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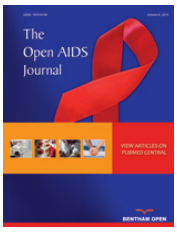

RESEARCH ARTICLE

Unintended Repeat Pregnancies Among HIV Positive Women in Rio De Janeiro, Brazil

Bernardo B. Wittlin[1], Alice W. Carvalho[1], Giulia P. Lima[1], Rune Andersson[2], Susanne Johansson[2], Elizabeth S. Machado[1], Tomaz P. Da Costa[1] and Cristina B. Hofer[1,*]

[1]*Department of Preventive Medicine - Instituto de Puericultura e Pediatria Martagão Gesteira, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil*

[2]*Department of Infectious Diseases, Institute of Biomedicine, Sahlgrenska Academy, Gothenburg University, Gothenburg, Sweden*

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Abstract:

Introduction:

High rates of unintended pregnancies among HIV positive women have been reported by several studies. Among repeated pregnancies, these rates may be higher. Our aim was to describe the unintended pregnancy rate in repeat gestations of the same group of HIV-positive women.

Methodology:

From a prospective cohort of HIV-infected pregnant women followed-up from 1995 to 2013 in an Antenatal Clinic (ANC) in Rio de Janeiro, we selected women who had at least two consecutive pregnancies. Patient data were prospectively obtained from standardized questionnaires. The main dependent variable was if the pregnancy was intended or unintended. Some of the other variables were: age, the interval between pregnancies, household income, CD4 cells count at admission in the ANC and at delivery, viral load<1000 copies/ml at admission and close to delivery, and attempts to illegal abortion.

Results:

From a total of 287 women included, the number of unintended pregnancies increased from 138 (63.6%) at first pregnancy to 198 (81.8%) at second pregnancy ($p < 0.01$). At first pregnancy, we observed 8 women who had made an attempt to illegal abortion (7 with an unintended pregnancy and 1 with a wanted pregnancy, $p = 0.06$), while at second pregnancy, 34 of them had made an attempt (33 with unintended pregnancy and 1 with a wanted pregnancy, $p < 0.01$). Regarding viral load suppression close to delivery, there was no statistic difference between first and second pregnancies (72,7% *vs*. 70,5%, $p = 0.36$) as well as between intended and unintended pregnancies (in first pregnancy: 80% *vs*. 86%, $p = 0.4$; in second pregnancy: 72% vs. 83%, $p = 0,1$).

Conclusion:

High rates of unintended pregnancies and illegal abortion attempts, along with their increase from one pregnancy to the subsequent, reinforce the need for continuous family planning practices in HIV-infected patients. The majority of the women were able to reach undetectable viral load at the end of the pregnancy, including those with unintended pregnancies.

Implications:

HIV infected patients presenting in antenatal care for sequential unintended pregnancies. Despite the fact that abortion is illegal in this country, a substantial number of women, still attempt it before attending antenatal care. Family planning actions should be performed during the antenatal care.

* Address correspondence to this author at the Department of Preventive Medicine - Instituto de Puericultura e Pediatria Martagão Gesteira, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil, Tel: 55-21-39382556; E-mail: cbhofer@hucff.ufrj.br

Keywords: Unintended, Unwanted, Pregnancy, HIV, Brazil, Illegal abortion.

1. INTRODUCTION

Eliminating HIV Mother-to-Child Transmission (MTCT) has been recently established as an objective in worldwide HIV national programs. This target was outlined in the 2011 Global Plan, conducted by the World Health Organization (WHO) and the United Nations Program on HIV/AIDS (USAIDS) [1]. Despite global efforts and significant results in reducing HIV newborn infections, there are still constraints to achieve it [2]. In summary, the scope of medical interventions carried out in order to prevent MTCT includes access to adequate antiretroviral treatment (ART) during pregnancy, proper delivery care including caesarian section and intrapartum prophylaxis when indicated, prophylaxis to the newborn for 4 weeks, and abstaining from breastfeeding. In absence of any intervention, the rates of HIV transmission vary from 20-45% [3], nevertheless, the risk can be reduced to less than 2% with all the measures above. Among others, high viral load close to delivery is a well-known risk factor for transmission of the virus from mother to child [4, 5]. This risk can be extensively reduced by the use of ART during pregnancy, which leads to undetectable viral loads at that point. Therefore, access to adequate ART and patient adherence are key issues to be addressed by any PMTCT program.

