Original Article

Incidence and determinants of pregnancy among women receiving HAART in Simiyu region: 14-year retrospective follow-up

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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]

Access this article online	
Website: www.tjogonline.com	Quick Response Code
DOI: 10.4103/TJOG.TJOG_92_19	

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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 km^2 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-STATA-PC) 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].

Table 1: Demographic characteristics, numbers, become pregnant, censored, proportion (percent, total) of women receiving HAART in Simiyu region, 2005-2018

Variable	Number	Become pregnant	Proportion pregnant (%)	Censored	Proportion censored (%)	Total frequency
Median age	34.2±7.8					
Age						
15-29	1617	324	58.48	1293	29.94	1617 (33.19)
30-39	2007	197	35.56	1810	41.92	2007 (41.19)
40-49	1248	33	5.96	1215	28.14	1248 (25.61)
Marital status						
Cohabited	16	3	0.54	13	0.30	16 (0.33)
Divorced/widowed	882	24	4.33	858	19.87	882 (18.10)
Married	3070	469	84.66	2601	60.24	3070 (63.01)
Single	904	58	10.47	846	19.59	904 (18.56)
District of treatment						
Bariadi	1759	270	48.64	1482	34.38	1751 (36.00)
Busega	1071	94	17.00	977	22.66	1071 (22.02)
Maswa	2042	190	34.36	1852	42.96	2042 (41.98)
Weight						
<45	886	19	3.43	867	20.08	886 (18.19)
45-55	1875	143	25.81	1732	40.11	1875 (38.49)
55+	2111	392	70.76	1719	39.81	2111 (43.33)
Who stage						
1	941	313	56.50	628	14.54	941 (19.31)
2	1663	157	28.34	1506	34.88	1663 (34.13)
3	1532	64	11.55	1468	34.00	1532 (31.44)
4	736	20	3.61	716	16.58	736 (15.11)
Cd4 count						
<50	320	14	2.53	306	7.09	320 (6.57)
50-199	975	42	7.58	933	21.61	975 (20.01)
200-349	1158	102	18.41	1056	24.46	1158 (23.77)
350-499	925	123	22.20	802	18.57	925 (18.99)
>=500	1494	273	49.28	1221	28.28	1494 (30.67)

Sources: CTC2 Database from Care and Treatment Clinics in Simiyu 2005-2018

Table 2: The number of subject, events, analysis time, incidence of pregnancy, and 95% confidence interval estimates for sociodemographic characteristics variables among female in care and treatment clinics in Simiyu region, 2005-2018

Variable	Number of female	Become pregnant	PYAR (per 100 PRAY)	PR (per 100 PRAY)	PR (95% CI)
Crude	4709	525	166.7918	3.15	2.88-3.43
Age					
15-29	1558	304	50.9017	5.97229	5.34-6.68
30-39	1944	190	71.9931	2.63914	2.29-3.042
40-49	1207	31	43.8969	0.70620	0.50-1.00
Marital status					
Cohabited	16	3	0.4914	6.10514	1.97-18.93
Divorced/widowed	865	22	31.5428	0.69746	0.46-1.06
Married	2971	445	104.6621	4.25178	3.87-4.67
Single	857	55	30.0954	1.82752	1.40-2.38
District of treatment					
Bariadi	1722	263	66.2744	3.9683	3.52-4.48
Busega	1061	93	33.5107	2.7752	2.26-3.40
Maswa	1922	169	66.8868	2.5267	2.17-2.94

Figures 1–4 show a difference in probability curve within different category of age, weight, WHO stage, and CD4 cells count.

