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Use of antiretrovirals in pregnant women living with HIV in Brazil: A retrospective cohort, 2014-2019

Uso de antirretrovirais em gestantes vivendo com HIV no Brasil: Coorte retrospectiva, 2014-2019

Uso de antirretrovirales en mujeres embarazadas que viven con VIH en Brasil: Coorte retrospectiva, 2014-2019

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Abstract
HIV cases in Brazilian women primarily occur during their reproductive years, with increasing detection rates among pregnant women in recent years. Changes in antiretroviral therapy (ART) protocols have influenced the management of pregnant women living with HIV (PWLHIV). Objective: To evaluate the use of antiretrovirals (ARVs) and the sociodemographic profile of PWLHIV in Brazil between 2014 and 2019. Methods: A retrospective cohort study was conducted using data from the Drug Logistics Control System (SICLOM). Women aged 14 years or older with at least one ARV dispensation during pregnancy were included. Pregnant women were categorized as those with prior ART use or those initiating ART during pregnancy. Descriptive and analytical statistics were applied. Results: The study included 34,659 pregnant women: 53.3% had prior ART use, and 46.7% initiated ART during pregnancy. Most were aged 30-39 years (32.6%), non-white (46.7%), without a partner (38.5%), and had 8-11 years of education (27.7%). The mean ART duration was 174.2 days, with adverse drug reactions reported by 14.3%. ARV regimens evolved during the study period, with lopinavir + ritonavir/zidovudine + lamivudine used until 2016, tenofovir + lamivudine + efavirenz in 2017, and tenofovir + lamivudine/raltegravir from 2018 onwards. Conclusion**:** ART use among PWLHIV aligned with national protocols, reflecting consistent practices. However, the findings highlight social vulnerabilities and the need for improved access to healthcare. Enhancing reproductive health services in Brazil remains essential to reduce vertical transmission and ensure comprehensive care.
Keywords: Pregnant women; Antiretrovirals; Brazil.

Resumo
No Brasil, o HIV em mulheres ocorre principalmente na fase reprodutiva, com aumento das taxas de detecção entre gestantes. Alterações nos protocolos de terapia antirretroviral (TARV) têm influenciado o manejo das gestantes vivendo com HIV (GVHIV). Objetivo: Avaliar o uso de antirretrovirais (ARVs) e o perfil sociodemográfico das GVHIV no Brasil entre 2014 e 2019. Métodos: Estudo de coorte retrospectivo com dados do Sistema de Controle Logístico de Medicamentos (SICLOM). Foram incluídas mulheres com 14 anos ou mais e ao menos uma dispensação de ARV durante a gestação. As gestantes foram classificadas entre usuárias prévias de TARV e iniciantes na gestação.

Análises descritivas e analíticas foram realizadas. Resultados: Incluíram-se 34.659 gestantes: 53,3% usaram TARV previamente e 46,7% iniciaram na gestação. A maioria tinha 30-39 anos (32,6%), era não branca (46,7%), sem parceiro (38,5%) e com 8-11 anos de estudo (27,7%). O tempo médio de TARV foi de 174,2 dias, com 14,3% relatando reações adversas. Os esquemas de ARVs variaram: lopinavir + ritonavir/zidovudina + lamivudina até 2016, tenofovir + lamivudina + efavirenz em 2017, e tenofovir + lamivudina/raltegravir a partir de 2018. Conclusão: O uso de TARV entre GVHIV seguiu os protocolos nacionais, refletindo práticas consistentes. Contudo, os dados destacam vulnerabilidades sociais e a necessidade de ampliar o acesso à saúde. Melhorar os serviços de saúde reprodutiva é essencial para reduzir a transmissão vertical e garantir cuidado integral.
Palavras-chave: Gestantes; Antirretrovirais; Brasil.

