

Incidence and Predictors of Sero-Conversion among HIV Discordant Couples at Amhara Region Selected Public Hospitals, Northwest Ethiopia, 2018: A Mixed Cohort Study

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Abstract

Background: Discordant couple refers to couples with mixed Sero status where one is positive and the other is HIV-negative. They are at permanent risk of getting the infection. But many individuals in healthy relationships are unaware of their partner and their own Sero status and chance of gaining the virus. Therefore, we conducted this cohort study to determine the incidence and predictors of Sero conversion among adult discordant couples at Amhara region selected public hospitals, Northwest, Ethiopia, 2019.

Methods: A mixed cohort study was conducted from October 2018 to November 2019 at selected public hospitals in the Amhara region. The study included two hundred twelve (212) discordant couples who had regular follow-up at selected ART clinics hospitals, and the data were collected using checklists. Epi-data 4.1 was used to data entry, and STATA 14 for analysis. Seroconversion incidence rate was 8/100 PY among discordant couples. Using the Kaplan-Meier curve the survival status between categorical variables were calculated and compared using the log-rank test. The Cox proportional hazard models used to examine independent time-related factors for HIV development.

Results: A total of 212 patients were followed and produced 598 person-years (PY) of observation, and 51 new HIV cases were observed during the follow up period with the overall incidence density of 8 per 100 PY. Female sex (AHR (95%CI: 1.67 (0.85, 3.3), not abstained within the last 12 months (AHR (95%CI: 2.11 (0.65, 6.75), viral load $\geq$ 1000 copies (AHR (95%CI: 1.33 (0.38, 1.49), being merchant 1.2 (0.3, 3), p : 0.01), desire to have children, AHR (95%CI: 2.27 (.89-5.81) P : 0.04) and having no history of alcohol (AHR (95%CI: 0.48 (0.21, 1.41) were independent predictors of Seroconversion. among discordant couples.

Conclusion: The overall incidence of Seroconversion among discordant couples is high and factors that affect the incidence are negative female spouse, not abstained in the past 12 months, high viral load, being merchant, desire to have children and having no history of alcohol.

Keywords: Incidence • Discordant couples • Predictor • Seroconversion

Abbreviations: AIDS • Acquired Immune Deficient Syndrome, ART • Anti-Retro Virus, EDHS • Ethiopian Health Survey, HIV • Human Immune Virus, OI • Opportunistic Infection, SDC • Sero Discordant Couple, SSA • Sub Saharan Africa, SSR • Sub Saharan Region, STI • Sexually Transmitted Infection, TB • Tuberculosis, UNAID • United Nation Aid, USA • United States of America, WHO • World Health Organization

Introduction

Discordant couples refer to couples with mixed Sero status in which one is positive and the other is negative for HIV. HIV/AIDS ranks among the most devastating diseases in the world since it spreads rapidly and affects mainly young people in their most productive years. Although remarkable progress has been made in the scale up of HIV treatment in low- and middle-income countries, particularly in sub-Saharan Africa, approximately 2 million individuals acquire HIV infection on an annual basis in 2010 and about 24 million individuals live with HIV/AIDS in 2017 [1-3].

In discordant couples the negative partners are at continuous risk to have the infection from their positive spouse (10% annual risk). Yet, many individu-

als in stable relations are unaware of their partner's status and their own HIV status. Approximately 40 per cent of the world's HIV-positive people know their result. Of that only 50% are projected to be part of the discordant couples since the addressing of the needs of such discordant couples is not readily available that might be contributed for the high incidence of Sero conversion [4-7].

According to the UNAIDS 2016 report, HIV has infected at least 60 million people since HIV / AIDS was discovered three decades ago and has been the leading cause of death in some parts of the world [8]. World Bank 2013 report showed that 2.5 million people worldwide were newly infected with HIV, and 1.5 million died in 2011 from HIV related causes thorough, HIV/AIDS remains a major concern in the global public health sector recently [9]. Approximately 940,000 people died from HIV related causes worldwide in 2017 and 37 million people living with HIV at the end of the year with 1.8 million newly infected people including those discordant individuals [10-12].