Predictors of pregnancy

Putting age into classes in this population was associated with high rate of pregnancy. Starting ART with age

Table 3: The number of subject, events, analysis time, incidence of pregnancy, and 95% confidence interval estimates for medical characteristics variables among female in care and treatment clinics in Simiyu region 2005-2018

Variable	Number of female	Become pregnant	PYAR (per 100 PRAY)	PR (per 100 PRAY)	PR (95%CI)
Weight					
<45	851	19	29.05	0.65	0.42-1.03
45-55	1824	139	65.79	2.11	1.79-2.49
55+	2034	367	71.95	5.10	4.61-5.65
Who stage					
1	917	302	26.64	11.33	10.13-12.69
2	1597	144	55.04	2.62	2.22-3.08
3	1475	59	52.48	1.12	0.87-1.45
4	720	20	32.63	0.61	0.40-0.95
Cd4 count					
<50	300	12	7.16	1.68	0.95-2.95
50-199	939	39	27.54	1.42	1.03-1.94
200-349	1123	98	40.95	2.39	1.96-2.92
350-499	910	122	34.09	3.58	3.00-4.27
>=500	1437	254	57.05	4.45	3.94-5.03

Table 4: Estimated hazard ratio (cHR and aHR) and 95% confidence intervals for age, marital status, district of residence, weight, WHO stage and Cd4 count categories from female enrolled into care and treatment clinics, 2005-2018

Variable	Being pregnant	CHR [95% confidence interval]	AHR [95% confidence interval]
Age			
15-29	304	8.42 [5.82-2.19]	4.92 [3.33-7.24]
30-39	190	3.57 [2.44-5.22]	2.96 [1.99-4.39]
40-49	31	1	1
Marital status			
cohabited	3	2.94 [0.92-9.40]	1.07 [0.37-3.37]
Divorced/widowed	22	0.38 [0.23-0.63]	0.28 [0.17-0.45]
Married	445	2.32 [1.75-3.07]	0.57 [0.42-0.75]
Single	55	1	1
Weight			
<45	19	1	1
45-55	139	3.19 [1.97-5.15]	1.46 [0.89-2.42]
55+	367	7.82 [4.93-12.40]	2.67 [1.63-4.36]
Who stage			
1	302	23.26 [14.51-37.31]	11.76 [6.46-21.41]
2	144	5.03 [3.10-8.15]	4.05 [2.23-7.38]
3	59	2.15 [1.28-3.61]	1.70 [0.91-3.17]
4	20	1	1
Cd4 count			
<50	12	1	1
50-199	39	0.87 [0.46-1.66]	0.60 [0.31-1.15]
200-349	98	1.47 [0.80-2.67]	0.71 [0.39-1.30]
350-499	122	2.19 [1.21-3.96]	0.78 [0.43-1.44]
>=500	254	2.72 [1.52-4.85]	0.92 [0.51-1.67]

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].

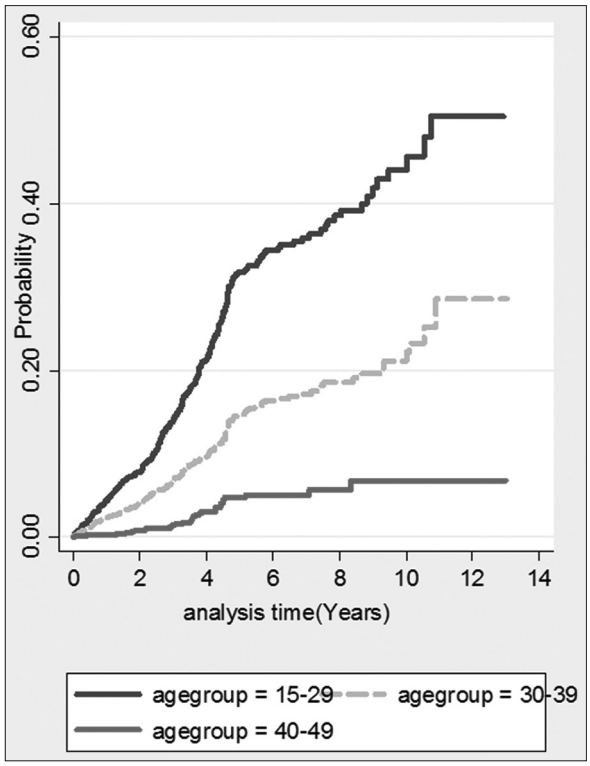

Figure 1: Kaplan-Meier plots of cumulative probability of pregnancy for HIV/AIDS women after ART start in Simiyu region by age category

