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Incidence and predictors of Pregnancy among HIV Positive women on ART in North West Ethiopia: A Retrospective Cohort Study

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Abstract

Objective: The objective of this study was to identify the prevalence and significant factors of incidence of pregnancy among HIV-positive women under ART follow-up.

Methods: A retrospective cohort study was employed and a sample size of 429 was selected using a simple random sampling technique. Both chi-square test of association and multiple binary logistic regression analysis was used.

Results: The study has shown that 21.2 % of women were pregnant during the follow-up. Variables like WHO clinical stage, spouse's HIV status, marital status, contraception use, body weight, occupation, CD4 count, age, and time of ART were significant predictors of incidence of pregnancy.

Conclusion: Women with advanced WHO clinical stages were less likely to be pregnant. Women, who are married, employed, and had never used contraceptive methods were more likely to have pregnant. When CD4 cell count and body weight increase, the incidence of pregnancy also increases and women who had a longer time on ART were more likely to be pregnant.

Health institutions and clinicians should be cautious when the patients have faced advanced WHO clinical stage and low CD4 count. We would like to put remarks on increasing the employment of HIV Positive women, providing effective services of ART health care, and studying further investigation for the general wellbeing of mothers and their respective potentially born children.

Keywords: Antiretroviral Therapy, Binary logistic regression, Incidence of Pregnancy

Introduction

HIV is the most serious disease that humankind has ever faced, and it is a social dilemma as well. It becomes one of the world's most serious health and development challenges for women under productive age **[1].** In 2020, an estimated 37.7 million people were living with HIV worldwide, and 27.5 million people were receiving HIV treatment in the year. In 2020, nearly three-fourths (73 %) of all people living with HIV were receiving life-saving antiretroviral therapy, and 85 % of pregnant women living with HIV had access to antiretroviral treatments to prevent transmission of HIV to their child. In 2020, about 680,000 death were recorded due to AIDS-related illnesses, which is a great declination compared with death in 2010 (1.3 million) worldwide. Out of the global number of pregnant women, 83 % were living with HIV and 68 % of them were receiving life-saving antiretroviral therapy in 2020. Two-thirds (67 %) of sub-Saharan African people were living with HIV in 2020 **[2]**.

In Ethiopia, 690,000 people were living with HIV and 65 % of them were on treatment in 2018. This year, 92 % of pregnant women with HIV received ART to prevent the disease's mother-to-child transmission during pregnancy and to the mothers' health.

In Ethiopia, seven regions and two administrative cities have HIV prevalence above one percent. In the regions, the prevalence of HIV was highest in Gambella (4.8 %), followed by Addis Ababa (3.4 %), Dire Dawa (2.5 %), and Harari (2.4 %) **[3]**. For HIV/AIDS infected women, significantly ameliorated having HIV-negative children by increasing the accessibility of ART; because, it has the potential to decrease the risk of HIV transmission from mother to child and prevents AIDS-related illness and death **[4]**. However, HIV-positive women are not volunteering to have the pregnancy and they are frightened to get HIV-negative children. Hence, it is significant to identify the prevalence and significant predictors of incidence of pregnancy under ART follow-up. So far, in different areas of the world, studies were conducted including in Ethiopia. However, most of the studies were done using descriptive statistics, and studies conducted in different parts of Ethiopia were not addressing the problem. Hence it is mandatory to conduct studies on the area under discussion. The study aimed to assess the prevalence and predictors of incidence of pregnancy among HIV-positive women under ART follow-up in Finote Selam general hospital.

Method

Description of the Study Area

The study was conducted at Finote Selam General Hospital, which is located in Finote Selam City administration, capital of west Gojjam zone, Amhara Region, Ethiopia. The town is located at about 387 km far from Addis Ababa and 173 km far from Bahir Dar Capital city of Amhara national regional state, Ethiopia. This hospital is the only general hospital in West Gojjam Zone that provides ART services for people living with HIV in the area of rural and urban surrounding the hospital.

