time, Brazilian guidelines recommended continuous use of cART for all patients living with HIV (Brazil, 2015). We excluded women who died during or after pregnancy and women who had become pregnant again when we queried SICLOM. The standard of care at HFSE is for pregnant women living with HIV to be prescribed antiretrovirals based on national guidelines.

Data collection

During routine obstetric visits, clinical and laboratory data were collected from participants in our ongoing cohort. These data were entered into a database and subsequently utilized in the present analysis. We included sociodemographic information (age at delivery, years of education, income, marital status, ethnicity, type of residence, and state of birth), data on illicit and licit drug use before and during pregnancy, clinical and obstetrical information (number of prenatal care appointments, delivery outcome, and history of HIV treatment before pregnancy) and laboratory data (viral load level – copies/mL – at delivery and other sexually-transmitted infections (STIs) during pregnancy). Ethnicity was divided into two categories: white and non-white.

In addition, we queried SICLOM to determine whether participants were regularly refilling the antiretrovirals that they were prescribed. SICLOM is an online platform of SUS used by public pharmacies to track antiretroviral prescription refills. Every person registered to receive antiretroviral medicines who does not refill a prescription for 90 days has his or her account deactivated, although the inactive account remains in the system. Treatment dropout was defined as having an inactive SICLOM record..

Based on SICLOM account status, we divided the cohort into two groups: those considered retained in care and those who interrupted treatment; data with these two possible outcomes were compared. In addition, we analyzed the dates when antiretroviral prescriptions were filled according to SICLOM in order to estimate the number of weeks between delivery and the interruption of cART uptake.

Data analysis

Socioeconomic, behavioral, clinical, obstetrical, and laboratory data were assembled for all participants. As noted above, we defined the interruption of cART as an inactive SICLOM record. Differences in categorical variables were quantified using Pearson's chi-squared test. Variables with a p-value less than 0.2 in the chi-squared test were included as the predictor variables in

a logistic regression model in which the response variable was whether the patient had an inactive record in SICLOM. A variable with an odds ratio whose confidence intervals did not overlap with one was considered a significant risk factor for an inactive SICLOM record. All analyses were performed using the Statistical Package for the Social Sciences (SPSS).

Results

Among the 469 women referred to specialized prenatal care at HFSE between January 2016 and December 2017, fifteen were excluded: thirteen because they had become pregnant again when we queried SICLOM and two died during or shortly after childbirth (Figure 1).

A total of 454 women living with HIV who received prenatal care at HFSE were included in the study. Most of participants were 20–34 years old (71.4%), approximately 20% were older than 35, and 8.6% were adolescents. The majority of the women were self-described as non-white (76%), from the southeast of Brazil (88.5%), in a stable relationship with a partner (62.5%), and had secondary (47.6%) or primary (45.8%) education.

Only 41.7% of women had any income and 82.5% reported household income less than three times the Brazilian minimum wage. Around 40% reported living in favela areas and 1.6% did not have indoor plumbing in the home.

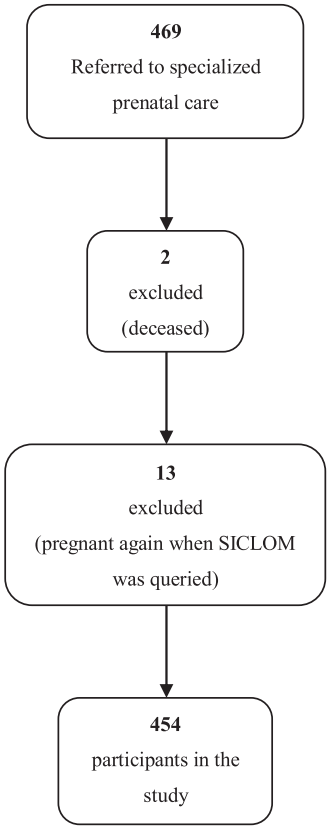

Figure 1. Flowchart of participants for analysis of postpartum cART interruption.

