

**ORIGINAL RESEARCH ARTICLE****Predictors of treatment failure among HIV positive clients in Webuye Sub-county, Bungoma County, in Kenya**

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ABSTRACT

Efforts to reduce AIDS-related mortality have been instrumental in providing antiretroviral therapy (ART) services. However, people are still dying while on treatment due to several factors. Recent studies have reported several treatment failures. Therefore, the main focus of the study was to determine predictors of treatment failure among HIV-positive clients through a case study of patients in Webuye sub-county, Bungoma County, Kenya. The study was carried out in the Webuye sub-county hospital and employed a cross-sectional study approach. The study included 3,975 adults who had been on ART for more than twelve months. The Mugenda and Mugenda (2003) formula was used to calculate the desired sample size, capturing a total of 361 respondents. A structured questionnaire and a face-to-face interview were used to collect data. Data entry was done on SPSS and analysed using version 23. Demographic characteristics such as age and sex were summarised into means and percentages. The odds ratio and chi-square test were conducted to investigate the correlation between prognostic factors and adherence to therapy. To account for potential confounding and effect modification, the p-value was set to $p < 0.1$. The results also found that patients who missed their appointments were more likely to have treatment failure than those who didn't have an appointment reminder. Clients who developed T.B. in patients admitted after ART initiation were at a higher risk of treatment failure, while opportunistic infections posed the same threat. The knowledge gained in this study will help make recommendations regarding developing appropriate health education strategies to empower clients about what can cause treatment failure.

1.0 Introduction

The human immunodeficiency virus (HIV) remains a significant global public health concern, claiming an estimated 27.2 to 47.8 million people (WHO 2021). At the end of 2020, 37 million people were living with HIV, with at least two-thirds (25.4 million) hailing from the WHO African region. HIV-related causes are estimated to have killed 480,000–1.0 million people (WHO, 2021). According to UNAIDS (2020), the new infections of HIV have been reduced by 52%, with an estimated 1.0–2.0 million newly infected in 2020 compared to 2.1–4.2 million at

the peak in 1997. (Nega et al., 2020) note that the global antiretroviral treatment (ART) rollout has been instrumental in halving the number of AIDS-related deaths and ensuring that the disease develops into a chronic, non-fatal condition. At least 23.3 million individuals have access to ART around the world. However, the effectiveness of this intervention is limited by a variety of factors, such as limited follow-up, limitations in manpower, poor monitoring of the intervention, and significant gaps in the programme data (Endalamaw et al., 2020).

In sub-Saharan Africa, ART usage has significantly reduced HIV-related morbidity and mortality. Similarly, it has been instrumental in prolonging the average life expectancy for individuals affected by HIV. Irrespective of these benefits, these interventions are challenged by the number of treatment failures associated with first- and second-line HIV therapies (Adal, 2019; Owusu et al., 2017). Immunological, clinical, or virological failures characterise HIV treatment failure. Immunological failure is defined as a drop in CD4 count of 50% or less than 100 cells/mL, whereas virological failure can be defined as definite or probable failure (Endalamaw et al., 2020). Clinical failures relate to the occurrence of new or recurrent stage III or stage IV.

In Kenya, the government and private health facilities provide ARVs for free to all patients. In addition, the United States of America provides annual assistance to help improve the Kenyan healthcare system and healthcare delivery (MOH, 2020). Waruru et al. (2021) also note that Kenya has the 3rd highest number of HIV infections in eastern and southern Africa, especially among adults 15 years of age and older. The prevalence of stunting was 33.0%, wasting was 15.1%, and underweight was 20.8% (Jane mbijiwe et al 2022). One of the most significant contributors to this trend is treatment failure in the country. Resistance to antimicrobial agents is widely considered a global public health threat (Philip M et al 2022). This is one of the contributing factors to the introduction of new forms of HIV infections that are resistant to medication. Levels lower than 95% suppress the HIV viral load and reduce the CD4 count. Therefore, the current study will investigate predictors of treatment failure among HIV-positive patients in Kenya, Bungoma County, and Webuye Sub-County.