Study Design and Data sources

A four-year institution-based retrospective cohort study was employed from October 2016 to September 2019 based on secondary data from medical charts of the ART clinic of the hospital.

The sources of data were HIV-positive women under ART follow-up in the Hospital. The data included all HIV-positive women under the follow-up of ART those who are aged between 15 and 49 years at the ART clinic of the hospital.

Variables in the Study

The response variable of the study was the incidence of pregnancy of HIV-positive women under ART follow-up (pregnancy occurred = 1, pregnancy not occurred =0).

The independent variables included in this study were age, educational level, occupation, marital status, religion, place of residence, child alive of women before ART follow-up, contraceptive use, WHO clinical stage, co-infection, body weight, time on ART follow-up, CD4 count and Spouse HIV status of women.

Sample Size Determination and Sampling Technique

In the research, the sample size is the core element, and it can be determined based on the following constraints: the objective of the research, design of the research, cost constraint, and degree of precision required. Considering these things, the sample size was determined using the following formula:

$$n = \frac{Z^2 P(1-P)}{1 + \frac{1}{N}\left(\frac{Z^2 P(1-P)}{d^2} - 1\right)}$$

Where n is the required sample size, Z = 1.96 from a standard normal distribution, the degree of precision, d is 0.04, and the proportion of success (P) is 0.5. Based on these values the final required sample was 429.

A simple random sampling technique was employed to select these 429 sample women from the ATR clinic for a total record of patient women in the given time frame.

Method of Data Collection

Secondary data was used and a structured data collection checklist was prepared in English to extract data from the records. Data were extracted from the main excel record and patient cards of the hospital. The data was collected by the data clerk of the ART clinic and health professionals of the hospital working on the ART database.

Statistical Analysis

The data were extracted from the medical chart of HIV-positive women and checked for completeness. After checking consistency and completeness, data were coded and analyzed using SPSS version 20 software. Descriptive statistics were used to assess the prevalence of incidence of pregnancy and to see the percentage of independent variables. Both chi-square test and binary logistic regression analysis were employed. A Chi-square test was used to identify the rough association between dependent and independent variables. Lastly, multiple binary logistic regression analysis was used to identify the significant variables for the incidence of pregnancy. The strength of association was interpreted using an odds ratio with a 95 % confidence interval; because the logistic regression model has a powerful analytic tool for medical research of the regression coefficients as log odds **[5]**. When odds ratio is the ratio of the probability of the occurrence of an event to the non-occurrence of an event **[6]**. From the result of multiple logistic regression analysis, variables with a *P*-value of ≤ 0.05 were considered significant predictors of incidence of pregnancy for HIV-positive women.

Ethical Approval and Informed Consent

This study received ethical approval from the institutional review board of Finote Selam general hospital. All study participants were informed that they have full right not to participate in the study or to stop the interview at any time they wish if that was their choice. All patients provided written informed consent before enrollment in the study.

Results

General characteristics

The objective of this study was to assess the prevalence and to identify the important predictors of incidence of pregnancy of women on ART follow-up. Of the total (n=429) sample women, 91 (21.2 %) were pregnant during the study time. The result showed that mothers who are under WHO stage I, stage II, stage III, and stage VI were 101 (23.5 %), 156 (36.4 %), 120 (28.0 %), and 52 (12.1 %), respectively.

More than half (n=225, 52.4 %) of HIV-positive women were married and most (n=384, 89.5 %) of the women were live in the urban area. Out of the total sample, about 160 (37.3 %) and 118 (27.5 %) reported their level of education as primary and secondary respectively. Nearly half (n=209, 48.7 %) of the respondents reported that their time duration in ART follow-up was less than 25 months. Furthermore, more than one-third (n= 160, 37.3 %) of women were unemployed and 271 (63.2 %) of women had children alive before ART follow-up (**Table 1**). Before multiple logistic regression analysis, the chi-square test of association was made to identify the rough association between the incidence of pregnancy and independent variables. From the Chi-

square Test of association, the incidence of pregnancy was associated with WHO clinical stage, illness due to co-infection, Spouse's HIV status, marital status, educational level, place of residence, Contraception use, CD4 cell count, time of ART, body weight, occupation, age and child alive before ART follow-up, at 5 % level of significance **(Table 1)**.