A total of 82 (18%) women admitted to having used an illicit drug (marijuana or cocaine) at some time in their lives and 27 (6%) had done so during pregnancy. About half, 231 (51.3%) reported that they had consumed alcohol before pregnancy and 64 (14%) during pregnancy. Approximately one-third of the participants (n=149, 33%) had used tobacco prior to conceiving and 68 (15%) during pregnancy.

A total of 262 (57.8%) knew their HIV positive status when they became pregnant, although only 172 (37.9%) were on cART at conception. A total of 36 (8%) lost at least one child at some point of in their lives and 146 (32.5%) reported that they had had an abortion. For 25.8% of the participants, the abortion was spontaneous, while for 4.7% it was intentional abortion, and a further 2% had had both kinds. Almost all participants were infected via sexual transmission (96.7%).

Clinical and laboratory data show that 311 (70.3%) had undetectable HIV viral load near delivery, 66 (14.6%) had at least one positive test result for syphilis during pregnancy, and 78 (17.3%) had another STI during pregnancy..

About 10% of the participants were hospitalized at some point during pregnancy and 4.8% experienced clinical complications postpartum (e.g., postpartum infections). Regarding specialized prenatal care appointments, about 73% attended at least six consultations and 11.2% had premature birth..

Almost all of the women delivered a single living child (99.3%) and 1.5% had twins. Regarding the mode of delivery, 181 (40.5%) of women had vaginal delivery and 266 (59.5%) had a C-section (data were missing for seven women). Approximately 13% of the participants had tubal ligation at delivery.

The prevalence of women with an inactive SICLOM account as of October 2018 was 18.3% (n=83). To examine these data in detail, we also analyzed the dates of cART prescription refills from delivery to 18 months after delivery for these women. The median duration of cART interruption after delivery of these women was 4 months [IQR=3–4]. Detailed analysis of the dates of cART withdraw revealed that 43% (n=160/369) of the women categorized as having an active register in SICLOM as of October 2018 interrupted treatment at least once up to 18 months after delivery. Considering the entire sample, around 50% (n=227/446) interrupted treatment at least once up to 18 months after delivery.

Bivariate analysis (Table 1) identified variables that were significantly associated with an inactive SICLOM account (p<0.05) or approached significance (p< 0.1).

Table 1. Bivariate analysis of baseline sociodemographic, virologic, behavioral, clinical, and obstetric characteristics of women living with HIV at a PMTCT center (HFSE) associated with treatment dropout after pregnancy using Fisher's Exact Test ($n = 545$).