Resumen
En Brasil, los casos de VIH en mujeres ocurren principalmente durante la etapa reproductiva, con un aumento en las tasas de detección entre mujeres embarazadas en los últimos años. Los cambios en los protocolos de terapia antirretroviral (TAR) han influido en el manejo de las mujeres embarazadas que viven con VIH (MEVVIH). Objetivo: Evaluar el uso de antirretrovirales (ARV) y el perfil sociodemográfico de las MEVVIH en Brasil entre 2014 y 2019. Métodos: Se realizó un estudio de cohorte retrospectivo con datos del Sistema de Control Logístico de Medicamentos (SICLOM). Se incluyeron mujeres de 14 años o más con al menos una dispensación de ARV durante el embarazo. Las embarazadas se clasificaron entre aquellas con uso previo de TAR y aquellas que iniciaron TAR durante el embarazo. Se aplicaron análisis descriptivos y analíticos. Resultados: Se incluyeron 34.659 mujeres embarazadas: el 53,3% usaron TAR previamente y el 46,7% lo iniciaron durante el embarazo. La mayoría tenía entre 30 y 39 años (32,6%), no eran blancas (46,7%), no tenían pareja (38,5%) y tenían entre 8-11 años de educación (27,7%). El tiempo promedio de TAR fue de 174,2 días, con reacciones adversas reportadas por el 14,3%. Los regímenes de ARV variaron: lopinavir + ritonavir/zidovudina + lamivudina hasta 2016, tenofovir + lamivudina + efavirenz en 2017 y tenofovir + lamivudina/raltegravir desde 2018. Conclusión: El uso de TAR entre las MEVVIH siguió los protocolos nacionales, reflejando prácticas consistentes. Sin embargo, los datos destacan vulnerabilidades sociales y la necesidad de mejorar el acceso a la atención médica. Fortalecer los servicios de salud reproductiva es esencial para reducir la transmisión vertical y garantizar un cuidado integral.
Palabras clave: Mujeres embarazadas; Antirretrovirales; Brasil.

1. Introduction

In Brazil, human immunodeficiency virus (HIV) infection is concentrated among sex workers, drug-injecting people, trans people, people deprived of liberty, gay people, and other men who have sex with men. However, a substantial increase in cases of HIV in pregnant women (Campany et al., 2021) has been reported in recent years.

The latest Clinical Monitoring Report on Pregnant Women Living with HIV (PWLHIV) published by the Ministry of Health in 2019 has reported an increase in the estimated number of these women from seven thousand in 2010 to 10.3 thousand in 2018 (Brasil, 2019).

HIV treatment in pregnant women and the rest of the population follows the recommendations of the Ministry of Health's clinical protocols for managing the virus. The currently recommended ART combines tenofovir/lamivudine (nucleoside analog reverse transcriptase inhibitors) associated with dolutegravir, an integrase inhibitor. Besides ART, PWLHIV must be linked to services that offer monitoring of their serological and immunological condition through HIV viral load (VL-HIV) tests, T-CD4+ lymphocyte count, and, if necessary, blood genotyping test (Brasil, 2022).

The studies that address the use of ARV in pregnant women or the profile of these women are local studies with municipal or state coverage or national studies performed to identify the prevalence of HIV in pregnant women. It is crucial to conduct studies with national coverage that provide more recent data on the use of ARV in the care of PWLHIV in Brazil. Thus, this study aimed to describe the use of ARV in PWLHIV from 2014 to 2019.

2. Methods

This descriptive and analytical retrospective cohort study (Toassi & Petry, 2021) was quantitative in nature (Pereira et al., 2018) and used descriptive statistics with mean values, standard deviations (Shitsuka et al., 2014).

This descriptive and analytical retrospective cohort study was conducted with national data from the Drug Logistics Control System (SICLOM) from January 2014 to December 2019. SICLOM is an administrative, online access system in which sociodemographic data and all ARV dispensations are recorded.

All individual data were anonymized for analysis. The anonymization process was conducted using the Python language's Dedupe package. Thus, the variable name, mother's name, date of birth, and individual tax registration number (CPF) were anonymized and used to create the SICLOM ID variable, employed to identify each individual in the cohort.

Women living with HIV/AIDS, on ART in the SUS, aged 14 years or over, and with at least one ARV dispensation in the pregnant category in SICLOM from January 2014 to December 2019 were included in the study. Pregnant women who used ARV in 2014 but started pregnancy in 2013 were excluded from the study. The pregnant women included in the study were classified according to when they started ART:

i. Pregnant women previously using ART: Women registered in SICLOM in the "Pregnant" category during the follow-up period but who had previously been dispensed ARV in the "Adult" category in SICLOM.
ii. Pregnant women who started ART during pregnancy: Women registered in SICLOM in the "Pregnant" category during the follow-up period and had not previously been dispensed ARV.

