Pediatric Health, Medicine and Therapeutics

Dovepress

open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Factors Affecting Virological Failure in Children Receiving First-Line Antiretroviral Therapy in Ethiopian Healthcare Facilities: A Retrospective Analysis

Mitiku Desalegn[1], Tewoderos Shitemaw[2], Mesfin Tesfaye[3], Genanew Kassie Getahun[3]

[1]Department of Anesthesia, College of Medicine and Health Science, Wachemo University, Hossana, Ethiopia; [2]Menelik II Medical and Health Science College, Addis Ababa, Ethiopia; [3]Department of Public Health, Menelik II Medical and Health Science College, Addis Ababa, Ethiopia

Correspondence: Mitiku Desalegn, Email mitikudesalegn44@gmail.com

Background: The causes of virological failure are poorly recognized and investigated. This study aimed to identify determinant factors of viral failure in children taking first-line ART at a randomly selected federal hospital in Addis Ababa, Ethiopia.

Methods: A facility-based unmatched case–control study was carried out from May 10, 2022, to July 20, 2022, G.C. among HIV-infected children on first-line antiretroviral therapy. There were 209 HIV-positive youngsters in the study's overall sample size, comprising 53 cases and 156 controls. Data was gathered by chart review using an organized checklist in English. The data were entered using Epi-data 4.2 and exported into SPSS version 24 for analysis. The relationship between each explanatory variable and the result variable was described using both bivariate and multivariate analysis. An adjusted odds ratio with 95% confidence intervals was conducted, and a p-value <0.05 was considered statistically significant.

Results: Being male (AOR= 4.504; 95% CI: 1.498, 13.539), duration on ART exceeding 47 months (AOR=40.6; 95% CI:9.571,172.222), fair and poor drug adherence (AOR=16.348; 95% CI:4.690,56.990), missed clinical appointments (AOR = 3.177; 95% CI: 1.100–9.174), and baseline WHO clinical stage 4 disease (AOR = 6.852; 95% CI: 1.540–30.49) were associated with an increased risk of virological failure. Conversely, a history of drug change and a CD4 count ranging from 250 to 500 cells/mm3 were significantly protective factors (AOR = 0.071; 95% CI: 0.024–0.214 and AOR=0.118; 95% CI: 0.030, 0.464, respectively).

Conclusion: Being male, duration on ART >47 months, fair and poor adherence, missed clinical appointments, and baseline WHO Stage 4 are factors that increase the odds of virological failure. History of ART Drug change and a CD4 count between 250 and 500 cells/mm3 are factors that decrease the odds of virological failure.

Keywords: retrospective, virological failure, antiretroviral therapy, children, Ethiopia

Introduction

A plasma viral load above 1000 copies/mL based on two consecutive viral load measures following three months of adherence support and at least six months of antiretroviral therapy (ART) is considered virological failure, which is a therapeutic failure (clinical and immunological).[1] If the patient is stable on antiretroviral therapy, viral load testing can be performed at six months, twelve months, and then every twelve months following that. A viral load test can also be performed if there is a suspicion of treatment failure and the initial viral load result is greater than 1000 copies/mL.[2] The quantity of HIV copies in the body is known as the viral load. The viral load test is the best method for assessing and tracking the effectiveness of antiretroviral therapy (ART) and shows how HIV is progressing in the body. A high viral load could be a sign of an untreated or uncontrolled HIV infection or a recent HIV transmission.[3]

Anti-HIV medication treatment is occasionally referred to as combination therapy since patients typically take three separate medications concurrently, frequently consolidated into a single tablet. It is also referred to as antiretroviral therapy (ART). Suppressing HIV replication to a point where medication resistance mutations do not arise is the aim of

Received: 27 December 2023
Accepted: 9 May 2024
Published: 13 May 2024

antiretroviral therapy (ART). However, the efficiency of ART is reduced due to drug resistance mutation, and viral suppression failure may occur.[4] HIV-infected children are considered a priority group for routine viral load monitoring.[5] Poor ART adherence, acquired or transmitted resistance to ART, or problems with pharmacokinetics (inadequate absorption, underdosing, and drug interactions) may be the cause of virological non-suppression.[6] The percentage of Ethiopian pediatric patients using ART who experience viral failure (VF) is 18.3%.[7]