Compliance of HIV positive pregnant women to PMTCT programs and its medical recommendations can be affected by several factors. One potential associated factor is women's reproductive intentions. Thus, unintended pregnancy may increase vertical transmission rates [6], besides its general risks irrespective of HIV status, which leads to increased morbidity and mortality to both mothers and children [7]. High rates of unintended and unwanted pregnancies among HIV positive women have been reported by several studies [8 - 12]; some have shown greater rates for this group comparing to HIV negative women [10, 12], while some have not [11]. Other studies focused on repeat pregnancies among HIV positive women and its predictors. For instance, younger age was one of the predictors more consistently found beside others, including lower educational status and decreased rank order of living conditions [13 - 16]. Hence, these predictors can be especially taken into account by family planning programs.

In Brazil, access to antenatal care, as well as to ART is free of charge. Family planning options are offered in primary care settings, also free of charge but not integrated with the antenatal care. However, abortion is illegal and is not considered in the Brazilian regular health system. Illegal abortion is still an important etiology of maternal mortality in this country [17].

Considering, high rates of unintended pregnancies, in HIV infected women, described in other studies [10, 12] and repeated pregnancies are considered possibly associated with an unwanted pregnancy, the present study aimed to study the pregnancy intentions in a group of HIV positive women, through two pregnancies in the same antenatal clinic. In order to evaluate the hypothesis that unwanted pregnancy would be more frequent among women in their second pregnancy, and to study possible consequences of it (illegal abortion attempts).

2. METHODS

This study was a prospective cohort study of HIV-infected pregnant women who had been referred to Instituto de Puericultura e Pediatria Martagão Gesteira (IPPMG) Antenatal Clinic (ANC) from 1995 to 2013. Inclusion criteria for this study were: being HIV positive; being pregnant and followed up for at least two antenatal care visits at the IPPMG Clinic; had at least two pregnancies followed up in the IPPMG antenatal care clinic.

Patient data were prospectively obtained from standardized questionnaires used in the antenatal care of HIV-infected pregnant women. The health care professional responsible for the care of the patient filled in the questionnaire based on the patient's responses, laboratory results, and medical records. Information from these questionnaires was thereafter manually transferred into different variables of interest.

The main dependent variable studied was if the pregnancy was intended or unintended. Unintended pregnancies are defined as those unwanted or mistimed. This was assessed by a direct question in the study entry (in the first visit of antenatal care for the followed up pregnancy), transcribed as follows: "Did you want this pregnancy?". In order to understand possible differences between first and second pregnancies, we performed comparisons between repeated pregnancies.

The independent variables were: age, interval between pregnancies, household income, CD4 cells count at admission to the Antenatal Center (ANC) and at delivery, viral load<1000 copies/ml at admission in the ANC clinic and close to delivery, trimester when ART was initiated, history of Sexually Transmitted Infections (STI) (including history

of HPV/ cervical intraepithelial neoplasia, syphilis), attempts to induce abortion. Comparisons between wanted and unwanted pregnancies, as well as first and second pregnancies, were performed by Mann-Whitney test, and the Chi-square or Fisher exact tests for continuous and categorical variables, respectively. To evaluate CD4 cell count and viral loads from admission to delivery within the two different pregnancies, paired Student t-test or McNemar test was used.

This data was then processed and analyzed using STATA statistics 13.0, Texas, USA.

