ABSTRACT

Introduction: The introduction of highly active antiretroviral therapy has so far led to a comparable reduction in disease progression and restoration of normal functioning of reproductive system in female living with HIV infection. The main objective of this study was to find out the magnitude of pregnant and its determinants among ART-registered clients in Simiyu region, Tanzania.

Methods: We used a retrospective cohort study of HIV/AIDS women initiated ART in Simiyu region from 2005 up to 2018. Kaplan–Meier survival graphics were used to explain the difference pregnancies experiences among different groups. Cox proportion hazard was used for model building to determine the predictors of pregnancy.

Results: A total number of 525 women became pregnant, giving an overall incidence rate of 3.1/100 person year at risk (PYAR) (95% CI 2.84–3.37). The incidence of pregnant was higher between the age 15 and 29 years (5.86/100 PYAR, 95% CI: 5.23–6.55). Cohabited and those who are married were associated with high incident rate of pregnant (5.62/100 PYAR, 95% CI: 1.81–17.43 and 4.16/100 PYAR, 95% CI: 3.79–4.57). Weight >55 kg were associated with high incidence of pregnant (5.03 PYAR, 95% CI: 4.54–5.57), and WHO stage one have high incidence of pregnant (11.14/100 PYAR, 95% CI: 9.95–12.47).

Conclusion: Young age and being healthier were the main predictors of pregnancy after ART initiation in this population. Policy for integration of family planning services into HIV care and treatment clinics should be strengthened but focused to young women. More follow-up is needed for pregnant and newborn outcome.

Key words: HAART; HIV/AIDS; pregnancy incidence.

Introduction

The decline of the new HIV infections among adults observed globally has rapidly slowed in the recent years. In sub-Saharan Africa, adolescent girls and young women accounted for 25% of the new HIV and adult women accounted for 56% of the new HIV infections.[1] In Tanzania, it was estimated that approximately 1.35 million people were infected with HIV in the country by the year 2016. Women were more affected, with an HIV prevalence of 6.3% versus 3.9% among men.[2] In 2017, it was reported that up to 80%[61–>95%] of pregnant women living with HIV in the country had an access to antiretroviral medicines that prevents transmission of HIV infection from mother to child.[3]

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Mageda K, Mohamed MA, Kulemba K. Incidence and determinants of pregnancy among women receiving HAART in Simiyu region: 14-year retrospective follow-up. Trop J Obstet Gynaecol 2020;37:38-45.

Received: 30-09-2019 Revised: 01-11-2019 Accepted: 25-03-2020 Published Online: 14-08-2020
The introduction of highly active antiretroviral therapy (HAART) has so far led to comparable reductions in disease progression and mortality. This results into backup of normal human functioning of various body organs and system such as reproductive system.[3-6]

Currently there is evidence that initiating ART among women of reproductive age increases child bearing desire and sexual activities. It was also found that increased numbers of sexually active female attending care and treatment clinic (CTC) are reported to use modern contraceptive methods.[7]

Access to HAART and the prevention of mother to child transmission of HIV (PMTCT) services has been one of the important determinants of fertility desires and behaviors.[8] Thus, availability of HAART encouraged patients to have children as their risk of transmitting the virus has been substantially decreased.[9] It is possible that the rapid improvements in health and quality of life that take place with HAART initiation lead to increased sexual activity, particularly for those with stable partnerships.[10] However, studies show that treatment of HIV patient with HAART does not influence the desire for having children by the patients using the drugs.[11] Researches conducted in developed countries show that HIV infection is associated with a decline in fertility and that HAART initiation reverses this decline.[12,13] Incidence of pregnancy among women receiving routine HIV care and treatment has increased and is almost comparable to that in the general population.[14] It is higher after initiating HAART compared to prior to could be due to an improved immune status or reduced HIV viral load in the body, and this tended to increase when both women and their spouses desired more children and decreased with older age.[15]

Although researchers have shown many important insights on the association between HAART use and childbearing desire, little work has been carried out to find out the impact of its use and occurrence of pregnancy in Tanzania. This study aimed at finding out the magnitude of pregnancy and its determinants among CTC-registered women in Simiyu region. The findings of this study will lead to the development of a conceptual framework on HIV women unmet needs, which will be used by policy makers.

Materials and Methods

Study design and population

This was a retrospective cohort study of HIV-infected women initiated with HAART from three districts, namely Maswa, Bariadi, and Busega in Simiyu region between 2005 and 2018. Eligibility was based on reproductive age between 15 and 49 years.