The practice of viral load testing to inform the diagnosis of treatment failure in Ethiopia is poor. This is a result of the highly developed, pricy laboratory facilities and staff training required to assess viral load. Because of this, treatment failure in environments with limited resources like Ethiopia is frequently identified using clinical or immunological markers that appear long after virological failure does. When treatment fails, more costly and less palatable second-line medications become necessary. It is crucial for children with co-infections associated with AIDS who have a decreasing viral load.[8]

Virological Failure (VF) among paediatric population taking ART in Ethiopia is 18.3%.[9] Keeping patients on a failing regimen leads to the reversal of clinical conditions of patients to the pretreatment state and development of drug-resistant strains. Once drug-resistant virus starts transmitting in the population, the consequences will be devastating. ART failure is not a common diagnosis in most centres in Ethiopia, very few patients among the needy started on second-line ART regimens, high viral load leads to low CD4 cell count, increasing the risk of illnesses such as severe infections and some cancers.[10] The occurrence of treatment failure leads to the need for more expensive and less-tolerable second-line drugs. Sustaining a low viral load is important for children with the progression of AIDS and associated co- infections.[11]

For this study, cases and controls were determined based on viral load values defined as a viral load above 1000 copies/mL based on two consecutive tests within 3 months adherence support after at least 6 months on ART. Cases are Children having virological failure and Controls are Children having no virological failure.

The causes of virological failure in young Ethiopian Children's have not been extensively studied. In order to better understand the factors that contribute to virological failure in children with HIV receiving first-line antiretroviral medication in Addis Ababa, Ethiopia, this study set out to gather data.

Methods and Materials

Study Design and Settings

A facility-based unmatched case–control study was conducted from May 10, 2022, to July 20, 2022. Ethical clearance was obtained from the ethical review committee of Yanet Health science College with the approval reference No: Y/C/6010/14 and a support letter no: Y/C/7002/11/2014 dated on May 19, 2022. Data were from medical records/charts and all the data source of patients' medical record numbers was anonymously registered using codes without personal identifiers such as names of patients.

The study was conducted in Addis Ababa, the capital city of Ethiopia, in three randomly selected federal hospitals (Army Force Comprehensive Specialized Hospital, St. Peter's Specialized Hospital, and St. Paul's Hospital Millennium Medical College). The Army Force Comprehensive Specialized Hospital serves paediatric, gynaecologic, and obstetric services for Ethiopian military personnel and their family members. The ART clinic is providing both adult and paediatric HIV care and treatment for about 2215 patients. St. Peter's Specialized Hospital provides a variety of services, which include medical, surgical, gynaecological, and obstetric services, tuberculosis (TB), multidrug-resistant tuberculosis (MDR-TB), human Immunodeficiency Virus (HIV) care, and toxicology. St. Paul's Hospital Millennium Medical College was established through a decree of the Council of Ministers in 2010. The paediatric ART clinic provides for more than 200 children's.

Participants

All children (Age≤15) taking first-line ART at randomly selected federal hospitals were the source population. All children (Age≤15) taking first-line ART for at least 6 months at the randomly selected hospital were the study population. Children taking ART for at least 6 months and having viral load determination (result) with (case) or without (control)

virological failure were included in this study. Children taking ART for less than 6 months or without viral load determination (result) were excluded from the study.

Sample Size and Sampling Procedure

An unmatched case–control formula called Epi Info TM 7 Stat-calc was used to calculate the sample size. The following assumptions were made: a 1:3 case-to-control ratio, 80% power, and a 95% confidence interval. Assuming prior research, the proportion of being non-disclosed of HIV status (control exposed 31.5 and cases exposed 56.4).[12] The calculated sample size was 190 (142 controls and 48 cases). By adding 10% of the sample, the final sample size was found to be 209 (53 cases and 156 controls).

The necessary sample size for every research site was obtained using the proportionate sampling allocation (Figure 1). Then, prior to data collection, the cases and controls were determined using the viral load values. The patient's medical record number served as the sampling frame once the cases and controls were determined. The list sample frame was used to pick cases and control groups using a computer-generated basic random sampling procedure. Using a straightforward random sample method, study participants were chosen from a book of registrations for viral loads.