WHO estimates that up to the end of 2016 more than 70 million people worldwide were diagnosed with HIV / AIDS, 35 million of whom suffered from HIV / AIDS and related complications. In 2017 about 722,248 people were living with HIV, 22,827 of whom have been newly infected and 14,872 deaths a year. With 25.7 million people living with HIV in 2017, Africa is the worst affected area accounted for 68 percent of all new infections and nearly

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half of all deaths globally occurred in Southern Africa among heterosexual couples [13-16]. About 30% of married HIV positive spouses have a negative (discordant) spouse and are at 10% annual risk of transmitting HIV to their negative spouses [17].

According to EDHS 2016 report although the magnitude of HIV decreases from 2011 to 2016, the burden of the disease is still high across Ethiopia. Regionally, the prevalence of HIV in Gambelia (4.8%), Addis Ababa (3.4%), Dire Dawa (2.5%) and Harari (2.4%) is higher than in other regions. The sero-negative partners of people with HIV are at greatest risk of contracting HIV through sexual transmission, in which about 60% of new HIV infections occur in Sero-discordant couples with HIV [18-20].

Methods

Study area and period

The study was conducted at selected government hospitals in east Gojjam, west Gojjam, and Awi district from October 2018 to November 2019. Amhara region is one of nine ethnic divisions in Ethiopia, containing the homeland of the Amhara people, formerly known as Region 3 and its capital is Bahir Dar. The region has 21.5 million inhabitants (19.7 million urban and 1.8 million rural) and comprises of 27 percent of the Ethiopian population, based on the 2016 Amhara Region Health Office report. There are 4,244 public health facilities in the district of Amhara (69 hospitals, 839 health centers and 3,336 health posts) and five of those hospitals are referral in the region (Debre Markos, Felege Hiwot, Gondar, Dessie, and Debre Birhan), serving approximately 15 million people in the catchment area [21].

Study design

Mixed cohort study design was used

Study population

The study populations were all HIV discordant couples registered in Amhara region selected public hospitals" ART follow-up care clinic and full fill the inclusion criteria.

Inclusion and exclusion criteria

All discordant couples who met the inclusion criteria in the ART follow-up clinic of selected public hospitals in the Amhara region were included in the study. However, HIV discordants with incomplete data on the clinical status of their positive partners, unavailable medical records for positive couples and couples who had no follow-up for the negative partners were excluded from the study.

Study variables

The dependent variable of the study was incidence of Sero conversion among discordant couples and the independent variables were Socio-demographic characteristics (Age, Sex, Residence, Marital status, occupation, Educational status, Ethnicity), Personal Behavior characteristics (Substance use, Condom use, Abstinence, Drug users, Multiple sexual partners, Desire to have children) and Clinical characteristics of the positive spouse (HAART status, CD4 cell count, Viral load, Clinical stage, Sero status of spouse, Duration of HIV infection, History of STI, History of OI).

Data collection tools and procedures

Data collection checklists (risk scoring tools) were used which was adapted from the previous studies. The tools consisted of both closed and open-ended checklists which were prepared in English version and had three parts (socio demographic and behavioral characteristics of the negative partners and clinical characteristics of the positive partners). Negative partners were prospectively followed for one year from October 30, 2018 to November 1, 2019 for their Sero status, and the positive partners' medical record was also reviewed retrospectively for five years (September 2014-November 2019) using the data collection checklist, which consists of patient information that was important to the study.

Data quality assurance

Data collectors and supervisors were given one day training to ensure the

quality of data before data collection. The questionnaire was carefully designed and the English version was used for data collection. Before actual data collection time, the questionnaire was checked for clarity, comprehensiveness and content validity by experts. During data collection, the supervisors were monitored the data collection process by checking completeness of the data and take the correction on the site of data collection when any problem happened. The principal investigator checked data for its completeness during data entry and the cleaning process.

Data analysis

The baseline data was collected from the medical records of the positive partners and the negative partners were followed for one year. Epidata3.1 was used for data entry and exported to STATA14 for analysis. Descriptive statistics such as frequencies, proportions, means and medians were calculated. The risk of HIV among negative partners was assessed by using the person time method and incidence rate. Seroconversion was calculated as number of positive cases per 100 person years observed. HIV free survival was calculated by months from the first follow-up visit to the diagnosis of the negative partners for HIV. The Kaplan-Meier curve was used to estimate the median duration of occurrence and the Log rank test was used to compare survival curves between different categories of explanatory variables. Cox proportional hazards models was used to examine independent factors associated with time to HIV development. Univariable analysis was used to assess the relationship between the independent variables and the risk of Seroconversion. Before fitting the covariate into the model all the proportional hazard model assumptions were checked by plotting Schoenfeld residuals and by examining log plots. To estimate the association between associated factors and Seroconversion, hazard ratio (HR) with 95% confidence intervals (CIs) was used. Variables at p value < 0.25 with Sero conversion among Discordants couples in the bivariable analysis were entered in to the multivariable analysis model. The finding was expressed with 95% CIs and significant variables were declared at p < 0.05 which was statically significant