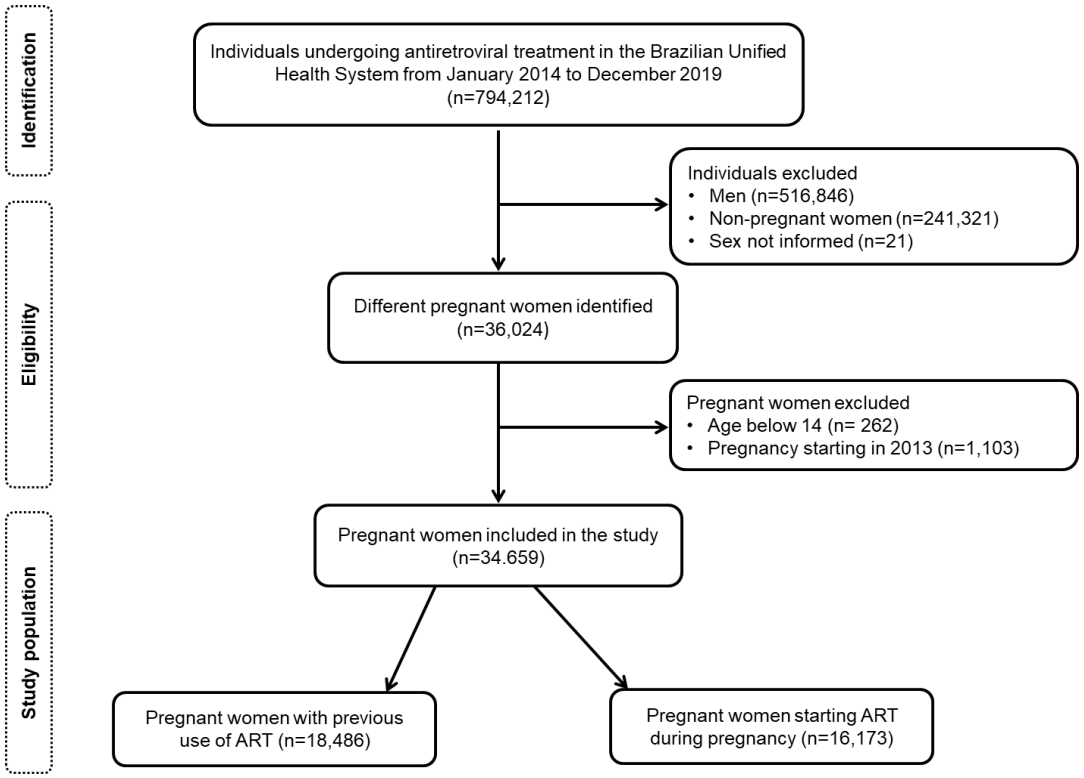
The variables investigated were ART-related variables (ART onset year, antiretroviral regimen used, women on ART before pregnancy, women starting ART during pregnancy, adverse drug reaction, and mean ART treatment time), sociodemographic variables, and number of pregnancies during the study period. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) software version 22. The descriptive analysis comprised the distribution of frequencies for categorical variables and measures of central tendency for quantitative variables. Data normality was assessed using the Shapiro-Wilk test to determine whether the data were parametric or non-parametric. The Student's T-test was used for parametric data, and the Mann-Whitney test was adopted for non-parametric data to compare medians for quantitative variables. Pearson's chi-square test (x^2) was performed to compare the proportions of categorical variables. A significance level of 5% ($p<0.05$) was considered in all analyses.

3. Results

Pregnant women

A total of 794,212 thousand individuals on ART were identified in the SICLOM database from 2014 to 2019: 516,846 men and 277,345 women, and 34,659 women living with HIV on ART met the eligibility criteria for the study (Figure 1).

Figure 1 – Flowchart of inclusion of individuals in the cohort. Brazil, 2014-2019.



Source: Prepared by the authors.

Pregnancies

The characteristics of PWLHIV undergoing treatment in the SUS are shown in Table 1. Pregnant women aged 30-39 (32.6%) prevailed in the total population. We identified a higher proportion of non-white pregnant women (46.7%). When assessing whether or not they had a partner, most women were without a spouse (38.5%). The highest percentage of pregnant women (27.7%) had 8-11 schooling years. The pregnant women had between one and five pregnancies, most with a single pregnancy during the study period (88.3%). A 14.3% adverse drug reaction (ADR) was recorded in these pregnant women. Practically all pregnant women were Brazilian (99.9%), and the highest percentage (34.6%) lived in the Southeast region. The pregnant women included in the study had a median age of 27 years and a mean ART time of 174.2 days during pregnancy. Among the 34,659 pregnant women included in the study, when comparing pregnant women according to previous exposure or not to ART, we can observe that 18,486 (53.3%) pregnant women had previously used ART and 16,173 (46.7%) pregnant women had started ART during pregnancy. A statistically significant difference was observed for all variables analyzed between these two populations.

Table 1 - Sociodemographic and related characteristics of pregnant women living with HIV, using ART. Brazil, 2014-2019.