The Dependent variable is Virological failure and the independent variables include Gender, Age, Residency, Care giver relations, Care giver HIV status, Vital status of mother and father, HIV disclosure status, Recent CD4, Recent Hgb, Baseline viral load, Functional status (for age ≥5 yrs), Developmental status (for age <5 yrs), Baseline WHO Clinical stage, Current TB status, Opportunistic Infections, Anthropometric Assessments of Nutritional status of children (z-scores of weight for age (WAZ) and height for age (HAZ)), Duration on ART, Recent Adherence, Missed Clinical appointment, Co-trimoxazole prophylaxis use, Isoniazid prophylaxis use, History of ART drug change, Current ART regimen and Reason for ART regimen change.

Data Collection Tool and Procedure

A pretested, structured questionnaire that was built from earlier research and the Ethiopian National Comprehensive ART Guidelines (need reference number) which are available at ART clinics in reporting and recording formats was used to retrieve data. The data collectors were three clinical nurses with ART foundational training. A questionnaire created from patient charts and registration books was used to collect the data. Data collectors received one-day trainings on variables to be gathered and methods for data extraction or gathering. Every day, the lead researcher kept a careful eye on the entire data collection procedure and provided input. Prior to statistics entry, the data were examined for accuracy, consistency, and missing values.

Data Processing and Analysis

For analysis, the data were exported from Epi Data 4.2 and imported into Statistical Package for the Social Sciences (SPSS) version 24. Following basic frequency analysis and cross-tabulation, the data were cleaned and edited, and descriptive statistics were generated to present the clinical and demographic traits of the cases and controls. To determine whether there was a rough correlation between the independent and outcome variables, bivariate analysis was used. To find independent drivers of virological failure, a multivariate binary logistic regression analysis was performed for

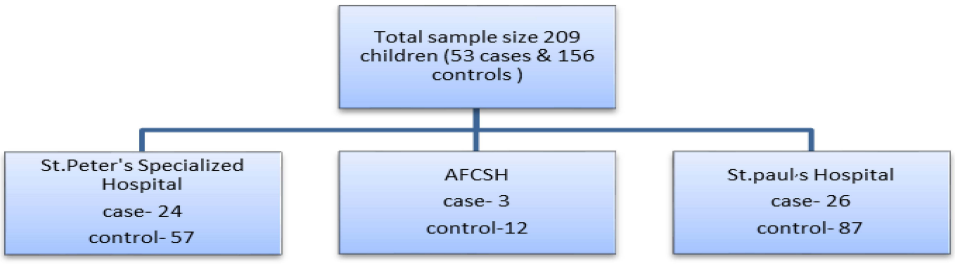

Figure 1 Proportional allocation of sample size in the study site.

variables exhibiting a P-value ≤0.25 in the bivariate analysis. The Hosmer–Lemeshow goodness-of-fit test was used to verify the model's goodness of fit. Additionally, the independent variables' multicollinearity was examined. Strongly associated variables with virological failure were found using odds ratios (OR) and their 95% confidence intervals.

Results

Socio-Demographic Characteristics

During our data extraction process, medical charts of 209 children's taking ART were included. A total of 53 cases and 156 controls were included in the study. Thirty-nine (73.6%) of cases and 78 (50%) of controls were males. Thirty-one (58.5%) of cases and 60 (38.5%) of controls were age groups ≥10 years. The majority (41, or 77.4%) of the cases and 122 (78.2%) of the controls were living in urban areas. Fifty (94.3%) of the cases and 135 (86.5%) of the controls were living with their parents (mother or father). The majority of 48 (90.6%) of cases and 137 (87.8%) of controls had HIV-positive caregivers. About 45 (84.9%) of the cases and 134 (85.9%) of the controls had a mother. Thirty-two (60.4%) of the cases and 79 (50.6%) of the controls disclosed their HIV status (Table 1).