Table 1: Socio-demographic and clinical characteristics of HIV positive women on ART follow up in Finote Selam general hospital, Oct. 2016 to Sep. 2019 (n=429) and Chi-square Tests of association.

Variables	**Categories**	**Pregnancy not occurred**	**Pregnancy occurred**	**Total**	**Pearson Chi-square (Sig.)**
		Count (%)	**Count (%)**	**n (%)**	
WHO clinical stage	Stage I	47 (13.9)	54 (59.3)	101 (23.5)	91.791 (0.000)
	Stage II	127 (37.6)	29 (31.9)	156 (36.4)	
	Stage III	115 (34.0)	5 (5.5)	120 (28.0)	
	Stage IV	49 (14.5)	3 (3.3)	52 (12.1)	
Illness due to co-infection	No	154 (45.6)	78 (85.7)	232 (54.1)	46.546 (0.000)
	Yes	184 (54.4)	13 (14.3)	197 (45.9)	
Spouse's HIV status	Negative	91 (26.9)	26 (28.6)	117 (27.3)	29.950 (0.000)
	Positive	49 (14.5)	35 (38.5)	84 (19.6)	
	Unknown	198 (58.6)	30 (33.0)	228 (53.1)	
Marital status	Married	144 (42.6)	81 (89.0)	225 (52.4)	62.014 (0.000)
	Unmarried	43 (12.7)	3 (3.3)	46 (10.7)	
	Divorced	81 (24.0)	4 (4.4)	85 (19.8)	
	Windowed	70 (20.7)	3 (3.3)	73 (17.0)	
Educational level	No education	84 (24.9)	10 (11.0)	94 (21.9)	27.392 (0.000)
	Primary	134 (39.6)	26 (28.6)	160 (37.3)	
	Secondary	88 (26.0)	30 (33.0)	118 (27.5)	
	College and above	32 (9.5)	25 (27.5)	57 (13.3)	
Residence	Rural	41 (12.1)	4 (4.4)	45 (10.5)	4.568 (0.033)
	Urban	297 (87.9)	87 (95.6)	384 (89.5)	
Contraceptive use	Never	206 (60.9)	67 (73.6)	273 (63.6)	18.352 (0.000)
	Rarely	29 (8.6)	15 (16.5)	44 (10.3)	
	Mostly	38 (11.2)	5 (5.5)	43 (10.0)	
	Always	65 (19.2)	4 (4.4)	69 (16.1)	
CD4 cell count	< 250	136 (40.2)	4 (4.4)	140 (32.6)	66.558 (0.000)
	250-350	74 (21.9)	10 (11.0)	84 (19.6)	
	351-500	60 (17.8)	31 (34.1)	91 (21.2)	
	> 500	68 (20.1)	46 (50.5)	114 (26.6)	
Time of ART follow-up	≤ 24 months	185 (54.7)	24 (26.4)	209 (48.7)	26.229 (0.000)
	25-48 months	76 (22.5)	41 (45.1)	117 (27.3)	
	> 48 months	77 (22.8)	26 (28.6)	103 (24.0)	
Occupation	Employed	68 (20.1)	49 (53.8)	117 (27.3)	46.716 (0.000)
	Unemployed	147 (43.5)	13 (14.3)	160 (37.3)	
	Housewife	123 (36.4)	29 (31.9)	152 (35.4)	
Body Weight	< 50 kg	113 (33.4)	8 (8.8)	121 (28.2)	36.462 (0.000)
	50-60 kg	153 (45.3)	38 (41.8)	191(44.5)	
	> 60 kg	72 (21.3)	45 (49.5)	117 (27.3)	
Age	15-24	45 (13.3)	24 (26.4)	69 (16.1)	22.942 (0.000)
	25-29	102 (30.2)	39 (42.9)	141 (32.9)	
	30-35	92 (27.2)	19 (20.9)	111 (25.9)	