Characteristics	All pregnant women (n=34,659)		Pregnant women with previous ART use (n=18,486)		Pregnant women with ART start during pregnancy (n=16,173)		P-value
	n	%	n	%	n	%	
Age group (years)							
14-19	4,640	13.4	2,153	11.6	2,487	15.4	
20-24	8,155	23.5	3,744	20.3	4,411	27.3	
25-29	8,712	25.1	4,588	24.8	4,124	25.5	<0.001
30-39	11,315	32.6	6,622	35.8	4,693	29.0	
40 and over	1,837	5.3	1,379	7.5	458	2.8	
Ethnicity/skin color							
White	12,829	37.0	7,499	40.6	5,330	33.0	
Brown	12,046	34.8	5,754	31.1	6,292	38.9	
Black	3,843	11.1	1,926	10.4	1,917	11.9	<0.001
Yellow	222	0.6	113	0.6	109	0.7	
Indigenous	92	0.3	41	0.2	51	0.3	
Unknown	5,627	16.2	3,153	17.1	2,474	15.3	
Cor white/non-white							
White	12,829	37.0	7,499	40.6	5,330	33.0	
Non-white	16,203	46.7	7,834	42.4	8,369	51.7	<0.001
Unknown	5,627	16.2	3,153	17.1	2,474	15.3	
Marital status							
Without spouse	13,347	38.5	7,687	41.6	5,660	35.0	
With spouse	9,666	27.9	4,725	25.6	4,941	30.6	<0.001
Unknown	11,646	33.6	6,074	32.9	5,572	34.5	
Schooling (years)							
None	319	0.9	198	1.1	121	0.7	
1-7	9,038	26.1	5,108	27.6	3,930	24.3	
8-11	9,608	27.7	5,130	27.8	4,478	27.7	<0.001
12 and over	3,006	8.7	1,684	9.1	1,322	8.2	
Unknown	12,688	36.6	6,366	34.4	6,322	39.1	
Region of residence							
Southeast	12,007	34.6	6,799	36.8	5,208	32.2	
South	10,597	30.6	6,101	33.0	4,496	27.8	
Northeast	6,260	18.1	2,878	15.6	3,382	20.9	<0.001
Midwest	2,371	6.8	1,162	6.3	1,209	7.5	
North	3,359	9.7	1,515	8.2	1,844	11.4	
Unknown	65	0.2	31	0.2	34	0.2	
Birth Country							
Brazil	34,630	99.9	18,469	99.9	16,161	99.9	
Other countries	27	0.1	15	0.1	12	0.1	<0.001
Unknown	2	0.0	2	0.0	0	0.0	
ADR*							
Yes	4,963	14.3	3,185	17.2	1,778	11.0	<0.001
No	29,696	85.7	15,301	82.8	14395	89.0	

Number of pregnancies							
1	30,615	88.33	16,533	89.4	14,082	87.1	
2	3,745	10.81	1,830	9.9	1,915	11.8	<0.001
3	283	0.82	118	0.6	165	1.0	
4	15	0.04	5	0.0	10	0.1	
5	1	0.00	0	0.0	1	0.0	

*ADR- Adverse Drug Reaction. Source: Elaborated by the author. Data: SICLOM 2014-2019.

A total of 39,019 pregnancies was observed during the study period, with a mean of 1.13 ± 0.37 pregnancies per woman. As shown in Table 2, the highest number of pregnancies was observed in 2018, with 7,195 registered cases. The lowest number of pregnancies was recorded in 2014, with 5,896 cases.

After stratifying the pregnancies, we observed that the percentage of pregnancies in women who started ART during pregnancy (51.3%) was higher than those who had previously used ART (48.7%) in the first year (2014) of the study only. All other study years revealed a higher percentage of pregnancies among pregnant women who had previously used ART.

Table 2 - Total number of pregnancies stratified per pregnant women with previous ART use and pregnant women starting ART during pregnancy. Brazil, 2014-2019.

Pregnancy onset	Total number of pregnancies (n=39,019)	Number of GUP* pregnancies at the beginning of the cohort (n=20,567)		Number of GIG** pregnancies at the beginning of the cohort (n= 18,452)	
	nº	nº	%	nº	%
2014	5,896	2,874	48.7	3,022	51.3
2015	6,216	3,170	51.0	3,046	49.0
2016	5,929	3,265	55.1	2,664	44.9
2017	6,683	3,633	54.4	3,050	45.6
2018	7,195	3,847	53.5	3,348	46.5
2019	7,100	3,778	53.2	3,322	46.8

*GUP – Pregnant women with previous ART use. **GIG – Pregnant women who started ART during pregnancy.
Source: Elaborated by the author. Data: SICLOM 2014-2019

Table 3 summarizes the ARV regimens that showed at least 2% dispensing. When analyzing the ARV regimens used in the total number of pregnancies in the study, we could observe that the most dispensed regimen from 2014 to 2016 was the lopinavir + ritonavir/zidovudine + lamivudine combination. This regimen had a percentage of 76.2% in 2014, 67.4% in 2015, and 42.1% in 2016 among all regimens dispensed for PWLHIV in the period studied. In 2017, the tenofovir + lamivudine + efavirenz regimen corresponded to 56.0% of dispensations, corresponding to the most dispensed regimen. In 2018 and 2019, the tenofovir + lamivudine/raltegravir regimen was the most dispensed, representing 40.2% in 2018 and 50.5% in 2019.