Clinical and Laboratory Related Characteristics

About 45 (84.9%) of the cases and 108 (69.2%) of the controls had a recent hemoglobin ≥12.5 g/dl. Thirty-six (67.9%) of the cases and 90 (57.7%) of the controls had a recent CD4 count of ≥500 cells/mm^3. Sixteen (30.2%) of the cases and

Table 1 Socio-Demographic Characteristics of Children on First-Line ART and Their Caregivers

Variables	Category	Cases, N (%)	Controls, N (%)	Total, N (%)
Sex	Male	39(73.6)	78(50)	117(56.0)
	Female	14(26.4)	78(50)	92(44.0)
Age group	<5 years	4(7.5)	40(25.6)	44(21.1)
	5–10 years	18(34)	56(35.9)	74(35.4)
	≥10 years	31(58.5)	60(38.5)	91(43.5)
Residency	Urban	41(77.4)	122(78.2)	163(78.0)
	Rural	12(22.6)	34(21.8)	46(22.0)
Care giver relation	Parents(mother/father)	50(94.3)	135(86.5)	185(88.5)
	Other	3(5.7)	19(12.2)	22(10.5)
	Orphan	0(0.0)	2(1.3)	2(1.0)
Care giver HIV status	Positive	48(90.6)	137(87.8)	185(88.5)
	Negative	1(1.9)	9(5.8)	10(4.8)
	Unknown	4(7.5)	10(6.4)	14(6.7)
Vital status of the mother	Alive	45(84.9)	134(85.9)	179(85.6)
	Dead	6(11.3)	15(9.6)	21(10.0)
	Do not know	2(3.8)	7(4.5)	9(4.3)
Vital status of the father	Alive	29(54.7)	97(62.2)	126(60.3)
	Dead	7(13.2)	21(13.5)	28(13.4)
	Do not know	17(32.1)	38(24.4)	55(26.3)
Disclosure status of the child	Disclosed	32((60.4)	79(50.6)	111(53.1)
	Undisclosed	21(39.6)	77(49.4)	98(46.9)

twenty (12.8%) of the controls had a baseline viral load >1000 copies/mL. According to functional status at age 5years, the majority of cases (72.9%) and controls (66.1%) were ambulatory. For age <5 years, about 3 (60%) of the cases and 21 (63.6%) of the controls had appropriate age and developmental status. Thirty-one (58.5%) of the cases and 67 (43% of the controls) had baseline clinical stages 3 and 4 at ART initiation. The majority of 51 (96.2%) of cases and 142 (91%) of controls had negative current TB status. Eight (15.1%) of the cases and 23 (14.7%) of the controls had a history of opportunistic infection. Twenty-five (47.2%), 22 (41.5%) of the cases, and 63 (40.4%) and 57 (36.5%) of the controls were wasted and stunted, respectively (Table 2).

Treatment and Drug Related Characteristics

The majority 44 (83%) of the cases and 87 (55.8%) of the controls had >47 months of duration from the start of ART. Thirty-five (66%) of the cases and 52 (33.3%) of the controls had a history of missed clinical appointments. Twenty-nine (54.7%) of the cases and 27 (17.3%) of the controls had fair and poor drug adherence. Forty-one

Table 2 Laboratory and Clinical Related Information's Among HIV-Infected Children

Variable	Category	Cases, N (%)	Controls, N (%)	Total, N (%)
Recent Hgb	Hgb<12.5g/dl	8(15.1)	48(30.8)	56(26.8)
	Hgb≥12.5g/dl	45(84.9)	108(69.2)	153(73.2)
Recent CD4	<250cells/mm3	4(7.5)	15(9.6)	19(9.1)
	250–500cells/mm3	13(24.5)	51(32.7)	64(30.6)
	≥500cells/mm3	36(67.9)	90(57.7)	126(60.3)
Baseline viral load result	≤1000 copies/mL	8(15.1)	14(9.0)	22(10.5)
	>1000 copies/mL	16(30.2)	20(12.8)	36(17.2)
	Unknown	29(54.7)	122(78.2)	151(72.3)
Functional status of the child (for age≥5yrs)	Working	13(27.1)	42(33.9)	55(32.0)
	Ambulatory	35(72.9)	82(66.1)	117(68.0)
Developmental status of the child (for age<5 yrs.)	Appropriate for the age	3(60.0)	21(63.6)	24(63.2)
	Delay	2(40%)	12(36.4)	14(36.8)
Baseline WHO Clinical Stage	Stage 1	16(30.2)	61(39.1)	77(36.8)
	Stage 2	6(11.3)	28(17.9)	34(16.3)
	Stage 3	16(30.2)	46(29.5)	62(29.7)
	Stage 4	15(28.3)	21(13.5)	36(17.2)
Opportunistic infection	Yes	8(15.1)	23(14.7)	31(14.8)
	No	45(84.9)	133(85.3)	178(85.2)
Current TB history	Positive	2(3.8)	14(9.0)	16(7.7)
	Negative	51(96.2)	142(91.0)	193(92.3)
z-score of weight for age	Wasted	25(47.2)	63(40.4)	88(42.1)
	Normal	28(52.8)	93(59.6)	121(57.9)
z-score of Height for age	Stunted	22(41.5)	57(36.5)	79(37.8)
	Normal	31(58.5)	99(63.5)	130(62.2)

