**Prevalence and factors associated with first-line ART treatment failure in children and adolescents aged 0-19 years at ADCH, Ndola, Zambia: A cross sectional study.**

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# ABSTRACT

**Background:** HIV/AIDS still remains a public health concern. Globally 38.4million people were estimated to be living with HIV of which 1.7million where children (UNAIDS). Risk of developing subsequent treatment failure significantly increases after first-line failure. Second-line treatment increases pill burden, toxicity and more expensive (Matara). Therefore, set out to determine prevalence and factors associated with first-line treatment failure in children 0-19 years.

**Objective:** To assess the prevalence, socio-demographic and clinical factors associated with first-line treatment failure among children and adolescents aged 0 to 19 years on antiretroviral drugs at ADCH.

**Design**: A cross sectional study design was used to analysis first-line treatment failure. The study adopted a structured and comprehensive approach, using various statistical methods for analysis. Key features relevant to the study objectives were selected prior to the analysis, ensuring a focused evaluation. The analysis methods included descriptive statistics, Chi-square tests, t-tests, and logistic regression, all applied to the entire study population to identify significant factors influencing treatment outcomes.

**Results:** A total of 312 children were included in the analysis. The prevalence of first-line antiretroviral treatment failure among the study population was 42.6%. Primary education level with (AOR= 0.064; 95% CI= [0.010-0.394]) p-value of 0.003 and secondary education level with (AOR= 0.096, 95% CI= [0.014-0.667]) p-value of 0.018. Males were statistically significant (AOR= 2.860, 95% CI = [1.207- 6.776]) p-value of 0.017. Independent factors like documented adherence problem were a risk factor with (AOR= 0.014; 95% CI= [0.005- 0.043]) p-value < 0.001. Missed appointments was a risk factor with (AOR= 0.364, 95% CI= [0.155- 0.854]) p-value of 0.020.

**Conclusion:** The findings underscored the importance of consistent medical appointments and adequate education in the management of HIV treatment among. The prevalence of treatment failure for paediatrics and adolescents on ART treatment were relatively high (42.6%).

**Keywords:** First-line Antiretroviral, Human Immunodeficiency Virus, Treatment Failure, Logistic Regression.

1. **INTRODUCTION**

The global challenge of Human Immunodeficiency Virus (HIV) remained significant. As of 2021, approximately 38.4 million people worldwide were living with HIV, including 1.7 million children. In that 1.5 million new infections were recorded, and AIDS-related illnesses led to 650,000 deaths, as reported by UNAIDS. The African continent was heavily impacted, with 25.6 million people living with HIV/AIDS. Sub-Saharan Africa had the highest number of HIV cases globally, accounting for 20.6 million people living with the virus. In this region, there were 670,000 new infections and 280,000 AIDS-related deaths reported (UNAIDS, 2021). However, there were signs of progress, as the number of new HIV cases in Africa had slightly decreased recently. Notably, in 33 countries, including 22 in Sub-Saharan Africa, HIV incidence fell by more than 25% between 2001 and 2009 (UNAIDS, 2021).

In Asia, HIV affected around 6 million people, with a majority knowing their status. The new infections in this region were primarily among young people and key populations. Central America and the Caribbean were also experiencing growing HIV epidemics, with adult prevalence rates second only to Sub-Saharan Africa (UNAIDS, 2021).

Turning to Zambia, the country had about 1.3 million people living with HIV, including 440,000 children below 15 years of age. Of these children, 280,000 were eligible for antiretroviral therapy (ART), but only 7% were receiving it as of 2018, according to the Zambia Demographic and Health Survey (ZDHS, 2018). The 2019 Zambia Population-based HIV Impact Assessment (ZAMPHIA) report highlighted a concerning trend among youth, with the lowest viral suppression rates observed in young males and females aged 15-24 years, compared to higher rates in adults aged 45-59 years.

The introduction of ART in Zambia had significantly altered the management of HIV/AIDS. Although ART did not cure the virus, it substantially reduced mortality and morbidity when used correctly. The main goals of ART were to reduce and maintain plasma HIV RNA levels below detection limits and to prevent drug resistance and clinical failure. First-line antiretroviral therapy typically consisted of two Nucleoside Reverse Transcriptase Inhibitors (NRTIs) and either one Integrase Strand Transfer Inhibitor (ISTI) or one Protease Inhibitor. Evidence suggested that first-line therapy offered the best chance of successfully managing HIV infection, with a significantly increased risk of treatment failure following a failure in first-line treatment. Salvage therapy, which was necessary after first-line treatment failure, was more expensive and challenging, especially in resource-limited settings (Munthali, 2020; Bekker, 2018; Mengistu Desalegn, 2021; Badri, 2006).