Study area

Simiyu Region covers an area of 23,807.7 km² and administratively it consists of 5 district councils and 1 town council, 12 divisions, 111 wards, 475 villages, and 17 Mitaa (in Bariadi Town Council). The region is located North of Tanzania and South East of Lake Victoria; it lies between latitude 2°1’ and 4° South of Equator and between 33°3’ and 35°1’ East of Greenwich.

The region is bordered by Manyara and Singida regions in the east, south by Shinyanga region, west by Mwanza region, and north by Mara region. Also, eastern and part of northern boundaries lie the famous Serengeti National Park.

HIV/AIDS care and treatment started in Simiyu 2005 at Maswa District Hospital. Currently, there are 53 care and treatment centers of 214 health facilities (24.7%) in the region.

The HIV prevalence in the region is estimated to be 3.9% (THIS2016/17) below the National average that is 4.7%. According to Regional HIV and AIDS profile, there are 4 hospitals, 17 health centers, and 193 dispensaries, making a total of 214 health facilities in the region.

Subject characteristics

The anticipated number of clients was 4872 with the age ranging from 15 to 49 years regarded as reproductive age range. Those women identified to be HIV positive and initiated ART in the 25 CTCs.

Women with age <15 and >49 years were excluded from the study. Women with missing observation such as weight, World Health Organization (WHO) stage, and pregnancy status were also excluded.

Sampling and data collection

We included all 25 health facility providing care and treatment for HIV/AIDS clients in Busega, Bariadi, and Maswa districts. Data were extracted from the electronic database CTC2 and exported for analysis to the excel software. At the time of data collection, we found a cumulative total of 16,344 clients enrolled. After checking for eligibility, only 4872 were eligible and sampled for the study.

The electronic database (CTC2) contained several files. We extracted three files: one that contained the sociodemographic characteristics such as sex, date of birth, height, and marital status; the second file that contained the medical characteristics and progression of the client such as date of visit, weight, WHO stage, and pregnancy status; and the third that showed the final status of the patient at the time of data extraction.

Data clerks in the respective clinic were trained for data collection from the electronic database. Data were screened
for missing value and those observed with the missing values were removed. All collected data were stored in an Excel data sheet (Microsoft corporation, One Microsoft way/Ridmond/WA 98052 USA) in a computer.

**Operation definition of variable**

**Indicator variable**: The indicator variable in this study that was used in modeling was pregnancy status, that is, a variable is equal to 0 or 1, where a value of 1 indicates that the women become pregnant at a certain time during observation, whereas a value of 0 indicates that the women does not experience pregnancy.

**Incident of pregnancy**: Incidence of pregnancy was considered in this study as when the indicator variable had the value of 1 during follow-up period. This variable was measured by using person years at risk time (PYAR).

**Categorical variable**: In this research, all categorical variables were given values to represent the membership in form of values 1, 2, 3, and 4. Categorical variables used were marital status and WHO stage.

**Continuous variable**: In this study, variables were measured on a well-defined, cardinal scale, such as age in years and immunology as in CD4 count.

**Time to event**: In this research, it was a time when the women free from pregnancy identified to have HIV infection and start HAART until when she becomes pregnant, and it was measured by person year.

**Dependent variable**: The dependent variable in this research was the incidence of pregnancy and this was considered when the women become pregnant at first time after HAART start.

**Independent variable**: In this study, variables such as weight, WHO stage, CD4 count, and district of residency were used as independent variables and entered in to the model.

**Data analysis**

Data from Excel were transferred to Stata software version 12.0 (StataCorp 4905 Lakeway Drive College Station, Texas 77845 USA, 800-STATAPC) for analysis and transformation was carried out. Categorical variables were grouped and given values of 1, 2, 3..., and measured using proportion. Continue variables were given ranges and converted into group by given values of 1, 2, 3..., and measured using proportion, mean, and median.

Kaplan–Meier survival graphics were used to explain different pregnancy experiences among groups. The log-rank, Wilcoxon, and Tarone–Ware tests were used to test the hypothesis of no-difference pregnancy experience among groups.

Cox proportion hazard was used for model building to determine the predictors of pregnancy and graphical method was used for Cox model diagnostics.

**Results**

**Baseline characteristics**

A total of 4872 women of 16,344 women (29.8%) were eligible and they were enrolled in the study. The mean age for this population was 34 years ± 8 standard deviation (SD).