(77.4%) of cases and 112 (71.8%) of controls completed co-trimoxazole prophylaxis. Thirty-nine (73.6%) of the cases and 105 (67.3%) of the controls completed isoniazid prophylaxis use. Twenty-three (43.4%) of the cases and 110 (70.5%) of the controls had a history of drug change. About 67.9% of the cases were on the LPV (R)-based regimen, and 88.5% of the controls were on the DTG-based regimen (Table 3).

Factors Associated with ART Virological Failure

The bivariate logistic regression analysis showed that being male in sex, age of the child >120 month, Non-disclosure HIV status of the child, recent hgb>12.5mg/dl, CD4 count of 250–500 cells/mm3, baseline viral load, baseline WHO Stage 4 disease, having positive TB history, those having duration on ART >47 month, having fair and poor adherence, missed clinical appointment and history of drug change were associated with virological failure. After Adjustment of possible effect of confounding variables, being male in sex (AOR = 4.504; 95% CI: 1.498, 13.539), duration on ART >47 month (AOR=40.6; 95% CI: 9.571, 172.222), having fair and poor drug adherence (AOR=16.348; 95% CI: 4.690, 56.990), missed clinical appointment (AOR=3.177;95% CI;1.100,9.174), baseline WHO clinical sage 4 disease (AOR=6.852;95% CI:1.540,30.49), history of drug change (AOR=0.071: 95% CI: 0.024, 0.214), CD4 count 250–500 cells/mm3 (AOR=0.118; 95% CI: 0.030, 0.464) were found to be significantly associated with virological failure (Table 4).

Discussion

The finding of this study revealed that the odds value of virological failure among male HIV infected child is 4.504 times more compared to female child. This result is similar but some higher than the study done in western Kenya (AOR=2.1),[11] Rural Cameron (AOR=2.0),[13] Ethiopia[7] and against with the finding that was done in south Ghana

Table 3 HIV Treatment and Drug-Related Characteristics Among HIV-Infected Children

Variables	Category	Cases, N (%)	Controls, N (%)	Total, N (%)
Duration on ART	≤47 month	9(17)	69(44.2)	78(37.3)
	>47 month	44(83.0)	87(55.8)	131(62.7)
Recent adherence	Good (>95%)	24(45.3)	129(82.7)	153(73.2)
	Fair (85–95%) and poor (<85%)	29(54.7)	27(17.3)	56(26.8)
Missed clinical Appointment	YES	35(66.0)	52(33.3)	87(41.6)
	NO	18(34.0)	104(66.7)	122(58.4)
Co-trimoxazole prophylaxis use	Completed	41(77.4)	112(71.8)	153(73.2)
	Not completed	12(22.6)	44(28.2)	56(26.8)
Isoniazid prophylaxis use	Completed	39(73.6)	105(67.3)	144(68.9)
	Not completed	14(26.4)	51(32.7)	65(31.1)
History of ART Drug change	Yes	23(43.4)	110(70.5)	133(63.6)
	No	30(56.6)	46(29.5)	76(36.4)
Reason for ART regimen change	Drug side effect	11(44.0)	13(11.4)	24(17.3)
	New drug availability	14(56.0)	101(88.6)	115(82.7)
Current regimen	DTG based	8(15.1)	138(88.5)	146(69.9)
	EFV based	0(0.0)	3(1.9)	3(1.4)
	LPV/R based	36(67.9)	15(9.6)	51(24.4)
	Others	9(17)	0(0.0)	9(4.3)

Table 4 Factors Associated with ART Virological Failure Among Children on First-Line ART