3. RESULTS

1240 HIV positive pregnant women attended IPPMG during the study period: 287 (23%) of them had at least one repeat pregnancy and 953 (77%) did not have any repeated pregnancies. Of the 287 women, 68 (24%) had a third, 8 (3%) a fourth and 2 (0.7%) a fifth pregnancy. The total of 287 women was included in the study, and the first pregnancy was compared to the second. Their median age was 24, in the first pregnancy and 27 at the second (Table **1**).

Table 1. Descriptive data on the first and second pregnancy.

Variable	Median (IQR)		*p*-value
	1st Pregnancy	2nd Pregnancy	
Age - years n=287	24 (20-28)	27(23-31)	<0.01
Household income - minimum wage/month[1] n=260	2 (1-3)	2 (1-3)	0.51
Interval between pregnancies - years n=287	2 (1-4)		
Number of previous pregnancies[2] n=227	2 (1-4)		
Number of previous births[2] n=227	1 (0-2)		
Number of woman with history of STI[3] (%) n=287	88 (30.6)		

Note: IQR = Interquartile range
[1]One minimum wage was equal to 283 US dollars per month in 2014
[2]Before knowledge of HIV status and attending IPPMG
[3]Sexually transmitted infections

During the baseline visit, we included viral load and CD4 cells count in the antenatal laboratory routine, but due to logistic problems, the women needed to return to the clinic in another day, to perform these exams. At first pregnancy, 240 women came to test their viral load at admission and 251 at second pregnancy. The number of women with HIV viral load <400 copies/ml on admission increased from 50 (20.8%) at first pregnancy to 90 (35.9%) at second pregnancy.

The same laboratory routine is ordered to be performed at the 34 weeks of gestational age. The results are shown in Table **2**.

Table 2. Laboratory results in the first and second pregnancies.

-		1st Pregnancy	2nd Pregnancy	p-value
Undetectable viral load at admission	Number of women (%)	50 (20.8%) N = 240	90 (35.9%) N = 251	<0.01
Undetectable viral load close to delivery	Number of women(%)	120 (72.7%) N = 165	141 (70.5%) N = 200	0.36
Viral load at admission (copies/ml)	Median (IQR)	4479 (640-18750) N = 240	2500 (96-14907) N = 251	0.17
Viral load close to delivery (copies/ml)	Median (IQR)	undetectable (undetectable -509) N = 165	undetectable (undetectable -1159) N = 200	0.46
CD4+ cell count at admission (cells/mm^3)	Median (IQR)	430 (306-604) N = 270	427 (280-592) N = 272	0.27
CD4+ cell count close to delivery (cells/mm^3)	Median (IQR)	534 (351-702) N = 157	509 (350-677) N = 282	0.40

Treatment was initiated earlier during second pregnancy. For those who were not already on treatment before first or second pregnancy, ART was initiated on average 8.5 weeks earlier (95% CI -7.8-10 weeks). Results are shown in Table **3**.

From a total of 287 women included in the study, 217 answered about their pregnancy intentions for the first pregnancy and 242 for the second pregnancy.

Table 3. Laboratory results in the first and second pregnancies.

-	1st Pregnancy	2nd Pregnancy	*p*-value
Already on treatment before pregnancy	45 (16.2%)	94 (33.8%)	p <0.01
First trimester	7 (2.5%)	12 (4.3%)	p = 0.25
Second trimester	110 (39.6%)	120 (43.2%)	p = 0.39
Third trimester	116 (41.7%)	52 (18.7%)	p <0.01
Total pairs	278 (100%)	278 (100%)	

Many pregnancies were unintended during both the first and second pregnancy. The number of unwanted pregnancies increased from 138 (63.6%) at first pregnancy to 198 (81.8%) at second pregnancy ($p < 0.01$). Of the 217 women who answered about their pregnancy intentions at first pregnancy, 118 also had viral load measured close to delivery, and out of the 242 women at second pregnancy, 165. Regarding viral load suppression close to delivery, there was no statistic difference between first and second pregnancies (72,7% vs. 70,5%, $p = 0.36$). We observed in first pregnancy group that 80% of the women who intended to be pregnant presented viral load under 1000 copies/ml close to delivery compared to 86% of the women who didn't intend ($p = 0.4$). At the second pregnancy, 72% of the women who wanted the pregnancy presented the same result, compared to 83% of the women with an unintended pregnancy ($p = 0.1$).