Among 4872, 3070 (63%) were married, 886 (18%) weighed <45 kg, and 3986 (72%) weighed >45 kg. 736 (15.11%) were in WHO stage IV, whereas 1494 (30.67%) had CD4 count >500 copies per deciliter [Table 1].

Of the 4872 population, 524 (11.4%) women experienced the event of having pregnant during the entire follow-up period [Table 2].

**Incidence rate of pregnancy**

A total number of 525 women became pregnant over 16679.17591 person year of follow-up, giving an overall incidence rate 3.1/100 PYAR (95% CI: 2.84–3.37). The incidence rates of pregnant by sociodemographic and clinical character are shown in Table 3.

The incidence of pregnancy was higher between the age 15 and 29 years (5.86/100 PYAR, 95% CI: 5.23–6.55) having five times higher than the age >40 years (0.7/100 PYAR, 95% CI: 0.49–0.99).

Cohabited and those who are married were associated with high incident rate of pregnant (5.62/100 PYAR, 95% CI: 1.81–17.43 and 4.16/100 PYAR, 95% CI: 3.79–4.57) as compared to those who are single and divorced (1.81/100 PYAR, 95% CI: 1.39–2.35 and 0.69/100 PYAR, 95% CI: 0.45–1.04).

Weight >55 kg were associated with high incidence of pregnancy being five times higher as compared to lower weigh (5.03 PYAR, 95% CI: 4.54–5.57), and WHO stage I have 11 times high incidence of pregnancy compared to other WHO stages (11.14/100 PYAR, 95% CI: 9.95–12.47).

In this population, having CD4 cell count >200 copies per deciliter was associated with high incidence of pregnancy [Table 4].
Predictors of pregnancy

Putting age into classes in this population was associated with high rate of pregnancy. Starting ART with age
ranging from 15 to 29 years in this population was found to be significant predictors of pregnancy in multivariate (HR = 4.92 [95% CI: 3.33–7.24]), compared to age 40 years and above.

Body weight stratified by categories was significantly associated with occurrence of pregnancy. Starting ART with body weight high at 55 kg was associated with three times hazard of pregnancy compared with lower weight (HR = 2.67 [95% CI: 1.63–4.36]).

Disease stage based on WHO staging was the predictors of pregnancy in this population. WHO stage I during start of ART was significantly associated with 12 times higher hazard of pregnancy as compared to both stages 3 and 4 (HR = 11.76 [95% CI: 6.46–21.41]) [Table 4].
Simiyu is one of the region providing care and treatment services to patient identified with HIV/AIDS since 2005. Due to scaling to HAART and accessibility to clients in Tanzania, the line of HIV infection has shifted from a lethal to a chronic disease as a result of this. This encouraged women to have children as their risk of transmitting the infection was substantially decrease; thus, patients with HIV infection consider having offspring as do other women without the infection within the reproductive age.

This study was an attempt to identify the magnitude and the factors determining the occurrence of pregnancy among HIV patient initiated HAART.

The incidence of pregnancy in this study found to be 3.15/100 PYAR; this highlights that women infected with HIV/AIDS on stable ART become pregnant like their neighbor who are not infected with HIV. This implies that there is an increase in probability of maternal to child transmission of the virus; thus, they need services such as PMTCT and family planning. Our study is similar to other studies that documented HIV women of reproductive age become pregnant when initiated.
ART[10,12,15,18-22] However, our magnitude is low compared from other countries in Sub-Saharan Africa[12,14] and Ethiopia.[23] In contrast, some studies observed that initiation of HAART was not associated with occurrence of pregnant.[24]

This study provides significant evidence that the incidence of pregnancy is higher from age 15 to 39 years. This is the normal age of highly biological reproductive period when the women desire more offspring. When the women infected with HIV and has an advanced disease, the biological reproductive system is impaired and the physiological/psychological desire for bearing children is lost.[25-27] After initiating HAART, the normal functioning of reproductive system is reverted and the women become normal.[15,28] This necessitates that the region put more efforts for primary prevention of HIV for the young group who are not infected to stay free from HIV and those who are affected should kept on lifelong ART and keeping close follow-up to their newborns. Our finding was similar to other studies showing that age was a significant predictor of pregnancy,[10,12,14,15,19,20,22] because this also was a predictors of fertility desire.[17]

Marital status is the clear indicator of sexual activity of an individual. This study showed that the incidence of pregnancy is more among cohabited/married women. Nevertheless, it has no statistical significance in a multivariate analysis. This entails that like other none infected couples, they need reproductive health services such as family planning, PMTCT, and social and behavioral communication changes. However, our study was dissimilar with the several studies, which show that marital status was significantly associated with occurrence of pregnancy.[10,12,14,23] however, what is needed is the frequency sexual contact[29] which does not depend on marital status.