Results

Socio demographic characteristics of study participants

Two hundred twelve (212) discordant couples were included in the study. From this about 126 (59.43%) of them were females and 116 (54.72%) were rural residents. In addition, occupation about 99 (46.28%) were farmers and about 131 (61.79%) of them had children (Table 1).

Behavioral characteristics of study participants

From the total participants about 174 (82.1%) of them have used condom correctly and consistently and 173 (81.6%) of them did not miss any appointments at all (Table 2).

Clinical characteristics of study participants

This study revealed that about 92 (43.6%) of the positive spouses use AZT-3TC-NVP combination therapy and 181 (85.38%) were with CD4 count of >= 200. About 72 (33.96%) of them were at first clinical stage (Table 3).

Incidence of Seroconversion among discordant couples

There were 51 new HIV cases (events) were observed during the follow up period with the overall incidence density of 8 per 100 PY (Figure 1). From those 34 (67%) were females and 29 (56.8%) were rural residences. Regarding to their educational status 31 (60.8%) of them were complete primary school and 42 (82.4%) of them do not miss any of their appointment. About 8 (15.7%) of them had desire to have children and 11 (21.6%) had history of STI. In addition, about 12 (23.5%) of the study participants had history of OI and 14 (27.5%) used Cotrimoxazol. About 31 (60.8%) were screened for TB and 9 (17.6%) of them were positive. Additionally, 18 (35.3%) of respondents were at clinical stage II.

Predictors of time to Seroconversion among discordance patients

In the bi-variable Cox-regression analysis model significant predictors

Table 1. Socio-demographic of the HIV discordance couples at Amhara region selected public hospitals, Ethiopia 2019.

Variables	Characteristics	Frequency	Percent (%)
Sex	Male	86	40.57
	Female	126	59.43
Age	18-35	120	56.6
	36-50	81	38.21
	>50	11	5.19
	Median		
Place of residence	Urban	96	45.28
	Rural	116	54.72
Occupation	Farmer	99	46.7
	Employer	69	32.55
	Merchant	29	13.68
	Driver	3	1.42
	Other	12	5.66
Having children	Yes	131	61.79
	No	81	38.21
Educational status of the negative partners	Unable to read and write	55	25.94
	Primary school	132	62.26
	Secondary school	13	6.13
	College and above	12	5.66
Educational status of positive partner	Unable to read and write	56	26.42
	Primary school	131	61.79
	Secondary school	20	9.43
	College and above	5	2.36

Table 2. Behavioral characteristics of the HIV discordance couples at Amhara region selected public hospitals, Ethiopia 2019.

Variables	Characteristics	Frequency	Percent (%)
Correct and consistent condom use	Always	24	11.32
	Sometimes	174	82.08
	Never	14	6.6
Missing of appointment	Yes	39	18.4
	No	173	81.6
Abstinence in the last 12 months	Yes	23	10.85
	No	189	89.15
Ever drink alcohol	Yes	18	8.49
	No	194	91.51
Life time sexual partner	1	36	16.98
	2	166	78.3
	03-Apr	9	4.25
	>=5	1	0.47
Number of alcohol drinks	1	1	5.56
	2	10	55.56
	03-Apr	4	22.22
	>= 5	3	16.67
Ever chew chat	Yes	8	3.77
	No	204	96.23
Desire to have children	Yes	40	18.87
	No	172	81.13
Sero-conversion	Yes	51	24.06
	No	161	75.94