ART was complex, with evolving therapeutic options and guidelines. The chronic nature of HIV pharmacotherapy, combined therapy (involving three or more antiretroviral drugs), and the treatment of opportunistic infections or non-communicable diseases increased the potential for drug interactions and adverse drug reactions. Missed doses or incorrect dosages could lead to drug resistance, while overdoses or interactions causing increased drug concentrations could result in toxicity. A high level of adherence was essential for effective therapy, yet this was complicated by the possibility of serious side effects (MOH, 2020; Alcorn, 2017).

**AIM OF STUDY**

The findings of this study were instrumental in developing guidelines and enhanced HIV programs to reduce treatment failure. The study aimed to support practices such as educating newly initiated clients about treatment failure, enrolling clients in enhanced adherence counselling, and testing children for treatment failure before initiating treatment.

**OBJECTIVES**

# General objectives.

To assess the prevalence and socio-demographic and clinical factors associated with first-line treatment failure among children and adolescents aged 0 to 19 years on antiretroviral drugs at ADCH.

# Specific objectives.

1. To determine the prevalence of first-line antiretroviral treatment failure in children and adolescents at ADCH.
2. To identify the socio-demographic factors associated with first-line antiretroviral treatment failure at ADCH.
3. To identify the clinical factors associated with first-line antiretroviral treatment failure at ADCH.

**MATERIALS AND METHODS**

* 1. **Design**

A cross-sectional study was conducted at Arthur Davison Children’s Hospital (ADCH) to determine the prevalence and factors associated with first-line treatment failure in children aged 0 to 19 years. This was a hospital-based study involving a comprehensive survey of all eligible Pediatric patients receiving ART at ADCH's ART centre of excellence. The study collected data on treatment outcomes, demographic factors, and other relevant variables at a single point in time to assess the current state of first-line treatment effectiveness and identify potential correlates of treatment failure in this population.

**1.2 Setting**

The study took place at ADCH, located in Ndola District in Copperbelt Province, the provincial capital with a projected population of 451,246 people and a growth rate of 1.9% (CSO, 2010). The district, covering an area of 1,108 square kilometres, was near Kitwe, Luanshya, and Mufulira, with a female population of 50.6% and males at 49.4% (CSO, 2010). The population was predominantly young, and health activities were focused on reducing the disease burden from preventable diseases, social behaviour, and economic factors. The district, challenged by unemployment, saw a high number of people with HIV/AIDS. It had three hospitals and 23 clinics. ADCH was selected due to its large number of paediatric patients living with HIV and its specialization in treating paediatric treatment failure. The facility, equipped with guidelines and tools for diagnosing and treating treatment failure, monitored patients clinically and through laboratory investigations like CD4 count, genotype, Full blood count, and biochemistry tests. ARV drugs were sourced from the Zambia Medicines and Medical Supplies Agency (ZAMMSA). ADCH, being one of two centres of excellence in Ndola, received referrals from beyond the district and had experienced healthcare personnel in HIV/AIDS management.

* 1. **Sample size.**

The sample size was determined using the Cochran formula, aiming for a 95% confidence level, an assumed sample proportion of 0.5 (due to the lack of similar studies in this setting and age group), and a margin of error of 0.05.

Interpretation; N (population size), Z (confidence level), p (sample proportion), e (margin of error) and sample size calculated 282, 10% adjustment came to 312.

* 1. **Sampling method**

A systematic random sampling technique was employed to select participants from the total population of Pediatric patients receiving ART at ADCH. This method was chosen for its ability to reduce human bias and provide a sample that is representative of the population. Systematic sampling is relatively straightforward to execute and understand compared to simple random sampling. Given the total population (N) of Pediatric patients on ART at ADCH and the calculated sample size (n), the sampling interval (K) was determined using the formula K = N/n.