Weight is a proximal measure of progression of the disease and nutrition status of an individual. This study shows that weight was significantly associated with occurrence of pregnancy. This entails that for the women to become pregnant should have good nutritional status. Thus, our work is to promote nutrition promotion to women initiated HAART; thus, they cannot go to advanced stage of the disease. And for those with advanced disease initiated HAART and getting better nutrients can become healthier reverting normal reproductive system. Our study was dissimilar to the studies that did not show the association of weight and occurrence of pregnancy.[12]

The WHO set criteria for classification of the severity of disease in patients with HIV/AIDS. This study provides evidence that women with less-advanced disease (stages 1 and 2) were significantly more likely to become pregnant compared to women with advanced stage of disease (stages 3 and 4). Findings indicate in women with less-advanced stage of the disease; their reproductive systems are well functioning, both biologically and physiologically. Thus, once there is sexual relation between the women and their partner, the chance of getting pregnant is high. Our work is to improve counseling the women when to get pregnant for those who need child bearing. This study had similar findings with other work indicating that WHO stage was significantly associated with incidence of pregnancy.[10]

When women are infected with HIV virus, it depletes the immunity. CD4 cells count is used to measure the immunological pattern of the patient infected with HIV. This study shows that CD4 cells count was not significantly associated with incidence of pregnancy in multivariate analysis. These findings were not similar with the findings of study conducted in Uganda, which shows that the levels of CD4 count were one of the determinants of pregnancy.[14] However, study conducted by Mmbaga et al.[30] showed that fertility desire increases when CD4 cells count are higher, which subsequently increases the possibility of HIV infected women to became pregnant.

Limitation of the study
In view of the fact that this is a retrospective study using already recorded data, some of the variables are missing such as family planning uptake, body mass index, adherence to ART, missing weight, CD4 count, and unknown pregnancy status; thus, some of the observation was deleted and this could affect the predictors of pregnant.

Conclusion
With regard to this finding, the incidence of pregnant in Simiyu region among women taking antiretroviral treatment was found to be considerably present in young women.

Predictors of pregnant after ART initiation in this population were young age and being healthier.

Recommendation
Policy for integration of family planning services into HIV CTCs should be strengthened but focused on young women. More follow-up study is needed to see the pregnant and new-born outcome.