(p -value ≤ 0.25) of Seroconversion included: sex, occupation, educational status, missing of appointments for HAART, condom use, abstinence during last 12 months, history of alcohol use, type of HAART they use, clinical stage of the positive spouse, having history of STI, high viral load (>1000) and high CD4 count was significantly associated with Seroconversion. Accordingly, females were 1.7 (AHR (95%CI: 1.7 (8.5- 33)) times more likely to have Sero-conversion than males. Couples who did not abstain within the last 12 months were 1.6 (1.6 (1.7-9.4), 0.04) times more likely to have Sero-conversion than abstained couples. In addition, positive spouses with high viral load (≥ 1000

copies) were 7.5 times more likely to transmit for their negative spouses (7.5 (3.8-14.9), 0.02) than the its counterparts., Merchants were 1.2 times more likely (1.2 (1.3-33), p : 0.04) to have Seroconversion than farmers., Besides this, couples who have desire to have children were 2.3 times more likely (2.3 (1.9-5.81)) P : 0.04) to have high Sero-conversion than its counterparts. Moreover, couples who had history of alcohol were 4.8 (4.8 (2.1-14.1), 0.02) times more likely to be positive than its counterpart. Furthermore, patients with high CD4 count (≥ 200) of indexed spouses were less likely (0.44 (2.1-9.4), 0.03) to acquire HIV than its counterpart (<200) (Table 4).

Table 3. Frequency distribution of clinical characteristics of the HIV discordance couples at Amhara region selected public hospitals, Ethiopia 2019.

Variables	Characteristics	Frequency	Percent (%)
Type of HARRT	1e (AZT-3TC-NVP)	92	43.6
	1c (TDF-3TC-EFV)	49	23.22
	1d (AZT-3TC-EFV)	51	24.17
	1f (TDF-3TC-NVP)	20	9.4
CD4 count	< 200	31	14.62
	>= 200	181	85.38
Viral load	<500	87	41.04
	500-1000	34	16.04
	>1000	91	42.92
Clinical stage of the positive partners	Stage 1	72	33.96
	Stage 2	70	33.02
	Stage 3	61	28.7
	Stage 4	9	4.25
Duration of HIV Infection	< 2 years	132	62.26
	2-5 years	61	28.77
	>5 years	19	8.96
History of sexually transmitted disease	Yes	55	25.94
	No	157	74.06
History of opportunistic infection	Yes	54	25.47
	No	158	74.53
Tuberculosis screening	Yes	134	63.21
	No	78	36.79
Result of tuberculosis screening	Negative	101	75.37
	Positive	33	24.63
Factional status of patients	Factional	76	35.85
	Ambulatory	131	61.79
	Bedridden	5	2.36
Cotrimoxazol use	Yes	61	28.77
	No	151	71.2
Use of INH prophylaxis	Yes	63	29.72
	No	149	70.28
Body mass index	<18.5	65	30.66
	18.5-25	123	58.02
	>25	24	11.32

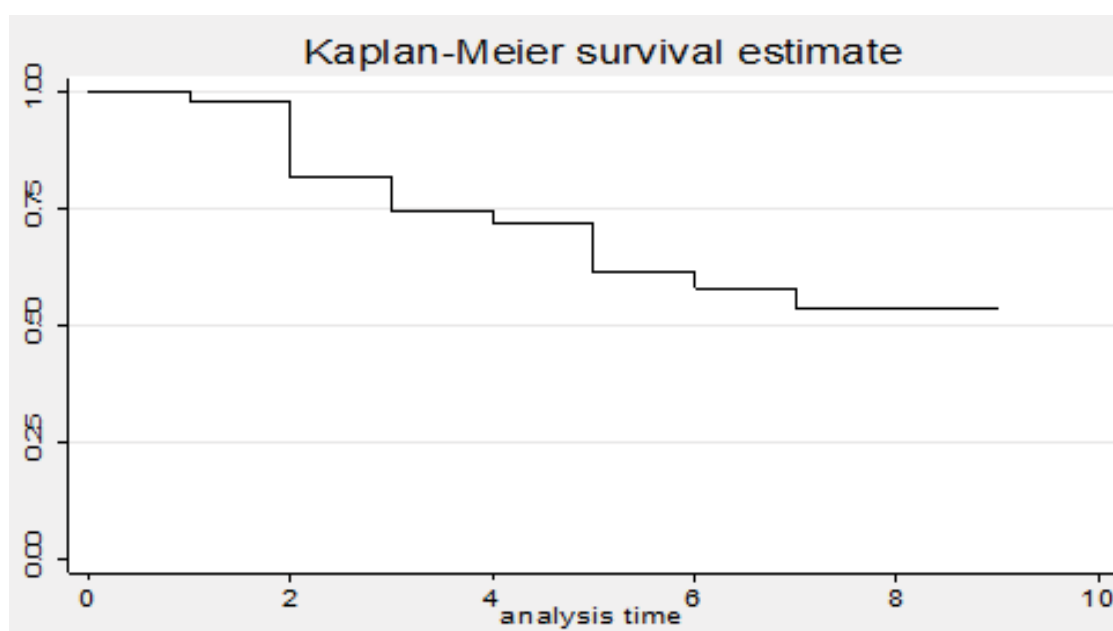
**Figure 1.** Kaplan-Meier curve of sero-conversion survival proportion for discordant couples at Amhara region public hospitals hospital, 2019.