The laboratory results of intended and unintended pregnancies were also compared (Table **4**), on each pregnancy. CD4+ cell count close to delivery among wanted pregnancies was higher than among unintended pregnancies (*p*-value <0.01).

Table 4. Descriptive data and laboratory results comparison between wanted and unwanted pregnancies.

-	1st Pregnancy			2nd Pregnancy		
Variable	**Wanted**	**Unwanted**	***p*-value**	**Wanted**	**Unwanted**	**p-value**
Age- years median (range)	24 (23-25) n=79	24 (23-25) n=138	0.88	23 (22-25) n=44	24 (23-24) n=198	0.7
Viral load at admission – copies/mL median (range)	22261.2 (10355.4-341667) n=64	16813.3 (10412.1-23214.6) n=113	0.38	8606 (4505.3-12706.6) n=41	20587.0 (11532.4-29641.7) n=171	0.21
Viral load close to delivery – copies/mL median (range)	3436.24 (1931.49-8803.98) n=45	865.849 (277.59-1454.10) n=73	0.23	6702 (44.8-13359.2) n=29	1029.1 (450.8-1607.4) n=136	0.47
Undetectable viral load close to delivery - Number of women(%)	63 (86.3)	36 (80)	0.37	42 (77.8)	74 (79.6)	0.80
CD4+ cell count at admission – cells/mm^3 median (range)	497.0 (443.7-550.4) n=72	449.9 (413.7-486.0) n=130	0.17	471.1 (383.7-558.6) n=42	460.2 (428.2-492.2) n=186	0.9
CD4+ cell count close to delivery – cells/mm^3 median (range)	590.6 (524.1-657.2) n=46	481.1 (424.2-538.1) n=72	<0.01	546.5(434.3-658.7) n=29	541. (495.3-586.8) n=125	0.98
Household income – minimum wage/month median (range)	2.1 (1.6-2.5) n=74	2. (1.7-2.5) n=134	0.9	2.4 (1.5-3.4) n=43	2.2 (1.8-2.6) n=190	0.6

Along with the increase of unintended pregnancies proportion at the second gestation, the increase of unsuccessfully attempts to induced abortion was also observed. At first pregnancy, 7 women from the unintended pregnancy group had made an attempt to induce abortion comparing to 1 on the wanted pregnancy group (p=0.06). At second pregnancy, 33 women from the unintended pregnancy group had also made an attempt, comparing to 1 from the unintended pregnancy group ($p < 0.01$).

4. DISCUSSION

Our results revealed an increase in the proportion of unintended pregnancies and attempts to abortion in second pregnancies compared to first pregnancies *i.e.* first-born children were more likely to be wanted than last-born children.

These findings suggest a lack of familiar planning following first pregnancies. Possibly, we could have found an opposite result, *i.e.* higher rates of unintended pregnancies in the first pregnancies, if we had younger enrolled women, considering young age is a classical risk factor for unintended pregnancies. As described above, our median age for first pregnancy was 24 years old.

Other studies have shown a high prevalence of unwanted and unplanned pregnancies and attempt to abortion among this group. In a study involving 113 HIV-positive women from Western India, 80 out of 158 pregnancies were reported as unwanted and 79 of them were voluntarily terminated [8]. Women from urban settings, and with two or more live births before HIV diagnosis were significantly more likely to report an unwanted pregnancy. Along to our results, the last finding suggests an influence of multiparity in pregnancy desires. A cross-sectional survey with postpartum HIV-positive women in Swaziland showed 67.9% of unintended pregnancy [11], while another survey in HIV antenatal care sites of Nigeria [9] have shown 37.2%. In another study in Pune, India, comparing HIV positive and HIV negative women coming for care for a repeat pregnancy in the same antenatal clinic, the likelihood of unplanned repeat pregnancies was significantly higher in HIV positive (70%) than HIV negative (36%) women [12].