When analyzing the most used ARV regimen per year, after stratifying the pregnancies, we observed that, in 2014, 2015 and 2016, the ARV combination lopinavir + ritonavir/zidovudine + lamivudine was the most dispensed for pregnant women who had previous ART use, with values of 64.8%, 55.6% and 37.6% respectively, and for pregnant women who started ART during pregnancy, with values of 87.1%, 79.6% and 47 .6%, respectively.

In 2017, the tenofovir + lamivudine + efavirenz regimen was the most dispensed for both categories of pregnant women, corresponding to 45.8% of dispensations for pregnant women who had previously used ART and 68.1% for those who started ART during pregnancy. In 2018, the most dispensed regimen for pregnant women who had previously used ART was tenofovir + lamivudine + efavirenz, with 36.7%. However, the tenofovir + lamivudine/raltegravir regimen was the most

dispensed (56.1%) for pregnant women who started ART during pregnancy. In 2019, the most dispensed regimen was the tenofovir + lamivudine/raltegravir combination for pregnant women who had previously used ART (35.7%) and pregnant women who started ART during pregnancy (67.3%).

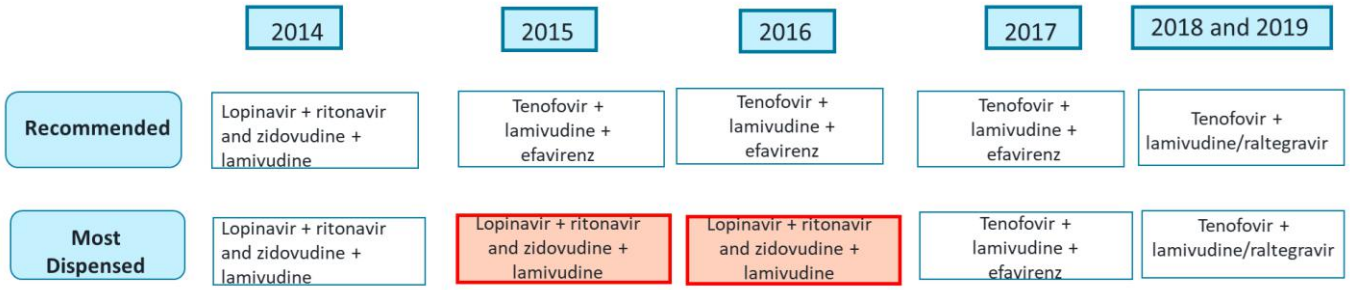
Table 3 - Antiretroviral regimens dispensed by year of onset of pregnancy in total and stratified pregnancies. Brazil, 2014-2019.