Table 4. Uni-variable and multivariable analysis of predictors of sero-conversion among discordant couples at Amhara region selected public hospitals, 2019.

Covariates	Survival status		Total	CHR (95%CI)	AHR (95% CI)	p-value
	Event (HIV)	Censored				
Sex						
Male	17	69	86	1	1	0.035*
Female	34	92	126	1.5(0.81-269)	1.67(.85- 3.30)	
Age						
18- 35	30	90	120	1	1	0.38
36-50	19	62	81	0.84 (.47 -1.5)	0.73(.36- 1.47)	
>50	2	9	11	0.49(0.11-2.04)	0.66(.14- 2.99)	
Residence						
Urban	22	74	96	1	1	0.28
Rural	29	87	116	1.24(0.71-2.20)	0.66(.31-1.40)	
BMI						
<=18.5	11	54	65	1	1	0.1
18.5-25	35	87	122	1.74(.86-3.53)	1.88(.88-4.03)	
>25	5	20	25	1.12(.39-3.30)	1.48 (.43-4.95)	
Occupation						
Farmer	27	72	99	1	1	0.04*
merchant	3	26	29	0.37(.11-1.22)	1.2(1.4-8.22)	
Employer	19	50	69	1.04(.57-1.88)	0.78(0.35- 1.72)	
Other	2	10	12	0.39(.05-2.90)	0.53(.06-4.61)	
Educational status						
unable to read and write	13	42	56	1		0.45
primary school	31	101	142	1.19(.59 -2.38)	0.71(.29-1.73)	
secondary school and above	7	18	25	2.4(1.05-7.08)	0.20(.02-1.95)	
Missing of appointments						
Yes	9	30	39	1	1	0.68
No	42	131	173	1.12(.54-2.30)	1.18(.52-2.63)	
Condom use						
Always	6	32	38	0.58(.25-1.35)		0.14*
Sometimes	45	129	174	1		
Abstinence						
Yes	4	19	23	1	1	
No	47	142	189	2.11(.65 -6.75)	1.6(1.72-9.44)	
Life time sexual partner						
1	10	26	36			
02-Mar	39	127	166			
>3	2	8	10			
Alcohol						
Yes	6	12	18	1	1	0.02*
No	45	149	194	0.48(.21-1.14)	0.25(.11-.806)	
Desire to have children						
Yes	8	32	40	0.84(.205-1.14)	2.27(1.9-5.81)	0.04*
No	43	129	172	1	1	
Type of HAART						
1 e	29	63	92	1		
1c	14	35	49	1.01(.53-1.91)		
1d	4	47	51	0.21(.08-.619)		
1f	5	15	20	0.74(.26-2.12)		
CD4 level						
<200	11	20	31	1	1	0.03*
>= 200	40	141	181	0.53(.27-1.03)	0.44(0.21-0.94)	
Viral load						
< 500	20	67	87	1	1	0.76
500-1000	5	29	34	0.73(0.27-1.95)	0.84(.28-2.52)	
>=1000	26	65	91	1.33(0.73-2.41)	7.5(3.8-14.9)	
Clinical stage						
Stage 1 and 2	32	110	142	1.85(.45-8.30)	1.28 (.57-2.8)	0.94

Stage 2 and 4	19	51	70	1	1	
History of STI						
Yes	11	44	55	1	1	
No	40	117	157	1.52(75-3.04)	1.25(.55-3.05)	0.54
History of OI						
Yes	12	42	54	1		
No	39	119	158	1.30(.67-2.53)		