Variable	Category	Case, (N)	Control, (N)	COR	AOR (95%)	p
Sex	Male	39	78	2.786	4.504(1.498,13.539)	0.007*
	Female	14	78		1	
RecentCD4 count	<250 cells/mm3	4	15	0.667	0.506(0.090,2.847)	0.439
	250–500cells/mm3	13	51	0.637	0.118(0.030,0.464)	0.002*
	>500 cells/mm3	36	90		1	
Duration on ART	<=47 month	9	69		1	
	>47 month	44	87	3.877	40.60(9.571,172.222)	0.001*
WHO Clinical Stage	Stage 1	16	61		1	
	Stage 2	6	28	0.817	1.613(0.298,8.739)	0.579
	Stage 3	16	46	1.326	3.073(0.947,9.970)	0.062
	Stage 4	15	21	2.723	6.852(1.540,30.491)	0.012*
Recent Adherence	Good (>95%)	24	129		1	
	Fair and poor	29	27	5.773	16.348(4.690,56.990)	0.001*
Missed Clinical appointment	Yes	35	52	3.889	3.177(1.100,9.174)	0.033*
	No	18	104		1	
History of drug change	Yes	23	110	0.321	0.071(0.024,0.214)	0.001*
	No	30	46		1	

Note: *Statistically significant at p-value <0.05:l, is a constant used as a comparison.

which revealed being female is 2.51 times as compared to male.[14] The finding in the south Ghana was the opposite of the result in this study reason might be because lower health seeking behavior in female children that lives in lower socioeconomic community. But the association between gender and virological failure may need further study.

This study find also that the odds value of virological failure among children whose duration on ART >47month is 40.6 times more compared to children whose duration on ART<47 month. The finding of this result is much higher than the study done in Swaziland (AOR=1.1)[15], Cameroon[13] and similar with study done in Ethiopia (AOR=11.2)[7] Bahir Dar (AOR=15.634).[16] This might be because long duration on treatment may increase drug resistance and adaptation of drugs finally got virologic failure.

The odds value of virological failure among children whose baseline WHO Clinical stage 4 Disease is 6.852 times more compared to children whose baseline WHO clinical Stage 1 disease. The finding is similar with this study[7,17] and much higher than the study done in Bahir Dar, Ethiopia (AOR=2.32).[16] This might be due to the fact that children presenting with advanced WHO clinical stage at ART initiation are at higher risk of opportunistic infections. The presence of opportunistic infections during ART initiation increases pill burden, which results in drug–drug interactions, and ultimately leads to virological failure.

The other finding of this study shows that the odds value among children who had fair and poor drug adherence is 16.348 times more compared to those children who had good drug adherence. The finding of this study goes with the study done in central Oromia (AOR=11.19)[18] and much higher than the study done in west Gojjam (AOR=6.05)[12] and similar with other studies.[16,18–21] The reason behind High viral load among those with poor adherence might be that optimal drug concentration is needed to control viral replication.

This study also shows that those children who had history of missed clinical appointment 3.177 times more likely to develop virological failure than those children who had no missed clinical appointment. This study is similar with the study done in Senegal (AOR=2.7)[22] and study done in west Gojjam which revealed that children with missed clinical Appointment had 8.03 times developing virological failure than children who had no missed clinical appointment.[12] This might be because missed clinical appointment leads to missing their dose, resulting in poor adherence causing periodic viral replication that result in the development of drug resistance.

This study also shows those children who had History of drug change have 97% less odds of virological failure in those who had no history of drug change. The result of this study aligned with the study done in Vietnam showed an association between the fixed-dose (single tablet daily) regimen with suppressed VL[23] and similar study also showed that, from non-nucleoside reverse transcriptase inhibitor, efavirenz use was associated with better virological outcome compared to nevirapine.[24] The finding of this study does not go with the study done in Ethiopia[7] and western Kenya.[11] Researchers identified higher odds of unsuppressed VL among children who were treated with TDF-3TC-NVP regimens compared to those on TDF-3TC-EFV. This could be due to the palatability of the preparation; sinceTDF-3TC-EFV formulation is a fixed-dose combination of a single pill taken once daily.

The odds value of virological failure among those children whose CD4 count is between 250 and 500cells/mm3 is 0.118 times less compared to those children >500 cells/mm3. The finding of this study might be despite ART mediated viral suppression, approximately 15%–20% of individuals who initiate ART at lower CD4 count (<200 cells/mm3) may plateau at abnormal low CD4 count.[25] The result of this study somewhat controversial needs further study.