Year of pregnancy start (Total pregnancies)	Antiretroviral regimen dispensed	Total		GUP*		GIG**	
		n	%	n	%	n	%
2014 (n=5,896)	Lopinavir + ritonavir/zidovudine + lamivudine	4,493	76.2	1,862	64.8	2,631	87.1
	Lopinavir + ritonavir/tenofovir/lamivudine	348	5.9	248	8.6	100	3.3
	Zidovudine + lamivudine/nevirapine	300	5.0	174	6.0	126	4.2
	Atazanavir/ritonavir/lamivudine/tenofovir	231	3.9	177	6.2	54	1.8
	Zidovudine + lamivudine/atazanavir/ritonavir	124	2.1	106	3.7	18	0.6
	Other regimens (90 different ones)	400	6.8	307	10.7	93	3.0
2015 (n=6,216)	Lopinavir + ritonavir/zidovudine + lamivudine	4,189	67.4	1,764	55.6	2,425	79.6
	Lopinavir + ritonavir/tenofovir + lamivudine	526	8.5	362	11.4	164	5.4
	Tenofovir + lamivudine/atazanavir/ritonavir	437	7.0	317	10.0	120	3.9
	Tenofovir + lamivudine + efavirenz	280	4.5	155	4.9	125	4.1
	Zidovudine + lamivudine/nevirapine	223	3.6	123	3.9	100	3.3
	Zidovudine + lamivudine/atazanavir/ritonavir	149	2.4	130	4.1	19	0.6
	Other regimens (89 different ones)	412	6.6	319	10.1	93	3.1
2016 (n=5,929)	Lopinavir + ritonavir/zidovudine + lamivudine	2,495	42.1	1,227	37.6	1,268	47.6
	Tenofovir + lamivudine + efavirenz	1,620	27.3	778	23.8	842	31.5
	Tenofovir + lamivudine/atazanavir/ritonavir	667	11.3	462	14.2	205	7.7
	Lopinavir + ritonavir/tenofovir + lamivudine	503	8.5	321	9.8	182	6.9
	Zidovudine + lamivudine/nevirapine	192	3.2	108	3.3	84	3.2
	Other regimens (77 different ones)	452	7.6	369	11.3	83	3.1
2017 (n=6,683)	Tenofovir + lamivudine + efavirenz	3,740	56.0	1,664	45.8	2,076	68.1
	Tenofovir + lamivudine/atazanavir/ritonavir	728	10.9	596	16.4	132	4.3
	Tenofovir + lamivudine/raltegravir	725	10.9	231	6.4	494	16.2
	Lopinavir + ritonavir/zidovudine + lamivudine	579	8.7	400	11.0	179	5.9
	Lopinavir + ritonavir/tenofovir + lamivudine	222	3.3	190	5.2	32	1.1
	Other regimens (79 different ones)	689	10.3	552	15.2	137	4.5
2018 (n=7,195)	Tenofovir + lamivudine/raltegravir	2,893	40.2	1,015	26.4	1,878	56.1
	Tenofovir + lamivudine + efavirenz	2,454	34.1	1,411	36.7	1,043	31.2
	Tenofovir + lamivudine/atazanavir/ritonavir	939	13.1	717	18.6	222	6.6
	Tenofovir + lamivudine/darunavir/ritonavir	150	2.1	122	3.2	28	0.8
	Zidovudine + lamivudine/atazanavir/ritonavir	145	2.0	118	3.1	27	0.8
	Other regimens (67 different ones)	614	8.5	464	12.1	150	4.5
2019 (n=7,100)	Tenofovir + lamivudine/raltegravir	3,583	50.5	1,347	35.7	2,236	67.3
	Tenofovir + lamivudine + efavirenz	2,067	29.1	1,295	34.3	772	23.2
	Tenofovir + lamivudine/atazanavir/ritonavir	775	10.9	581	15.4	194	5.8
	Tenofovir + lamivudine/darunavir/ritonavir	164	2.3	133	3.5	31	0.9
	Other regimens (63 different ones)	511	7.2	422	11.2	89	2.7

*GUP – Pregnant women with previous ART use. **GIG – Pregnant women who started ART during pregnancy. Source: Elaborated by the author. Data: SICLOM 2014-2019.

Figure 2 shows the ARV regimens recommended by the Ministry of Health compared to the most dispensed ARV regimens yearly. We observed that the most dispensed regimens differed in 2015 and 2016 from those recommended by the Ministry of Health. In other years, the most dispensed regimen follows the Ministry of Health's PCDT-TV recommendation.

Figure 2 - Antiretroviral regimens recommended by the Ministry of Health compared to the most dispensed antiretroviral regimens per year. Brazil, 2014-2019.



BRASIL (2010). Recomendações para Profilaxia da Transmissão Vertical do HIV e Terapia Antirretroviral em Gestante.
BRASIL (2015). Protocolo Clínico e Diretrizes Terapêuticas para Prevenção da Transmissão Vertical de HIV, Sífilis e Hepatites Virais.
BRASIL (2018). Protocolo Clínico e Diretrizes Terapêuticas para Prevenção da Transmissão Vertical de HIV, Sífilis e Hepatites Virais.
SICLOM 2014 -2019. Source: Prepared by the author.

4. Discussion

This nationally-based retrospective cohort study with PWLHIV on ART between 2014 and 2019 revealed that, in the six follow-up years, the profile of pregnant women monitored included women over 30 with previous ART use, predominantly non-white, with up to 11 schooling years, and without a spouse; most had only a single pregnancy during the period assessed and a mean ART use of approximately six months. Most resided in the Southeast and South. The main ARV regimens used were lopinavir + ritonavir/zidovudine + lamivudine between 2014 and 2016, tenofovir + lamivudine + efavirenz in 2017, and tenofovir + lamivudine/raltegravir between 2018 and 2019.

The results reveal that the age profile of pregnant women monitored in this cohort is per the Epidemiological Bulletin published in 2019 and other studies conducted with pregnant women in Brazil. In the Epidemiological Bulletin, the age group with the highest proportion of PWLHIV cases between 2014 and 2019 was also 30-39 years, with 29.9% of cases (Brasil, 2022). A study on HIV prevalence in pregnant women living in Brazil between 2010 and 2012 showed a higher proportion of pregnant women in this age group, 30-39 years (Pereira et. al., 2016). The median age of pregnant women followed in this study is close to the results of another study performed in Brazil, with a mean of 28 years (Domingues et al., 2018). Regarding ethnicity/skin color, the results of this study point to the highest percentage of non-white pregnant women. The same result was found in the Epidemiological Bulletin published in 2019.