	> 35	99 (29.3)	9 (9.9)	108 (25.2)	
Child of women	Have no child	104 (30.8)	54 (59.3)	158 (36.8)	25.157 (0.000)
	Have a child	234 (69.2)	37 (40.7)	271 (63.2)	
Incidence of pregnancy		338 (78.8)	91(21.2)		

Result of Multiple Logistic Regression Analysis

Multiple binary logistic regression was used to identify the important predictors of incidence of pregnancy. The result of this analysis showed the estimated coefficients, odds ratio, p-value, Wald statistic, and 95 % confidence interval. The significance of the Wald statistic tells the importance of the predictor variable in the model. The result revealed that variables such as WHO clinical stage, spouse's HIV status, marital status, contraception use, and time on ART follow-up, body weight, occupation, age, CD4 cell count, and child alive before ART follow-up were found the significant predictors of incidence of pregnancy at 5 % of the level of significance. Based on the result, the odds of incidence of pregnancy in women under WHO clinical stage II was 0.277 (95 % CI, 0.062-1.228) times less likely than in stage I. The odds ratio of unmarried, divorced, and widowed women were 0.013 (95 % CI, 0.002-0.101), 0.007 (95 % CI, 0.001-0.065), and 0.020 (95 % CI, 0.001-0.268) respectively, which indicates that unmarried, divorced and widowed women were 98.7 %, 99.3 % and 98 % less likely to be pregnant than married women respectively. Based on the result, CD4 count was a significant predictor of the incidence of pregnancy. HIV-positive women who had a CD4 count greater than 500 cells count were 9.522 (95 % CI, 1.265-71.674) times more likely to be pregnant compared to women who had a CD4 count of less than 250 cell/mm3. According to the time of ART follow-up, women who followed ART for 25-48 months were 21.363 (95 % CI, 3.750-121.681) times more likely to have pregnancy compared to the reference group. The body weight of women was positively and significantly related to the incidence of pregnancy. The odds ratio of women who had body weight between 50 and 60 kilograms was 55 % (95 % CI, 0.325-7.387) more likely to be pregnant than women who had body weight less than 50 kilograms. Moreover, occupation is also a significant predictor of the incidence of pregnancy; unemployed women were 0.097 (95 % CI, 0.019-0.490) times less likely to be pregnant than employed women. Finally, the odds of women having a child being pregnant were reduced by 84.9 % (95 % CI, 0.041-0.554) as compared to those women with no child before ART follow-up **(Table 2)**.

Table 2: Result of Multiple Logistic Regression Analysis of incidence of pregnancy among HIV positive women on ART in Finote Selam general hospital, Oct. 2016 to Sep. 2019

Covariate	**Category**	**B**	**S.E.**	**Wald**	**df**	**Sig.**	**Exp(B)**	**95.% CI EXP (B)**	
								Lower	**Upper**
WHO clinical stage	Stage I (ref.)			16.320	3	.001*			
	Stage II	-1.285	.760	2.857	1	.091	.277	.062	1.228
	Stage III	-5.085	1.310	15.065	1	.000*	.006	.000	.081
	Stage IV	-3.745	1.846	4.114	1	.043*	.024	.001	.882
Spouse's HIV status	Negative (ref.)			6.871	2	.032*			
	Positive	1.614	.742	4.725	1	.030*	5.023	1.172	21.526
	Unknown	-.464	.761	.371	1	.542	.629	.141	2.797
Marital status	Married (ref.)			25.368	3	.000*			
	Unmarried	-4.326	1.040	17.315	1	.000*	.013	.002	.101
	Divorced	-4.904	1.111	19.485	1	.000*	.007	.001	.065
	Widowed	-3.920	1.328	8.715	1	.003*	.020	.001	.268
Contraception use	Never(ref.)			19.940	3	.000*			
	Rarely	-.1.026	.978	1.102	1	.294	.358	.053	2.435
	Mostly	-4.100	1.105	13.774	1	.000*	.017	.002	.144
	Always	-3.671	1.106	11.019	1	.001*	.025	.003	.222
CD4 cell count	< 250 (ref.)			22.550	3	.000*			
	250-350	-2.700	1.286	4.410	1	.036*	.067	.005	.835
	351-500	1.594	1.060	2.263	1	.133	4.925	.617	39.322
	> 500	2.254	1.030	4.789	1	.029*	9.522	1.265	71.674