Strength and Limitation of the Study

The area selected for this study is facility providing Pediatrics ART care in Addis Ababa, which was selected randomly which is generalizable to similar setup in the study pilot areas. The fact that we used previously collected, regularly recorded facility data was one of the drawbacks. Consequently, certain potentially significant factors were either missed because of incomplete records or because they might not have been necessary for patient care. Since it was unknown what happened first, it was only able to establish a correlation between the risk factors and virological failure. That is to say, this study did not examine cause and effect relationships.

Conclusion

This study was intended to identify determinant factors of virological failure; those factors that increase the odds of virological failure were being male, duration on ART >47 month, Fair and Poor adherence, missed clinical Appointment and Baseline WHO Stage 4 And that decrease the odds of virological failure were History of ART Drug change and CD4 count between 250 and 500 cells/mm3. Based on this study, we recommend healthcare practitioners and policymakers to intervene and improve adherence, and develop a treatment strategy for reducing virological failure.

Data Sharing Statement

The data used to support the findings of the study can be obtained from the corresponding author upon reasonable request.

Ethics Statement

Ethical clearance was obtained from the ethical review committee of Yanet Health science College with the approval reference No: Y/C/6010/14 and a support letter no: Y/C/7002/11/2014 dated on May 19, 2022. All methods were performed in accordance with the relevant regulations and according to the criteria set by Declaration of Helsinki. Informed consent was waived by the review committee as all the data source of patients' medical record numbers were anonymously registered using codes without personal identifiers such as names of patients. Permission letters for the selected facilities were obtained from institutional review board of ethical clearance of each facility. The data were collected by maintaining confidentiality while reviewing the card of the patient.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors declare that they have no conflicts of interest.