We observed a higher percentage of pregnant women with 8-11 schooling years. The Clinical Monitoring of Pregnant Women published in 2019 found a higher percentage among women with 0-7 schooling years, followed closely by the 8-11 schooling years age group. Despite the slight divergence between this study and the Clinical Monitoring, both point to less educated women. Another national study in which prenatal care and HIV prevalence in pregnant women were evaluated (Domingues, et al., 2015) also pointed out that the prevalence of HIV in pregnant women occurs among less educated women. This finding and the more significant number of non-white pregnant women may signal greater social vulnerability in these populations. Most pregnant women in the study did not have a spouse. Another study in Brazil also showed that most PWLHIV did not have a spouse during pregnancy (Domingues, et. al., 2015).

This study revealed a mean ART use time of approximately six months during pregnancy. An article about the profile of 46 pregnant women using ART from a Drug Dispensing Unit (DDU) in Rio Grande do Sul state identified that most

pregnant women (29) had been using ART during pregnancy for more than six months (Beck et.al., 2018). This difference can be explained because pregnant women's medical records were used as a source of information in the study mentioned above, besides the fact that it is a study restricted to a single DDU with a much smaller number of participants than in this study.

In the distribution of PLWHIV between the states and the Federal District, we observed a high number of pregnant women undergoing treatment living in the southern states of the country. Although their population represents 14.2% (IBGE, 2021), the three states together accounted for 30.6% of all PWLHIV in the study. This result can be partially explained because the South's detection rate is 2.2 times higher than the national rate (Domingues et al., 2018). The values found in the South may derive from public policies that improved access to HIV diagnosis among pregnant women.

Most sociodemographic variables are similar when comparing pregnant women with previous use of ART and those who started ART during pregnancy. One divergent variable refers to ethnicity when observed in a stratified manner. In this variable, pregnant women with previous ART use are primarily white. In contrast, most are mixed-race pregnant women who started ART during pregnancy. This result may derive from a vulnerable population and, therefore, has less information and access to health services, which leads it to seek services later.

The results of the pregnancies found in the study indicate an increase in the number of pregnancies among pregnant women previously using ART compared to those who started ART during pregnancy between the first year of the study and the last. In the Ministry of Health's Clinical Monitoring Report on Pregnant Women (Brasil, 2019), which evaluated data from 2010 to 2018, an increase in pregnant women previously using ART was also observed against those who started ART during pregnancy. The clinical monitoring showed that, in 2014, pregnant women previously using ART had a percentage of 46.0%, which was 61.0% at the end of the period evaluated. The increased number of pregnancies among women previously using ART may signal improved public policies regarding women's reproductive health and a possible reduced risk of vertical transmission. It may also reflect the recommendation of immediate initiation of ART for all PLHIV, regardless of T-CD4+ lymphocyte count and viral load.

The use of ARV regimens was modified due to changes in the recommendations of the Clinical Protocols and Therapeutic Guidelines for the Prevention of Vertical Transmission (PCDT-TV) over the six years of study of our work. In 2014, the recommendation for first choice for PWLHIV was the combination of a PI/ritonavir and an NRTI, and the indication was that they were lopinavir + ritonavir and zidovudine + lamivudine. Lopinavir with ritonavir booster was safe during pregnancy and had a satisfactory virological suppression response (Senise et. al., 2008). The zidovudine/lamivudine combination was also safe in pregnant women (Connor et. al.,1994; El Beitune et.al., 2005). Most dispensations (76.2%) in the present study were per the PCDT-TV recommendation.

In 2015, the combination lopinavir + ritonavir and zidovudine + lamivudine remained the most dispensed, although the PCDT-TV indicated the ARV regimen tenofovir + lamivudine + efavirenz as the first choice. This mismatch between the recommendation of the Ministry of Health protocol and the dispensation can be explained by the fact that PCDT-TV/2015 was only published at the end of that year, per the Ministry of Health Ordinance N° 65 of November 9, 2015[12]. Lopinavir + ritonavir and zidovudine + lamivudine regimens accounted for 67.4% of all dispensations, while the ARV regimen recommended at the end of 2015 had only 4.5% of dispensations.

The modification of the first line of treatment, which since 2015, recommended efavirenz (EFV), a non-nucleoside analog reverse transcriptase inhibitor, replacing lopinavir/ritonavir was also not reflected in the Brazilian DDU dispensations in 2016. This year, lopinavir + ritonavir and zidovudine + lamivudine was the most dispensed regimen. This change in the PCDT-TV recommendation was an attempt to increase pregnant women's adherence to treatment. The tenofovir + lamivudine + efavirenz regimen was a combined fixed-dose tablet (CFDT), reducing six to just one tablet per day.