Time on ART follow up	> =24 months			11.978	2	.003*			
	25-48 months	3.062	.888	11.897	1	.001*	21.363	3.750	121.681
	> 48 months	2.135	.926	5.315	1	.021*	8.460	1.377	51.973
Body weight of women	< 50 kg (ref.)			6.284	2	.043*			
	50-60 kg	.438	.797	.303	1	.582	1.550	.325	7.387
	> 60 kg	1.949	.907	4.616	1	.032*	7.018	1.186	41.515
Occupation	Employed (ref.)			10.108	2	.006*			
	Unemployed	-2.334	.827	7.976	1	.005*	.097	.019	.490
	Housewife	-2.636	.904	8.499	1	.004*	.072	.012	.422
Age	15-24 (ref.)			16.401	3	.001*			
	25-29	.166	.761	.048	1	.827	1.181	.266	5.249
	30-35	-2.423	1.030	5.538	1	.019*	.089	.012	.667
	> 35	-5.035	1.333	14.255	1	.000*	.007	.000	.089
Child alive	Have a child	-1.892	.664	8.111	1	.004*	.151	.041	.554
Constant		1.569	2.442	.413	1	.520	4.804		

ref.=Reference category which is the first category; *=significant at 5 % significance level

Discussions

The objective of this study was to assess the prevalence and to identify the important predictors of incidence of pregnancy of HIV positive women on ART follow up. As per the result of descriptive analysis, out of 429 samples about 91 (21.2 %) of women had pregnancy during the follow up. From multiple logistic regression analysis, WHO clinical stage, spouse's HIV status, marital status, contraception use, body weight, child alive before ART, occupation, CD4 cell count, age and time of ART follow-up were significant predictors at 5 % level of significance.

The study has shown that WHO clinical stage was an important significant variable of incidence of pregnancy. According to the result of this study, women who are under advanced WHO clinical stage were less likely to become pregnant. That is, incidence of pregnancy was negatively related with WHO clinical stage, when the stages become increase, the incidence of pregnancy decrease. This implies that women who had WHO clinical stage I were more likely to be pregnant and this result is supported by the studies **[7,9]**. This difference might be due to those women in stage I at initiation of ART have a better health.

Marital status of women was also significant predictor for the incidence of pregnancy of HIV positive women. The result indicates that married women were more likely to be pregnant than other category. This finding is similar with the study in Ethiopia, Uganda and Brazil **[7,8,11,13,14]**. The possible reason for the explanation might be differences in the size of records reviewed, the study period, and marital status is the clear indicator of sexual activity of an individual.

From the result contraception use of women was a significant predictor of incidence of pregnancy. Women who ever-used contraception (mostly, always) were less likely to became pregnant than women who never use contraception and this is supported by the study of **[8,11]**.

As shown from the result, CD4 cell count was strong significant predictors and positively related with incidence of pregnancy. The incidence of pregnancy during ART follow-up was highest among women with CD4 count greater than 500 cell/mm3. The incidence of pregnancy of women was increased with increasing of CD4 cell count. The result is consistent with the study of **[10,13]** and inconsistent with the study of **[11]**. The possible justification might be due to that fertility desire increases when CD4 cells count are higher, which subsequently increases the possibility of HIV infected women to become pregnant.