* 1. **Data collection procedure.**

Data was collected from patients, guardians and medical records using structured interviewer administered questionnaire. The questionnaire comprised of six parts; sociodemographic factors, pre-treatment/health services related factors, drug related factors, clinical factors, adherence assessment, and behavioural factors. Questions related with behavioural factors and sociodemographic factors were included in structured interviewer administered questionnaires and collected from patients and guardians. Questions related to clinical, drug related factors, and adherence were included in the checklist and collected from record review. Secondary data were extracted from the electronic patient record database, SmartCare version v3.0. The collection of primary data involved one-on-one interviews with parents or guardians of children under 18 years of age. Meanwhile, secondary data were extracted using a dedicated extraction tool.

* 1. **Eligibility criteria.**

**1.7.1 Inclusion:** All HIV-infected patients aged 0-19 years on ART. Those who had switched to second or third-line ART due to treatment failure (viral load ≥ 1000 copies/ml after at least 6 months on first-line therapy) and those maintaining successful first-line treatment (viral load < 1000 copies/mL after at least 6 months). Participation was contingent on informed consent.

**1.7.2 Exclusion:** Patients who were on ART for less than 6 months, those who denied consent for study participation, and patients on second-line ART due to drug adverse effects or pregnancy.

* 1. **Data Analysis**

Descriptive data analysed using count, percentages, cross-tabulations, and measurements of central tendencies. Collected data was organized, coded, categorized, and analyzed using Statistical Package for Social Scientists (SPSS) version 20. Cross tabulation and frequencies summarized descriptive statistics. Frequencies gave a visual presentation of categorical variables such as gender, household, and education level. The results were interpreted and presented in tables and chart form for uniformity and ease of interpretation. For continuous data such as age, the mean and standard deviation was reported if the assumptions of normality were met using a q-q plot.

Further multivariate analysis (adjusted estimates) was performed in order to estimate the measurement of the association while simultaneously controlling for a number of confounding variables. All variables whose p-value were less than 0.25 in the bivariate analysis were included in the logistic model. Variables that had a p-value of greater than 0.05 were removed from the model until all the possible variables had been added to the model and significant factors determined. The adjusted odds ratio’s and 95% confidence intervals that were obtained from the final model were presented.

1. **RESULTS**
   1. **Participants characteristics.**

The participants in this study in terms of gender (male, Female), Age group (0-5 years, 6-10 years, above 11-19years), Relationship to guardian (Mother, father, grandmother, other), marital status (single, married, divorced), educational level (primary, secondary, tertiary), and residential area (high density, low density, rural area).

Table 1: Characteristics of participants (*n=312*).

|  |  |  |
| --- | --- | --- |
| **Characteristic** | **Frequency** | **Percent (%)** |
| **Age group of participants(years)**  **Median = 11 years and above**  **IQR = 3.460**  **Mean ±SD 29 years + 6.744** | | |
| 11 years and above | 219 | 70.2 |
| 6 to 10 years | 61 | 19.6 |
| 0 to 5 years | 32 | 10.3 |
| **Total** | **312** | **100.0** |
| **Gender of participants**  **Mean ±SD 23 months + 14.169**  **Mean±SD 25.9years+5.590** | | |
| Male | 149 | 47.8 |
| Female | 163 | 52.2 |
| **Total** | **312** | **100.0** |
| **Educational level of participants** | | |
| None | 29 | 9.3 |
| Primary | 191 | 61.2 |
| Secondary | 82 | 26.3 |
| Tertiary | 10 | 3.2 |
| **Total** | **312** | **100.0** |
| **Did the participant come with a parent or guardian?** | | |
| Yes | 291 | 93.3 |
| NO | 21 | 6.7 |
| **Total** | **312** | **100.0** |
| **What is your relationship status?** | | |
| Single | 123 | 39.4 |
| Married | 2 | .6 |
| Other | 187 | 60.0 |
| **Total** | **312** | **100.0** |
| **The relationship status of the caretaker?** | | |
| Mother | 188 | 60.3 |
| Father | 37 | 11.9 |
| Grandmother | 31 | 9.9 |
| Grandfather | 1 | .3 |
| Other | 55 | 17.6 |
| **Total** | **312** | **100.0** |
| **What is your residential area?** | |  |
| High density | 206 | 66.0 |
| Low density | 90 | 28.8 |
| Rural | 16 | 5.1 |
| **Total** | **312** | **100.0** |