2.0 Materials and method

2.1 Study site

The study was carried out at the Webuye sub-county hospital. The hospital has a bed capacity of 217 with an approximately 150% bed occupancy rate. Between 150 and 200 patients suffering from diverse conditions can be seen daily.

2.2 Study design

A cross-sectional study design was implemented given its effectiveness in determining the prevalence of a phenomenon, problem, attitude, or issue by taking a snapshot or cross-section of the population. This obtains an overall picture as it stands at the time of the study.

This study design was selected for its ease in assessing any association between predictors of HIV treatment failure between exposed and non-exposed patients. The study design was suitable since it allowed the study to be conducted within a relatively short period of time and

with limited resources.

2.3 Study population

The study targeted 3,975 adults who have been active clients on ART for more than twelve months. Clients must have had more than two viral loads performed and the results made available.

2.4 Sample size determination

The sample size was determined by the Mugenda and Mugenda (2003) formula for calculating the desired sample size, as stated below. When the target population is less than 10,000,

$$nf = \frac{N}{1 + Ne^2}$$

Where nf = desired sample size (population less than 10,000)

N = total population size (3782 clients on ART)

e = relative tolerable error (0.05)

1 = constant number

Therefore

$$nf = \frac{3782}{1 + (3782)0.05^2} = 361$$

The recommended sample size was 361

2.5 Sampling method

A simple random sampling technique was used to determine the study's sample population. A table of random numbers was used to select from the ART register, which was used as a sampling frame for all subjects that fulfilled the inclusion criteria for the participants.

2.6 Data collection methods and instruments

A structured questionnaire and face-to-face interview were used to collect data that recorded demographics, treatment failure data from patient files, medication-related factors, health care delivery systems, and adherence to therapy. Patients were interviewed in English or Kiswahili according to their preferences.

2.7 Data analysis

Data entry was done on SPSS version 23. Demographic characteristics such as age and sex were summarised into means and percentages. The odds ratio and chi-square test were conducted to investigate the correlation between prognostic factors and adherence to therapy. To account for potential confounding and effect modification, the p-value was set to $p < 0.1$. Qualifying factors were included in a multivariate logistic regression model to estimate adjusted odds ratios and identify the independent predictors of non-adherence (association) judged

significant at $p < 0.05$. The term "significant" refers to a chi-square p-value less than 0.05; "marginally significant" refers to a p-value between 0.05 and 0.10, inclusive; and "not significant" refers to a p-value greater than 0.10. $p < 0.1$

3.0 Results

3.1 Socio-demographic factors

In this study, 361 participants were enrolled, with 133 males and 228 females, as shown in Figure 1. Most of the clients under care and treatment were more than 45 years old: 43.8% (158/361); 35-44 yrs = 102; 25-34 yrs = 80; 15-24 yrs = 21; as shown in figure 2.