Time of ART follow-up was important predictor and positively related with incidence of pregnancy. Women on ART for 25-48 months were 21.363 times more likely to become pregnant than women on ART less than 25 months and women on ART for more than 48 months were 8.46 times more likely to become pregnant than women less than 25 months. This indicate that longer time on ART follow-up were associated with increasing probability of becoming pregnant. This finding was in line with the study in Malawi and Uganda **[9,12]**.

Body weight of women was significant predictor for incidence of pregnancy. From the output, women who had body weight between 50and 60 kilogram were more likely to be pregnant than women who had body weight less than 50 kilogram. Additionally, women who had body weight greater than 60 kilogram were more likely to be pregnant compared with the reference group and this study was similar with the studies of **[7, 11]**.

Based on the result, occupation of women was significant predictor of incidence of pregnancy. Both unemployed and housewife women were less likely to be pregnant compared to employed women. This

implies that incidence of pregnancy was higher in employed patient women than other groups on ART follow-up. This result was consistent with the study in sub-Saharan Africa and Ethiopia **[14]** and inconsistent with the study by **[9]** in Malawi. The possible explanation of this finding might be due to the fact that in most circumstances in Ethiopia employed women are those with better educational status and they could be financially secured.

The study revealed that age of women was a significantly and negatively related with incidence of pregnancy on ART follow-up. The prevalence of pregnancy during the follow-up was higher among younger women aged 15-24 and 25-29, than older women. This indicate that there was decreasing the probability of incidence of pregnancy with increasing age of women. These results are expected because women are generally most fertile between the ages of 20 and 24 years and as they get older the likelihood of getting pregnant decreases. This finding was supported by similar findings in sub-Saharan Africa, Malawi, Uganda and Brazil **[7,8,9,10,11,13]**. The explanation is probably that it is more common for women in having children at a younger age in Ethiopia and the fact that younger women are generally more fertile.

The result of our study indicates that number of child alive before ART follow-up was another important significant variable for incidence of pregnancy. Women who have no child were more likely to become pregnant compared to women who had child. Likewise, women who had fewer children were more likely to become pregnant compared to women who had more. This result was consistent with the finding of **[11,14]** and inconsistent with the study of **[13]**.

Conclusions

The aim of the study was to assess the prevalence and to identify the important predictors of incidence of pregnancy among HIV positive women under ART follow-up of reproductive ages in Finote Selam general Hospital. Both chi-square test and binary logistic regression analysis were employed. Out of total sample about 21.2 % of women had pregnancy during ART follow up. From logistic regression result, the significant predictors of incidence of pregnancy on HIV positive women under ART follow up were WHO clinical stage, spouse's HIV status, marital status, use of contraception, CD4 count, time of ART follow-up, body weight, occupation, age and child alive. Women with advance WHO clinical stage were less likely to be pregnant. Women being married, being employed, never use contraceptive, had HIV positive spouse, had child were more likely to have pregnancy on the follow up. When CD4 cell count and body weight increase, incidence of pregnancy also increases and women who had longer time on ART follow up were more likely to be pregnant.

Based on the findings of this study, the following recommendations were made:

- Zonal Health Department and health institutions should be cautious when the patients have faced advanced WHO clinical stage and low CD4 count.
- Effective counseling strategies have to be designed focusing on unemployed, housewife mothers and mothers with no children at enrollment to encourage pregnancy.
- We would like to put remarks of increasing employment of HIV Positive women, providing effective services of ART health care, and studying further investigation for the general wellbeing of mothers and their respective potentially born children.

Abbreviations

AIDS: Acquired Immunodeficiency Syndrome

ART: Antiretroviral Therapy

ARV: Antiretroviral Drugs

CD4: Cluster designation 4 positive lymphocytes

HIV: Human Immunodeficiency Virus

MLE: Maximum Likelihood Estimation

OR: Odds Ratio

UNAIDS: United Nations AIDS Programme

USAID: United State Agency for International Development

WHO: World Health Organization

Declarations

Availability of data and materials

The primary data set collected from households and analyzed during the current study is available from the corresponding author.

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