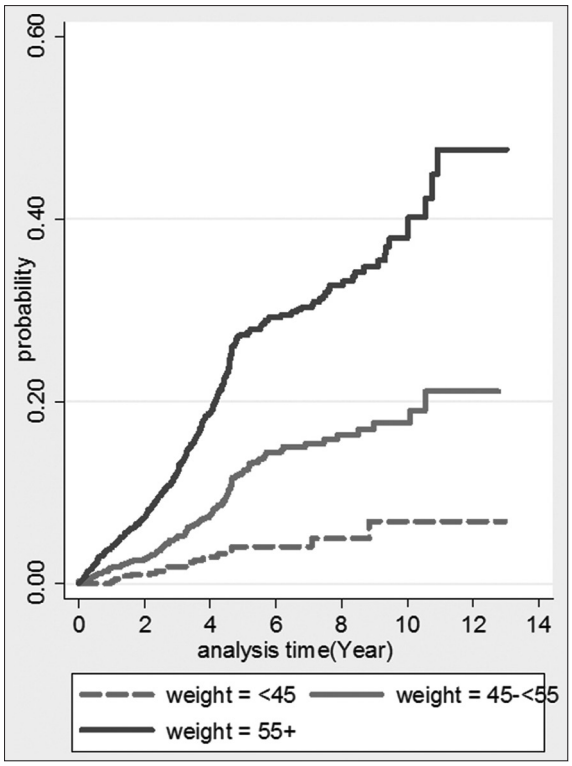

Figure 2: Kaplan-Meier plots of cumulative probability of pregnancy after ART start in simiyu region by Weight

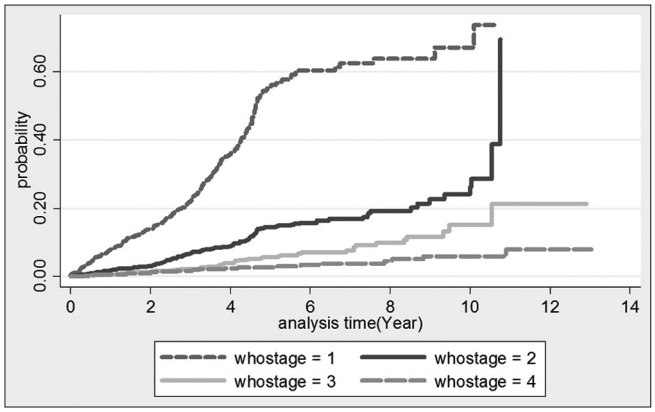

Figure 3: Kaplan-Meier plots of cumulative probability of pregnancy after ART start in simiyu region by WHO stage

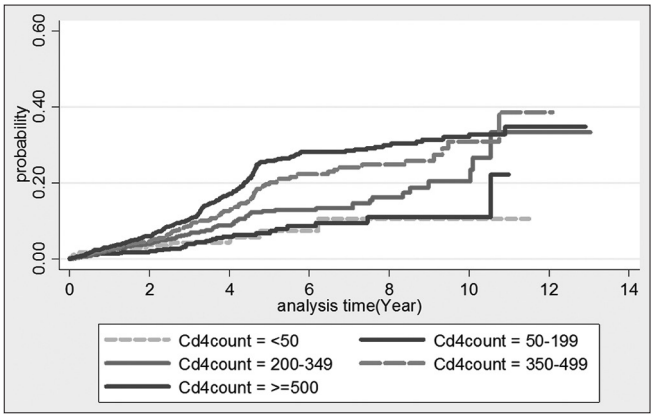

Figure 4: Kaplan-Meier plots of cumulative probability of pregnancy after ART start in simiyu region by Cd4 Count

Discussion

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.[4,6] This encouraged women to have children as their risk of transmitting the infection was substantially decrease;[9] thus, patients with HIV infection consider having offspring as do other women without the infection within the reproductive age.[12,16,17]

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;[10,14,23] 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.

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