Ethical policy and institutional review board statement
Ethical approval was obtained from the National Medical Institute of Research of Tanzania.
Acknowledgement
The authors acknowledge the Ariel Glaser Paediatric AIDS Healthcare Initiative (AGPAHI) for the long term support for care, treatment and prevention of HIV/AIDS in the Region.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References
1. UNAIDS (2018). Fact sheet, 2017 Global HIV statistics, and 2030 ending the AIDS epidemic.
2. Tanzania Commission for AIDS (TACAIDS), Zanzibar AIDS Commission (ZAC), National Bureau of Statistics (NBS), Office of the Chief Government Statistician (OCGS), and ICF International. 2013. Tanzania HIV/AIDS and Malaria Indicator Survey 2011-12. Dar es Salaam, Tanzania: TACAIDS, ZAC, NBS, OCGS, and ICF International.
3. Global report: UNAIDS report on the global AIDS epidemic 2010. “UNAIDS/10.11E | JC1959E.”
4. Matthäus E, Bernard H, Patrick F, Philippe S, Marc W, Markus F, et al. Impact of new antiretroviral combination therapies in HIV infected patients in Switzerland: Prospective multicentre study. BMJ 1997;315:1194-9.
5. Meg O, Katherine H, Eric G, Nathan F, Mariette S, Graeme M, et al. Immune restoration disease after the treatment of immunodeficient HIV-infected patients with highly active antiretroviral therapy. Human Reprod Update 2007;13:197-206.
6. French MA, Lemo N, James IR, Price P, Flexman JP, Tay Kearney M-L, et al. Immune restoration disease after the treatment of immunodeficient HIV-infected patients with highly active antiretroviral therapy. Human Reprod Update 2007;13:197-206.
7. Joy Noel B, Mackenzie G, Mark AW, Gottlieb M, Thecla WK, Christine L, et al. Integrating family planning services into HIV care and treatment clinics in Tanzania: Evaluation of a facilitated referral model. Health Policy Plan 2014;29:570-9.
8. Shrinivas D, Inge H, Sanjeevani K, Vinay K, Fanny J. Occurrence of pregnancies among HIV infected Indian women: Does knowledge about HIV status make a difference? Int J Population Res, Vol 2015, Article ID 578150.
9. Mujumdar V, Berman D, Schafer KR. Reproduction and fertility beliefs, perceptions, and attitudes in people living with HIV. AIDS Res Treatment Volume 2018, Article ID 5349793.
10. Myer L, Carter RJ, Katyal M, Toro P, El-Sadr WM, Abrams EJ. Impact of antiretroviral therapy on incidence of pregnancy among HIV-infected women in Sub-Saharan Africa: A cohort study. PLoS Med 2010;7:e1000229.
11. Kipp W, Heys J, Jhangri GS, Bosena T, Temamen T. Fertility desire and associated factors among people living with HIV attending antiretroviral therapy clinic in Ethiopia. BMC Pregnancy Childbirth 2014.
12. Arnel P, Arsène H, Aina K, Firmin K, Jacques Z, Adrien Bruno S, et al. Pregnancy rate and birth outcomes among women receiving antiretroviral therapy in Burkina Faso: A retrospective cohort study. Pan Afr Med J 2013;23:105.
13. Daniel W, Mhairy M, Dennis R, Ippa M, Imogen J, Pappie M et al. Incidence of pregnancy after initiation of antiretroviral therapy in South Africa: A retrospective clinical cohort analysis. Infect Dis Obstet Gynecol Volume 2012, Article ID 971059.
14. Homys J, Bunnell R, Moore D, King R, Malamba S, Nakityo R, et al. Reproductive intentions and outcomes among women on antiretroviral therapy in rural Uganda: A prospective cohort study. PLoS One 2009;4:e4149.
15. Schwartz SR, Rees H, Mehta S, Venter WDF, E Taha T, Black V. High incidence of unplanned pregnancy after antiretroviral therapy initiation: Findings from a prospective cohort study in South Africa. PLoS One 2012;7:e36039.
16. Blair JM, Hanson DL, Jones JL, Dworkin MS. Trends in pregnancy rates among women with human immunodeficiency virus. Obstet Gynecol 2004;103:663-8.
17. Meseret M, Shimeka A, Bekele A. Incidence and predictors of pregnancy among women on ART in Debre Markos referral hospital, Northwest Ethiopia: A Five-Year Retrospective Cohort Study. AIDS Res Treatment, Volume 2017, Article ID 3261205.
18. Elul B, Wool-Kaloustian KK, Wu Y, Musick BS, Nuwagabba-Biribonwoha H, Bash D, et al. Untangling the relationship between antiretroviral therapy use and incident pregnancy: A marginal structural model analysis using data from 47,313 HIV-positive women in East Africa. J Acquir Immune Defic Syndr 2016;72:324-32.
19. Huntington SE, Thorne C, Banski LD, Anderson J, Newell M-L, Sabin CA, et al. Predictors of pregnancy and changes in pregnancy incidence among HIV-positive women accessing HIV clinical care at 13 large UK clinics. AIDS 2013;27:95-103.
20. Amanda R, Lieve V, Rosemary L, Billy NM, Leigh Anne S, Jimmy W, et al. HIV-1 disease progression and fertility: the incidence of recognized pregnancy and pregnancy outcome in Uganda. AIDS 2004;18:799-804.
21. Kaida A, Matthews LT, Kantes S, Kabakyenga J, Muzoora C, Mocello AR, et al. Incidence and predictors of pregnancy among a cohort of HIV-positive women initiating antiretroviral therapy in Mbarara, Uganda. PLoS One 2013;8:e63411.
22. Beth SL, Howard M, Mardge HC, Roksana K, Deborah C, Elizabeth TG, et al. Relative time to pregnancy among HIV-infected and uninfected women in the Women's Interagency HIV Study, 2002–2009. AIDS 2011;25:707-11.
23. Salters K, Loutfy M, de Pokomandy A, Money D, Pick N, Wang L, et al. Pregnancy incidence and intention after HIV diagnosis among women living with HIV in Canada. PLoS One 2017;12:e0180524.
24. Mnmbaga EJ, Leyna GH, Ezekiel MJ, Kakoko DC. Fertility desire and intention of people living with HIV/AIDS in Tanzania: A call for restructuring care and treatment services. BMC Public Health 2013;13:86.