Discussion

Despite numerous interventions made to prevent HIV/AIDS, it remains a serious global public health concern, especially in low- and middle-income countries. Therefore, we conducted this mixed cohort study to determine Seroconversion at Debre Markos Referral Hospital, Ethiopia. Accordingly, the overall Seroconversion rate was found to be 8 per 100 PY among discordant couples. This finding aligns with the previous studies conducted in south Africa (7.75/100PY) [22] and Zambia (7.5/100PY) [23]. However, our finding is higher than studies conducted in china (2.52, 0.39, 0.63,1 and 1.02 per 100 person year) [24-28], Africa (3.02 per 100PY) [29], Uganda (4.9/100PY) [30] and with one systematic review (3.6/100 PY) in Cambridge [31]. Conversely, our finding is much lower than studies reported in Tanzania (59.3/1000 PY and 6.7/100 PY among female and male spouses respectively) [32], and sub-Saharan Africa (11.1/100PY) [33]. The above variations between studies could be explained, in part, by the differences in sample size, study settings, follow-up period, and socio-demographic characteristics of study participants.

In this cohort study, female sex was significantly associated with Seroconversion. Accordingly, male to female transmission was 1.7 times more likely (1.7 (8.5- 33)) than female to male transmission (Figure 2) which is in line with the study conducted in Zambia [23] and Tanzania [16,32]. It is known that the most important biological and anatomical influencing factors of HIV/AIDS is sex (females have short urethra and receptive for semen from males) which is supported by the study conducted in china [34]. However, this is contradicting with other study reported in china [25] that shows the odds of men with HIV-positive wives were higher among Serodiscordant couples. The possible explanation for these contradictory findings might be due to the difference in life style like substance utilization (amphetamines and heavy drinking) as well as sexual activity norms (enjoyment of more risky sexual practice and homosexuality) of males and good consistent condom utilization among females in china as evidence suggested that Seroconversion was significantly associated with substance utilization and unsafe sexual practice [35-37].

In addition, in this study occupation (being merchant) was one of the most important predictors for the occurrence of Seroconversion among discordant. Patients who were merchants are 1.2 times more likely (1.2 (1.3-33), p : 0.04), to have higher Seroconversion rate than farmers counterparts (Figure 3). Moreover, this study found that discordant couples who do not abstain in the last 12 months were at higher risk of Seroconversion (1.6 (1.7-9.4), 0.04) as compared to its counterparts (Figure 4). This finding is consistent with a study conducted in Pennsylvania reported that abstained individuals were less likely to engage in risky sexual practices [38]. In addition our study demonstrated that couples who had alcoholic history are 4.8 times more likely to have high Seroconversion rate (4.8 (2.1-14.1), 0.02) as compared to their counterparts which aligns with previous studies conducted in South Africa and other low and middle income countries [39,40]. It is known that alcohol causes greater suppression of CD4+ cells and poor ART adherence as well as engaging in risky sexual practice that might contribute for high Seroconversion rate [41,42]. This finding is supported by the study finding in Zambia showed that having sex under the influence of alcohol can compound the risk of HIV [43]. Desire to have children was significantly associated with Seroconversion. Accordingly, couples who have desire to have children are 2.3 more likely to have high Seroconversion rate (2.3 (1.9-5.81)) P : 0.04) as compared to their counterparts which is aligned with the findings reported in china [24]. This difference could be associated with frequent sexual intercourse without condom among couples who desired to have children. Additionally, this study finding reported that viral load is significantly associated with Sero-conversion. Accordingly, couples with viral load of >1000 copies/ml are 7.5 times more likely (7.5 (3.8-14.9), 0.02) to be positive as compared to their counterparts (Figure 5). This study finding is

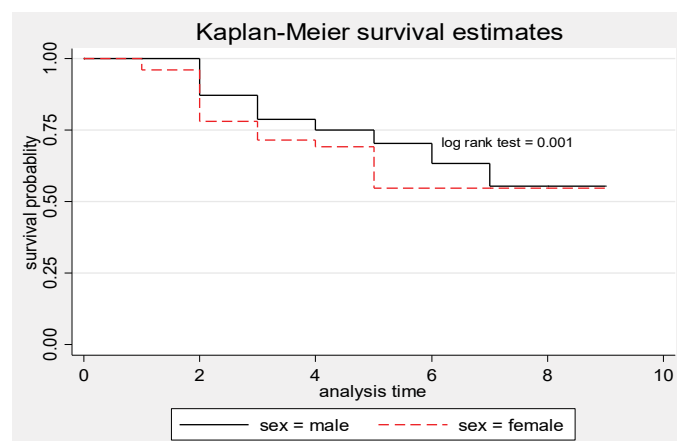


Figure 2. The Kaplan-Meier survival curves comparing the sero-conversion probabilities of discordant couples based on their sex.