References

1. Approach PH, On CG. Guidelines HIV prevention, testing, treatment, service delivery and monitoring; 2021.
2. World Health Organization. Global HIV, hepatitis and STIs programmes. HIV data Stat Geneva WHO; 2020.;
3. World Health Organization. *Guideline on When to Start Antiretroviral Therapy and on Pre-Exposure Prophylaxis for HIV*. World Health Organization; 2015.
4. Pennings PS. HIV drug resistance: problems and perspectives. *Infect Dis Rep*. 2013;5(Suppl 1):e5. doi:10.4081/idr.2013.s1.e5
5. Arpadi SM, Shiau S, De Gusmao EP, Violari A. Routine viral load monitoring in HIV-infected infants and children in low- and middle-income countries: challenges and opportunities. *J Int AIDS Soc*. 2017;20(S7):e25001. doi:10.1002/jia2.25001
6. Bulage L, Ssewanyana I, Nankabirwa V, et al. Factors associated with virological non-suppression among HIV-positive patients on antiretroviral therapy in Uganda, August 2014–July 2015. *BMC Infect Dis*. 2017;17(1):1–11. doi:10.1186/s12879-017-2428-3
7. Getaneh Y, Yizengaw A, Likie A, et al. Rate and predictors of treatment failure among pediatric population taking highly active antiretroviral therapy in Ethiopia. *medRxiv*. 2019;2:19005538.
8. Jiao K, Wang C, Liao M, et al. A differentiated digital intervention to improve antiretroviral therapy adherence among men who have sex with men living with HIV in China: a randomized controlled trial. *BMC Med*. 2022;20(1):1–15. doi:10.1186/s12916-022-02538-3
9. Zenebe E, Washo A, Addis Gesese A, Karwowski J. Time to first-line antiretroviral treatment failure and its predictors among HIV-positive children in shashemene town health facilities, Oromia Region, Ethiopia, 2019. *Sci World J*. 2021;2021:8868479. doi:10.1155/2021/8868479
10. Ethiopia FM. National consolidated guidelines for comprehensive HIV prevention, care and; 2018.
11. Kadima J, Patterson E, Mburu M, et al. Adoption of routine virologic testing and predictors of virologic failure among HIV-infected children on antiretroviral treatment in western Kenya. *PLoS One*. 2018;13(11):e0200242. doi:10.1371/journal.pone.0200242
12. Shumetie A, Moges NA, Teshome M, Gedif G. Determinants of virological failure among HIV-infected children on first-line antiretroviral therapy in West Gojjam Zone, Amhara Region, Ethiopia. *HIV AIDS Res Palliat Care*. 2021;13:1035–1044. doi:10.2147/HIV.S334067
13. Zoufaly A, Fillekes Q, Hammerl R, et al. Prevalence and determinants of virological failure in HIV-infected children on antiretroviral therapy in rural Cameroon: a cross-sectional study. *Antivir Ther*. 2013;18(5):681–690. doi:10.3851/IMP2562
14. Afrane AKA, Goka BQ, Renner L, et al. HIV virological non-suppression and its associated factors in children on antiretroviral therapy at a major treatment centre in Southern Ghana: a cross-sectional study. *BMC Infect Dis*. 2021;21(1):1–11. doi:10.1186/s12879-021-06459-z
15. Jobanputra K, Parker LA, Azih C, et al. Factors associated with virological failure and suppression after enhanced adherence counselling, in children, adolescents and adults on antiretroviral therapy for HIV in Swaziland. *PLoS One*. 2015;10(2):e0116144. doi:10.1371/journal.pone.0116144
16. Gelaw B, Mulatu G, Tesfa G, Marew C, Chekole B, Alebel A. Magnitude and associated factors of virological failure among children on ART in Bahir Dar Town public health facilities, Northwest Ethiopia: a facility based cross-sectional study. *Ital J Pediatr*. 2021;47(1):1–9. doi:10.1186/s13052-021-01030-7
17. Bacha T, Tilahun B, Worku A. Predictors of treatment failure and time to detection and switching in HIV-infected Ethiopian children receiving first line anti-retroviral therapy. *BMC Infect Dis*. 2012;12(1):1–8. doi:10.1186/1471-2334-12-197
18. Abdullahi IJ, Deybasso HA, Adlo AM. Determinants of virological failure among patients on first-line antiretroviral therapy in central Oromia, Ethiopia: a case–control study. *HIV AIDS Res Palliat Care*. 2020;12:931–939. doi:10.2147/HIV.S281672
19. Ahmed M, Merga H, Jarso H. Predictors of virological treatment failure among adult HIV patients on first-line antiretroviral therapy in Woldia and Dessie hospitals, Northeast Ethiopia: a case-control study. *BMC Infect Dis*. 2019;19(1):1–7. doi:10.1186/s12879-019-3924-4
20. Bitwale NZ, Mnzava DP, Kimaro FD, Jacob T, Mpondo BCT, Jumanne S. Prevalence and factors associated with virological treatment failure among children and adolescents on antiretroviral therapy attending HIV/AIDS care and treatment clinics in Dodoma Municipality, Central Tanzania. *J Pediatric Infect Dis Soc*. 2021;10(2):131–140. doi:10.1093/jpids/piaa030
21. Barry O, Powell J, Renner L, et al. Effectiveness of first-line antiretroviral therapy and correlates of longitudinal changes in CD4 and viral load among HIV-infected children in Ghana. *BMC Infect Dis*. 2013;13(1):1–10. doi:10.1186/1471-2334-13-476
22. Cissé A-M, Laborde-Balen G, Kébé-Fall K, et al. High level of treatment failure and drug resistance to first-line antiretroviral therapies among HIV-infected children receiving decentralized care in Senegal. *BMC Pediatr*. 2019;19(1):1–8. doi:10.1186/s12887-019-1420-z
23. Rangarajan S, Colby DJ, Bui DD, et al. Factors associated with HIV viral load suppression on antiretroviral therapy in Vietnam. *J virus Erad*. 2016;2(2):94–101. doi:10.1016/S2055-6640(20)30466-0
24. Crawford KW, Wakabi S, Magala F, Kibuuka H, Liu M, Hamm TE. Evaluation of treatment outcomes for patients on first-line regimens in US President's Emergency Plan for AIDS Relief (PEPFAR) clinics in U ganda: predictors of virological and immunological response from RV 288 analyses. *HIV Med*. 2015;16(2):95–104. doi:10.1111/hiv.12177
25. García F, de Lazzari E, Plana M, et al. Long-term CD4+ T-cell response to highly active antiretroviral therapy according to baseline CD4+ T-cell count. *JAIDS J Acquir Immune Defic Syndr*. 2004;36(2):702–713. doi:10.1097/00126334-200406010-00007