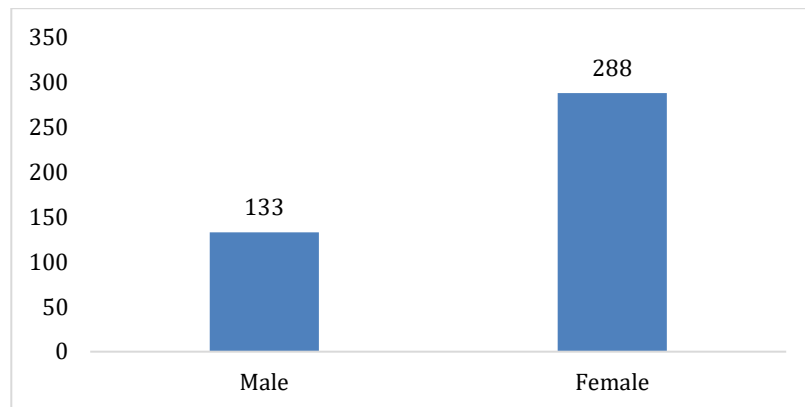


Figure 1: Distribution by Gender

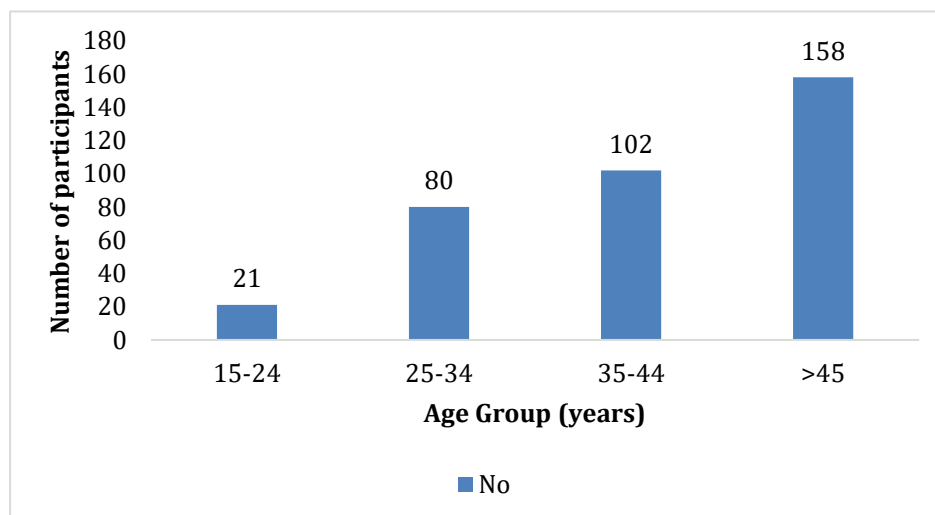


Figure 2: Age Distribution

3.2 Patient-related factors and clinical Characteristics

A higher proportion of clients who smoke, 71.9% (23/32), and use alcohol, 67.6% (46/68), experienced treatment failure. Patients with poor ARV adherence had the highest treatment failure rate of 63.0% (29/46). Clients who were enrolled in WHO stage 3 had higher failure rates, at 32.9% (46/140), as presented in Table 1.

Treatment failure among HIV positive clients

Table 1: Demographic Characteristics by Treatment failure

Factor	Treatment Failure (Viral Loads)			P-Value
	ALL	Success	Failure	
N	361	276	85	
Age (mean (SD))	42.7 (12.2)	42.1(11.7)	44.4(13.9)	
	n (%)	n (%)	n (%)	
Age group				
15-24	21 (5.8)	14 (66.7)	7 (33.3)	0.090
25-34	80 (22.2)	64 (80.0)	16 (20.0)	
35-44	102 (28.3)	85 (83.3)	17 (16.7)	
>45	158 (43.8)	113 (71.5)	45 (28.5)	
Gender				
Female	228 (63.2)	176 (77.2)	52 (22.8)	0.761
Male	133 (36.8)	100 (75.2)	33 (24.8)	
Marital status				
Divorced/Separated/Widowed	81 (22.4)	58 (71.6)	23 (28.4)	0.132
Married Polygamous	44 (12.2)	29 (65.9)	15 (34.1)	
Married Monogamous	195 (54)	157 (80.5)	38 (19.5)	
Single	41 (11.4)	32 (78.0)	9 (22.0)	
WHO Status				
WHO Stage1	116 (32.1)	98 (84.5)	18 (15.5)	0.009
WHO Stage2	99 (27.4)	79 (79.8)	20 (20.2)	
WHO Stage3	140 (38.8)	94 (67.1)	46 (32.9)	
WHO Stage4	6 (1.7)	5 (83.3)	1 (16.7)	
Smokes				
No	329 (91.1)	267 (81.2)	62 (18.8)	<0.001
Yes	32 (8.9)	9 (28.1)	23 (71.9)	
Takes Alcohol				
No	293 (81.2)	254 (86.7)	39 (13.3)	<0.001
Yes	68 (18.8)	22 (32.4)	46 (67.6)	
T.B. History				
No	332 (92.0)	260 (78.3)	72 (21.7)	0.005
Yes	29 (8.0)	16 (55.2)	13 (44.8)	
Time on ARVs (years)				
<2	28 (7.8)	25 (89.3)	3 (10.7)	0.128
2 - 3	18 (5)	16 (88.9)	2 (11.1)	
4 – 5	28 (7.8)	23 (82.1)	5 (17.9)	
>5	287 (79.5)	212 (73.9)	75 (26.1)	
ARV Adherence				
Good	315 (87.3)	259 (82.2)	56 (17.8)	<0.001
Poor	46 (12.7)	17 (37.0)	29 (63.0)	
CD4 count				
<200	159 (44)	116 (73)	43 (27)	0.108
201-300	74 (20.5)	54 (73)	20 (27)	
>300	128 (35.5)	106 (82.8)	22 (17.2)	