A study in which adherence was observed in the general population and not just in pregnant women showed a 14.0% increase in adherence to treatment with the change to DFC (Santos, S.F. 2018). Despite this, prescribers continued to avoid EFZ for pregnant women. A possible explanation for this may be because EFZ, until then, was not permitted for use during pregnancy as it was considered a teratogenic medication (CASTELO et al., 2001). However, a systematic review (Ford et.al., 2013) showed that the medication could be used during pregnancy, from the first trimester, without risk. The fear of recommending EFZ during pregnancy, even if there was a systematic review demonstrating its safety, may signal that the professionals involved in the treatment may require a refresher. In 2017, the most dispensed ARV regimen was the one recommended by PCDT-TV. The DFC regimen (tenofovir + lamivudine + efavirenz) was observed in 56.0% of all dispensations. That year, the ARV dolutegravir (DTG), an integrase inhibitor, became part of the first-line regimen for adults living with HIV in Brazil. However, its use in pregnant women was not recommended. Based on initial results from a prospective study in Botswana, the World Health Organization (WHO) issued a warning about potential neural tube defects in babies of mothers exposed to DTG at conception (WHO, 2018).

In 2018 and 2019, the first-line regimen recommended by PCDT-TV was the tenofovir + lamivudine/raltegravir combination, replacing EFZ with raltegravir (RAL), an integrase inhibitor. Although the presentation of DFC was introduced to improve adherence, despite having good efficacy, EFZ has a low genetic barrier and, thus, is prone to selecting viral resistance when adherence is not good. Furthermore, the most common side effects are neuropsychiatric symptoms (Vrouenraets et al., 2007). A 2009 study comparing RAL with EFZ in treatment-naive people showed significantly fewer side effects in individuals who used RAL (Lennox et al. 2009). Another study that investigated RAL's efficacy, safety, and pharmacokinetics in pregnancy showed that this ARV was safe and effective in pregnant women who used ART before pregnancy and in pregnant women who started ART during pregnancy (Maliakkal et al., 2016). Thus, at that time, the integrase inhibitor RAL began to be indicated instead of EFZ for PWLHIV. Dispensations in Brazil in these years followed the PCDT-TV recommendation, and tenofovir + lamivudine/raltegravir was the most dispensed regimen. In 2018 and 2019, it represented 40.2% and 50.5% of all dispensations, respectively.

In 2022, the Ministry of Health recommended the combination of tenofovir + lamivudine/dolutegravir as the first choice regimen for PWLHIV. The Botswana study update did not show statistically significant differences in neural tube defects among women exposed to DTG at conception against those who conceived using ARV regimens without DTG (WHO, 2019). A national cohort was also conducted in Brazil, in which no neural tube defects were observed with periconceptional exposure to DTG (Pereira et al., 2021). The DTG Brazilian Active Pharmacovigilance Project was also implemented in the country, which used SICLOM as a source of information (Batista et al., 2019). Furthermore, data from the DTG Brazilian Active Pharmacovigilance Project revealed that neural tube defects may be associated with several factors that cannot be attributed to DTG exposure (Mendes et al., 2023).

This study presented a large national cohort of PWLHIV using ARV in Brazil, which can provide important information about the characteristics of these pregnant women and the ARV regimens used. SICLOM was used as a system in which the sociodemographic and clinical data of people who use ARVs in Brazil are recorded, and data on dispensing these medications in the public health system.

Therefore, the results are representative of PWLHIV undergoing treatment. Another strength of the study is the identification and comparison of ARV regimens used by pregnant women. Although some studies address the profile of PWLHIV, we did not find another study with a national dimension on the sociodemographic profile of pregnant women or a national-based study that identifies ARV regimens in the period evaluated, which limited us in communicating with other studies.

5. Conclusion

Although the study shows an increase in pregnancies among women who previously used ART, compared to those who start ART during pregnancy, many pregnant women still start ART only during pregnancy. This situation shows that these people seek health services later, reiterating the characterization of a more socially vulnerable population. This profile of pregnant women points to the need to expand this population's access, listening, and reception to health services in the SUS, which are fundamental to improving care for women's reproductive health. Thus, despite advances in SUS strategies to combat HIV, the country still needs to improve the care provided to PWLHIV.

Regarding the ART regimens used, the ARVs dispensed for the management of HIV in pregnant women followed the recommendations of clinical protocols and therapeutic guidelines published by the Ministry of Health in most years, pointing to an alignment of conduct in the treatment of PWLHIV even in different regions of the country.

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