Variable	Active n (%) 371 (81.7)	Inactive n (%) 83 (18.3)	*p*-value
Ethnicity *n*=445			.116
White	93 (86.9)	14 (13.1)	
Non-white	270 (79.9)	68 (20.1)	
Geographic origin *n*=454			.704
Southeast of Brazil	327 (81.3)	75 (18.7)	
Other	44 (84.6)	8 (15.4)	
Age *n*=452			**.009**
Less than 35 years	287 (79.5)	74 (20.5)	
35 years or more	83 (92.2)	8 (8.8)	
Marital status *n*=445			.524
With partner	225 (80.9)	53 (19.1)	
Without partner	140 (83.8)	27 (16.2)	
Income *n*=444			.534
Any	154 (83.2)	31 (16.8)	
None	209 (80.7)	50 (19.3)	
Residence *n*=443			.526
Slum areas	141 (80.6)	34 (19.4)	
Not slum areas	223 (83.2)	45 (16.8)	
Illicit drug use before pregnancy *n*=450			.525
Yes	66 (79.5)	17 (20.5)	
No	304 (82.8)	63 (17.2)	
Illicit drug use during pregnancy *n*=450			**.038**
Yes	18 (66.7)	9 (33.3)	
No	352 (83.2)	71 (16.8)	
Alcohol use during pregnancy *n*=450			1.000
Yes	53 (82.8)	11 (17.2)	
No	317 (82.1)	69 (17.9)	
Smoking during pregnancy *n*=449			.120
Yes	51 (75.0)	17 (25.0)	
No	318 (83.5)	63 (16.5)	
Aware of HIV and not on ARV before pregnancy *n*=445			**.000**
Yes	69 (69.0)	31 (31.0)	
No	295 (85.5)	50 (14.5)	
Viral Load at delivery *n*=441			.598
Undetectable	256 (82.6)	54 (17.4)	
Detectable	105 (80.2)	26 (19.8)	
Syphilis *n*=451			1.000
Yes	54 (81.8)	12 (18.2)	
No	315 (81.8)	70 (18.2)	
HIV diagnosis during pregnancy *n*=449			.711
Yes	215 (81.1)	50 (18.9)	
No	152 (82.6)	32 (17.4)	
Prenatal consultations *n*=439			.325
More than 6	267 (83.4)	53 (16.6)	
Less than 6	94 (79.0)	25 (21.0)	
Gestational age at birth *n*=394			1.000
Up to 36 weeks	37 (84.1)	7 (15.9)	
37 weeks or more	294 (84.0)	56 (16.0)	
Pregnancy outcome *n*=453			1.000
Living newborn	368 (81.6)	83 (18.4)	
Stillbirth	2 (100)	0 (0)	
Delivery *n*=447			.104
Vaginal	155 (85.6)	26 (14.4)	
C-section	211 (79.3)	55 (20.7)	

Variables associated with an inactive account in the bivariate analysis were illicit drug use during pregnancy (p=0.03), being younger than 35 (p=0.09), and being aware of HIV serostatus at conception but not adhering to cART (p<0.001)..

Variables that showed a possible association with treatment dropout outcome (p<0.2) in the bivariate analyses as well as those that were described as associated with treatment dropout in the literature were included in the multivariate logistic regression analysis. Those variables were: age (divided into categories), ethnicity (white or not), marital status (with a partner or not), illicit drug use during pregnancy (yes or no), alcohol use during pregnancy (yes or no), awareness of HIV status and cART adherence at conception (yes or no), positive test for syphilis (yes or no), smoking during pregnancy (yes or no), number of specialized prenatal care consultations attended (more than 6 or less), and delivery type (vaginal or C-section). Of those, only age (p=0.01), illicit drug use during pregnancy (p=0.04), and being aware of HIV status but not using cART at conception (p=0.01) were significantly associated with treatment interruption postpartum in the multivariate regressionTable 2..

Discussion

Continuing antiretroviral treatment after pregnancy is important for maternal health and to reduce the chance of MTCT in future pregnancies. A number of studies have shown that the proportion of women retained in treatment decreases after delivery compared to during pregnancy (Nachega et al., 2018). Adherence to cART is often higher during pregnancy than in the postpartum period as the mother is concerned about transmitting the virus to the baby prenatally or during delivery (Vitalis, 2013).

Among our study participants, the rate of C-sections (58.6%) was higher than among the general population of Brazil (45%). In the present study, approximately 70% of pregnant women had < 400 copies of HIV RNA near delivery, defined as 34–36 weeks gestation. This proportion is similar to previous studies at our PMTCT center in Rio de Janeiro, in which the percentage ranged from 65 to 75% (Joao et al., 2012; Teixeira et al., 2015).

Our findings also indicate that illicit drug use during pregnancy is associated with postpartum treatment interruption. The use of alcohol, illicit drugs, and tobacco are strongly discouraged during pregnancy because they are harmful to the child's health. Kassada et al. (2013) reported that the feeling of guilt could be a barrier for pregnant women who use drugs to disclose this to health workers and receive treatment. This scenario is unfavorable to women who use drugs and can be an additional obstacle to adherence to antiretrovirals. Other studies conducted in Brazil (Batista et al., 2014;

Table 2. Multivariate regression analysis of the risk of treatment dropout after pregnancy of women living with HIV at a PMTCT center (HFSE).