On univariable analysis, the results shown in Table 2 indicate that, although not significant, clients aged 15–24 and those aged more than 45 years had higher odds of treatment failure [OR = 2.00 (95% CI 0.67–5.69)] and [OR = 1.59 (95% CI 0.59–3.53)], respectively. Although not significant, male clients had higher odds of treatment failure than female clients [OR = 1.12 (95% CI 0.67–1.84)]. Clients with a history of marriage (divorced, separated, and widowed) and those in polygamous relationships had higher odds of treatment failure [OR = 1.41 (95% CI 0.60-3.55)] and [OR = 1.84 (95% CI 0.71-4.99%)], respectively. The odds of treatment failure were significantly higher for clients who smoked and drank. [OR = 11.0 (95% CI 5.01-26.2)] and [OR = 13.6 (95% CI 7.50-25.5)], respectively. Clients with a poor history of ARV adherence were eight times more likely to have treatment failure [OR = 7.89 (95% CI 4.10–15.6)]. Clients with a history of T.B. were almost three times more likely to have treatment failure [OR = 2.93 (95% CI 1.33-6.38)].

On multivariable analysis, clients aged more than 45 years had significantly higher odds of treatment failure [OR = 2.59 (95% CI 1.07–6.75)]. Clients with a history of T.B. were two times more likely to have treatment failure [OR = 2.30 (95% CI 1.24–7.23)] compared to those that didn't have a history of T.B. Clients taking alcohol had significantly higher odds of treatment failure [OR = 21.1 (95% CI 9.08-52.7)]. Clients with a CD4 count of less than 200 and 201-300 had nearly three times the odds of failing treatment [OR = 2.91 (95% CI 1.33-6.72)] and [OR = 2.72 (95% CI 1.05-7.20)], respectively. Clients with a poor history of ARV adherence had significantly higher odds of treatment failure [OR = 15.2 (95% CI 6.32–39.6)] as presented in Table 2.

Table 2: Demographic & Clinical predictors for Treatment Failure (n= 361)

Covariate	Univariate Analysis			Multivariate Analysis			
	OR	95% CI	p-value	OR	95% CI	p-value	
Age group	25-34	1		1			
	15-24	2.00	(0.67-5.69)	0.200	1.69	(0.43-6.38)	0.441
	35-44	0.80	(0.37-1.72)	0.563	0.85	(0.32-2.24)	0.735
	> 45	1.59	(0.59-3.53)	0.159	2.59	(1.07-6.75)	0.041
Gender	Female	1					
	Male	1.12	(0.67-1.84)	0.665			
Marital Status	Single	1					
	Divorced/Separated/Widowed	1.41	(0.60-3.55)	0.446			
	Married Polygamous	1.84	(0.71-4.99)	0.217			
	Married Monogamous	0.86	(0.39-2.05)	0.720			
WHO Status	WHO Stage 1	1		1			
	WHO Stage 2	1.38	(0.68-2.80)	0.371	1.29	(0.54-3.12)	0.568
	WHO Stage 3	2.66	(1.46-5.02)	0.002	2.10	(0.94-4.87)	0.075
	WHO Stage 4	1.09	(0.06-7.29)	0.940	0.41	(0.02-4.22)	0.504
Smokes	No	1		1			
	Yes	11.0	(5.01-26.2)	<0.001	1.51	(0.51-4.51)	0.453
Takes Alcohol	No	1		1			
	Yes	13.6	(7.50-25.5)	<0.001	21.1	(9.08-52.7)	<0.001
TB History	No	1		1			
	Yes	2.93	(1.33-6.38)	<0.001	2.30	(1.24-7.23)	<0.001
Time on ARVs (years)	<2	1					
	2-3	1.04	(0.13-6.96)	0.966			
	4-5	1.81	(0.40-9.64)	0.449			
	>5	2.95	(1.00-12.6)	0.839			
ARV Adherence	Good	1		1			
	Poor	7.89	(4.10-15.6)	<0.001	15.2	(6.32-39.6)	<0.001
CD4 count	>300	1		1			
	<200	1.79	(1.00-5.76)	0.049	2.91	(1.33-6.72)	0.010
	201-300	1.79	(0.89-3.56)	0.099	2.72	(1.05-7.20)	0.040