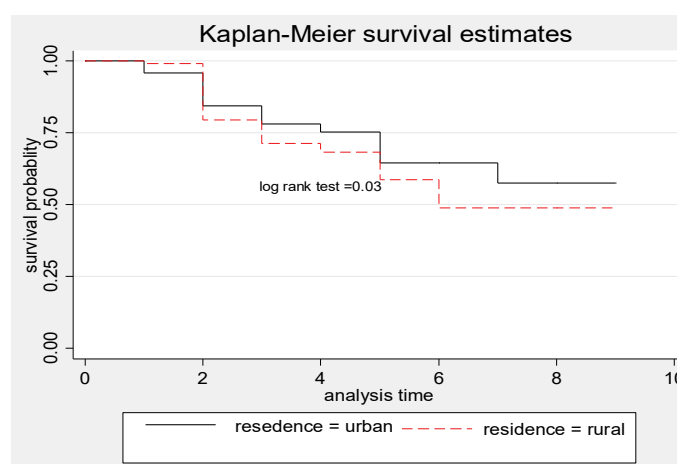


Figure 3. The Kaplan-Meier survival curves comparing the sero-conversion probabilities of discordant couples based on their residences.

supported with the studies reported in china [34,44] and Kenya [45]. It is known that; viral load is an important driver of HIV transmission among the discordant couples with enhanced HIV replication associated with the immune response. However, this study finding contradicts with the studies in china [46] and Uganda [47]. These variations could be explained, in part, by the differences in sample size, study settings, follow-up period, and socio-demographic characteristics of study participants. Another important predictor associated with increased risk of HIV Sero-conversion was CD4 count. Hence, HIV negative partners with high CD4 count (≥ 200) of indexed spouses were less likely (0.44 (2.1-9.4), 0.03) to acquire HIV than its counterpart (<200) (Figure 6). This finding is supported by study conducted in china [27] and Uganda [47]. High CD4 count strengthens the defense mechanisms of the body that prevents the viral replication. As a result, the transmission and Seroconversion rate from positive spouse to the negative spouse will be low.

Limitations of the study

The main strength of this study is conducted by using mixed cohort study design. Therefore, we were able to include a range of socio-demographic, clinical and behavioral factors, which were very important to determine

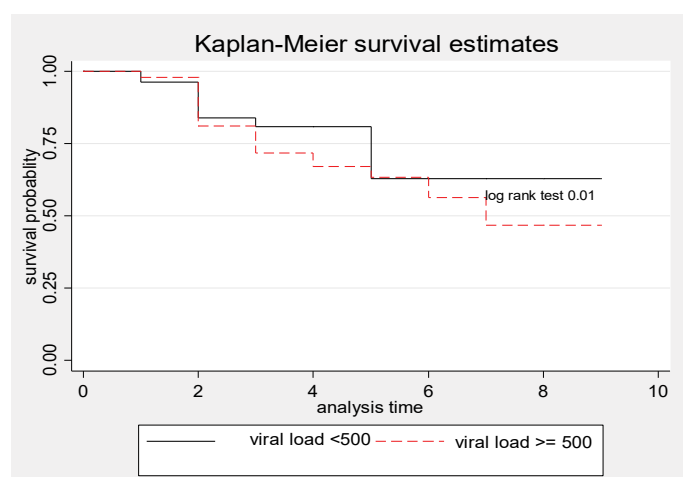


Figure 4. The Kaplan-Meier survival curves comparing the sero-conversion probabilities of discordant couples based on their abstinence status in the past 12 months.