Considering that illegal abortion is an important etiology of maternal mortality in our country, we were able to partially demonstrate the missing opportunity to prevent subsequent unwanted pregnancies (by family planning interventions) and thus abortion attempts. It is likely that illegal abortion, abortion attempts and complications rates were much higher. Women who successfully performed an illegal abortion or had severe complications usually do not look for an antenatal clinic. Besides, there is also the limitation of asking women to report on an illegal behavior, which should have a role in underestimating this information.

We observed differences between the two pregnancies regarding the trimester in which ART was initiated. We believe that this difference is partially due to women who obviously knew their HIV serostatus on the second pregnancy. Another important issue is that recommendations of PMTCT Brazilian guidelines regarding ART initiation have changed over time, and it was reflected on differences in ART initiation between first and second pregnancy (Table **3**). However, it did not reflect differences on the final aim of the ART use during pregnancies: the frequency of undetectable viral load close to birth was the same during first and second pregnancies, and even between intended and unintended pregnancies (Table **4**).

We did not find differences as for "undetectable VL close to delivery" between first and second pregnancies. Possible factors could explain hypothetical differences here presumably annulled, for instance: higher rates of undetectable VL at second pregnancies could occur due to changes on ART regimens over years (from mono/dual therapy to cART) and due to late ART initiation in first pregnancy (*i.e.* pregnant women diagnosed and enrolled in PMTCT program too close to delivery, while in second pregnancy they were already followed-up and early taking ART). On the other hand, lower rates of undetectable VL at second pregnancies could occur due to a possible decrease in ART adherence over time, possibly associated with pregnancy willingness. Even more curious was that we found higher rates of "undetectable VL close to delivery" in unintended pregnancies (vs. intended pregnancies). These last findings do not favor our original hypothesis, that is, the more unwanted or unplanned is a pregnancy, the more viral load suppression is not likely to be reached (due to poor compliance and adherence).

One of the particular advantages of our study is a relatively large number of HIV positive women enrolled and followed-up with two pregnancies. Therefore, while most of the other studies involving pregnancy intentions and/or repeat pregnancies among HIV positive women were sectional, our study was able to compare first and second pregnancies within the same group of women.

As a limitation of this study, we were not able to differentiate unplanned/mistimed pregnancy (*i.e.* women who did not plan but might have desired the child once pregnant) and unwanted pregnancy (did not plan and did not desire the child while pregnant). We were able to infer that the pregnancies were unwanted at the baseline visit (*i.e.*; the first antenatal visit to our Center). Refining the question and assessing pregnancy willingness throughout pregnancy (asking the same question in other visits) could also increase accuracy. Another limitation was that the proportion of women who did not collect all the samples required (*i.e.* CD4+ count and VL at admission and close to delivery, in both pregnancies) may have jeopardized statistical significance when comparing those parameters.

Finally, most of the enrolled women were from a low-income socioeconomic stratum, which denotes a certain profile of women with particular social issues. Poverty, low educational status, difficulties to access public health system, stigma and bias related to people living with HIV, risks related to illegal induced abortions are some of the issues which should be targeted by family planning practices, general antenatal care, and PMTCT/HIV care programs.

There is a particular concern with risky abortion practices in countries like Brazil, leading to high rates of maternal mortality [17]. As a conclusion of this present study, the high prevalence of unintended pregnancies and induced abortion attempts besides their increase from one pregnancy to another reinforce the need for continuous family planning practices in health care settings, with special attention to puerperal HIV positive patients.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This project was approved by IPPMG IRB.

HUMAN AND ANIMAL RIGHTS

No Animals were used in this research. All human research procedures followed were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013.

CONSENT FOR PUBLICATION

Written and informed consent was obtained for study.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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