4.0 Discussion

4.1 Patient-related factors

A positive correlation was captured between treatment failure and patient practises such as smoking and alcohol consumption. The study revealed that patients who smoked had a 9.77 percent chance of experiencing treatment failure compared to those who didn't smoke. These findings are similar to those of a study conducted in Ethiopia that revealed that ART users who smoked were at least 5.9 times more likely to experience treatment failure than those who were non-smokers (Asfaw et al., 2019). Another study in Korea focused on capturing the role of alcohol consumption on ARV treatment failure. The researchers distinguished the alcohol-consuming patients into non-hazardous, binge-prone, hazardous, and alcohol-dependent groups. The results captured from the study revealed that the odds ratio for low adherence to

ARV medication for binge drinkers, hazardous drinkers, and alcohol dependents was 4.65 (Kim, J. Y. et al., 2018). However, a study conducted in Kenya did not capture any significant relationship between smoking, alcoholism, and treatment failure (Mwamzuka, 2021).

4.2 Comorbidities

The study revealed that clients with a history of TB were three times more likely to encounter treatment failure than their counterparts. A similar study conducted by Getaway et al., 2021, concluded treatment failure, regimen change, being on ART for an extended period, being male, and co-infection with TB were associated with higher mortality. Another study in Ghana sought to determine the HIV viral non-suppression among children on antiretroviral therapy and sampled 250 children between 8 months and 15 years of age. The results revealed that gender and the history of TB were associated with severe CD4 immune suppression and treatment failure (Afrane et al., 2021). Similarly, a study in Ethiopia revealed that a history of TB first-line antiretroviral treatment failure was also related to co-infection.

4.3 Clinical characteristics

The study revealed that clients with a CD4 count of less than 200 and 201-300 had almost three times the significant odds of treatment failure. Similarly, clients with a poor history of ARV adherence had substantially higher odds of treatment failure. A baseline BMI of 18.5, a baseline CD4 cell count of 100 cells/ul, a history of loss to follow-up, poor medication adherence, and starting antiretroviral therapy after two years of HIV diagnosis were all predictors of first-line antiretroviral treatment failure (Zenu et al., 2021). Lailulo et al. (2020) also note that the likelihood of treatment failure was at least five times higher among clients with a CD4 < 200 cells/mm³, compared to their counterparts.

5.0 Conclusion

Comorbidities associated with HIV infection, such as TB, are common among HIV-positive clients, exposing them to treatment failure. Drug-related factors, such as adherence to medication, determine the risk of treatment failure among patients. Missed clinical visits affected medication adherence. System reminders are crucial in ensuring that patients adhere to their medication. Social practices such as smoking and alcoholism influence treatment failure and increase risk.

6.0 Limitations of the Study

Selection bias may have limited the representativeness of the findings. However, efforts were made to reach all the samples randomly selected within the ART register. Another limitation was that the study participants were drawn from only one health facility.

7.0 Acknowledgment

7.1 Funding

None



7.2 Declaration of interest

The Research approval was obtained from Jaramogi Oginga Odinga Teaching and Referral Hospital Ethical Review Committee. Reference number: ERC.IB/VOL.1/445

7.3 Conflict of interest

None.

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