	Unadjusted association			Adjusted association		
Variable	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Age	.629	.407–.972	.037	.539	.326–.892	**.016**
Non-white	.598	.321–1.113	.105	1.509	.753–3.021	.246
Without partner	1.221	.734–2.032	.441	.641	.352–1.167	.146
Illicit drug use during pregnancy	2.479	1.070–5.741	0.34	2.919	1.007–8.467	**.049**
Alcohol use during pregnancy	.954	.474–1.919	.894	.459	.158–1.333	.152
Aware of HIV but not on cART at conception	2.651	1.577–4.454	.000	2.668	1.471–4.836	**.001**
Tobacco use during pregnancy	1.683	.913–3.102	.096	1.493	.611–3.649	.380
Syphilis during pregnancy	1	.508–1.968	1.00	.716	.317–1.614	.420
< 6 prenatal care consultations	.746	.439–1.269	.280	1.095	.583–2.058	.777
C-section	1.554	.933–2.589	0.91	1.485	.841–2.629	.173

Lopes & Silva, 2012; Schilkowsky et al., 2011; Teixeira et al., 2013; Tiezmann et al., 2013 Zago et al., 2012) and in other countries (Amirkhanian et al., 2018; Bardeguez et al., 2008; Levison et al., 2017; Nachega et al., 2012) also reported an association between illicit drug use and treatment interruption among people living with HIV. Some studies discuss the association between drug use and social vulnerability (Nachega et al., 2012; Teixeira et al., 2013). Motherhood for a woman living with HIV can be complex and is influenced by multiple factors at different scales, including the individual, institutional, and interpersonal levels. As many cART regimens must be taken with food at the same time every day, the patient needs to have a relatively stable living situation. Our findings also show that the incidence of treatment interruption is higher among younger women; this association has been described in other studies (Meade et al., 2019; Siddiqui et al., 2014).

Within our study population, there was also a high rate of treatment interruption after pregnancy among women who were aware of their HIV status before pregnancy but were not in use of cART. We consider it unlikely that these women did not have a cART prescription at their last medical visit before becoming pregnant due to the fact that universal cART use was recommended after 2015 HIV guidelines for all people living with HIV (WHO, 2017). Investigating the reasons for treatment abandonment before conception was not the principal objective of this study. However, our results indicate that abandonment prior to pregnancy was associated with dropout from treatment during pregnancy. Zago et al. (2012) conducted a study with 250 patients in Vitória, Brazil, and observed that a history of previous abandonment was an important factor for predicting a new interruption in a study conducted with adults living with HIV.

The main findings of this study reveal that, for many women, retention in treatment may be a dynamic process with periods of cART adherence interspersed with interruption. The prevalence of treatment dropout in October 2018 was 18%. However, when we examined the dates when the study participants filled their antiretroviral prescriptions over the course of treatment, it became apparent that interruptions and resumptions occurred frequently after delivery. The factors associated with this dynamic process are not completely understood. Previous research on postpartum retention in HIV treatment has demonstrated the importance of acceptance and multidisciplinary intervention by healthcare providers who treat pregnant women living with HIV with the aim of ensuring continuation of care after pregnancy (Nachega et al., 2012; Phillips et al., 2018; Teixeira et al., 2013). It is crucial that health workers who treat this subpopulation in public hospitals attempt to identify women who do not accept their diagnosis, lack social support, report prior treatment abandonment, and use illicit drugs during pregnancy. Adequate support can reduce the anxiety and panic triggered by HIV diagnosis, diminish the deleterious effects of stigma, and promote self-sufficient adherence to cART.

Conclusions

The results of the current study revealed that 18% of women living with HIV had interrupted treatment in October 2018, despite having specialized prenatal care at a PMTCT Reference Hospital. According to our data, possible strategies to increase the retention of this population in care should include identification of illicit drug use and history of previous interruption of HIV treatment. Further studies focusing on these issues could help better elucidate factors underlying intermittent adherence.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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