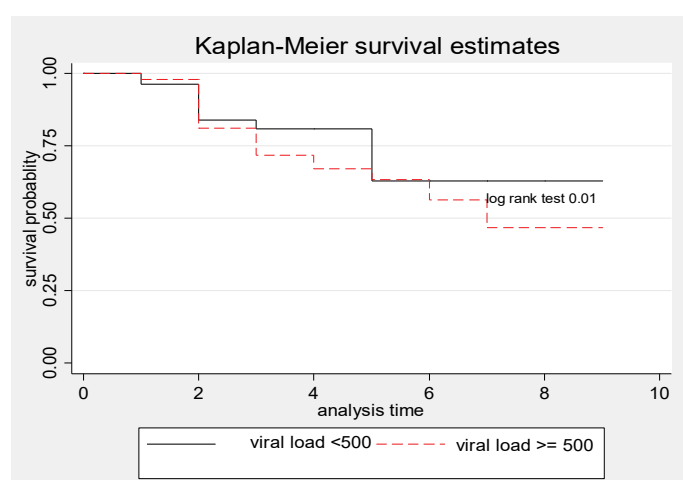


Figure 5. The Kaplan-Meier survival curves comparing the sero-conversion probabilities of discordant couples based on their viral load status.

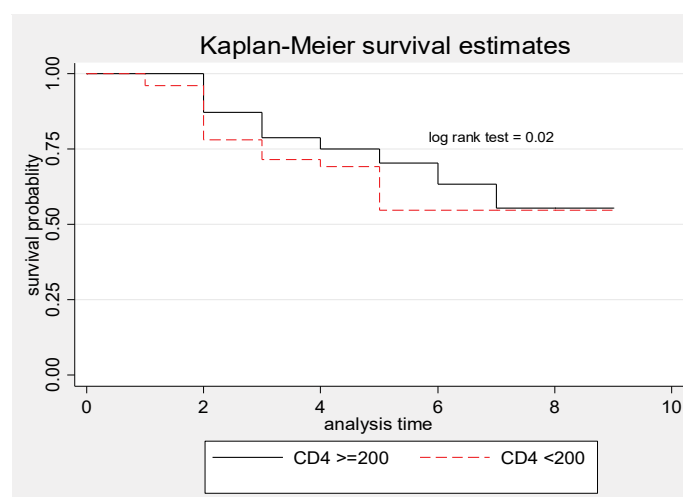


Figure 6. The Kaplan-Meier survival curves comparing the sero-conversion probabilities of discordant couples based on their CD4 count.

Seroconversion. Despite these strengths, this study has a number of limitations. Firstly, the study was conducted at hospitals; therefore, discordants at home could be missed. Moreover, secondary data were used for positive spouses consequently, important variables could be missed. Furthermore, the impact of providers' training, supplies, equipment, and hospital service contexts has not been explored.

Conclusion

In this study, we found a high rate of Seroconversion. Female Sex, being merchant, abstinence, history of alcohol, desire to have children, low CD4 count (<200), and high viral load (≥ 1000) were predictors significantly increase the risk of Seroconversion. Therefore, based on our findings, we strongly recommend that special emphasis should give to discordant couples for female Sero-negative spouses, merchants, patients who do not abstained for the last 12 months, having history of alcohol, who have desire to have children, with low CD4 (<200), and high viral load (≥ 1000) to reduce the rate of Sero-conversion. Lastly, further research is needed to explore the impact of provider training, supplies, equipment, and hospital management context.

Ethics approval and consent to participate

Ethical clearance was obtained from the Institutional Review Committee of the College of Health Sciences, Debre Markos University. Oral permission was obtained from hospital administrations. Each discordant couple received an explanation about the purpose of study, and verbal informed consent was obtained from each participant prior to proceeding. The ethical committee formally waived the need of formal written consent since the study was done through interviewing and reviewing of medical record of the couples. Therefore, the committee declared that this study is less invasive as much as confidentiality is maintained. To ensure confidentiality, all collected data were coded and locked in a separate room prior to the data entry process. After entering of data into the computer, all data were locked by password. Participant names were not included in the data collection format, and the data were not disclosed to any person other than principal investigators.

Consent to Publish

Not applicable.

Availability of Data and Materials

The dataset will not be shared in order to protect the participants' identities" but it is available from the corresponding author on reasonable request.

Competing Interests

The authors declared that no conflict of interest.

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Authors' Contributions

All authors contributed to data analysis, drafting, or revising the article gave, final approval of the revision to be published, and agree to be accountable for all aspects of the work.

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