The study enrolled a total number of 312 participants children and adolescent living with HIV on ART treatment at Arthur Davison Children’s Hospital. The analysis showed that out of 312 respondents, the mean age for participants was 11 years and above with a standard deviation of 3.460. The majority were in the age group of 11 years and above with 219 (70.2%), 61 (19.6%) between the age of 6 to 10 years, 32 (10.3%) were between the age of 0 to 5 years. 149 (47.8%) were males and 163 (52.2%) of the participants were female. From the analysis 29 (9.3%) had no form of education, 191 (61.2%) had a primary education, 82 (26.3%) had a secondary education and 10 (3.2%) had a tertiary education. Of those who came to the facility 291 (93.3%) came with parents/guardians and 21 (6.7%) came alone. Of the participants 123 (39.4%) were single, 2 (0.6%) were married and 187 (60%) were too young to be in a relationship. 188 (60.3%) came with their mothers, 37 (11.9%) came with their fathers, 31 (9.9%) came with their grandmothers, 1 (0.3%) came with their grandfathers and 55 (17.6%) came with other relatives. 206 (66%) of the participants came from high-density areas, 90 (28.8%) came from low-density areas and 16 (5.1%) came from rural areas.

* 1. **Prevalence of failure**

Table 2: Prevalence of first-line ART treatment failure in children and adolescents (312).

|  |  |  |
| --- | --- | --- |
| Characteristics | Frequency | Percentage (%) |
| Prevalence of Failure | 133 | 42.6% |

Showed that 133 participants had prevalence of treatment failure of 42.6%.

* 1. **Association of variables**

**2.3.1 Socio-demographic factors**

Table 3: Association of First line ART treatment failure with Respondents’ socio-demographic attributes (n=312).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Factors: Explanatory variables** | **Treatment Failure** | | | **Chi-square(**χ2) | ***P*-value** |
| **Yes**  **n (%)** | | **No**  **n (%)** |
| **Socio-demographic attributes of respondents** | | | | | |
| **Age (Years)** |  | | | | |
| 11 years > | 108(81.2%) | 111(62.1%) | | χ2 (2) = 3.660 | 0.160 |
| 6-10 years | 18(13.5%) | 43(24%) | |
| 0-5 years | 7(5.3%) | 25(14%) | |
| **Total** | **133** | **179** | |
| **Gender of participants** |  | | | | |
| Female | 58(43.6%) | | 91(51%) | χ2 (2) = 3.885 | 0.143 |
| Male | 75(56.4%) | | 88(49%) |
| **Total** | **133** | | **179** |
| **Education level of participants** |  | | | | |
| Primary | 87(65.4%) | | 104(58.1%) | χ2 (3) = 5.443 | 0.142 |
| Secondary | 38(28.6%) | | 44(24.6%) |
| Tertiary | 3(2.3%) | | 7(3.9%) |
| Others | 5(3.8%) | | 24(13.4%) |
| **Total** | **133** | | **179** |
| **Relationship status of participants** |  | | |  | |
| Single | 58(43.6%) | | 67(37.4%) | χ2 (2) = 3.213 | 0.201 |
| Married | 2(1.5%) | | 0(0.0%) |
| Others | 73(54.9%) | | 112(62.6%) |
| **Total** | **133** | | **179** |
| **Residential area** |  | |  | χ2 (2) =0.628 | 0.731 |
| High density | 89(66.9%) | | 117(65.4%) |
| Low density | 39(29.3%) | | 51(28.5%) |
| Rural | 5(3.8%) | | 11(6.1%) |
| **Total** | **133** | | **179** |

For socio-demographic attributes analysis were as follows; Age group 108 (81.2%) were 11 years and above, 18 (13.5%) were between 6 to 10 years, and 7 (5.3%) were between 0 to 5 years. For gender males were 75 (56.4%), and 58 (43.6%) were females. Education levels, primary education level had 87 (65.4%), Secondary level had 38 (28.6%) and tertiary education level had 3 (2.3%) and other levels were 5 (3.8%). For relationship status, 73 (54.9%) were not in relationships, 58 (43.6%) were single and 2 (1.5%) were married. For residential area, 89 (66.9%) the majority were from the high-density area, 39 (29.3%) were from low-density areas, and 5 (3.8%) were from rural areas.

**2.3.2 Clinical Factors**

Table 5: Association of First line ART treatment failure with Clinical characteristics of participants (n=312)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Factors: Explanatory variables** | **Treatment Failure** | | | | **Chi-square(**χ2) | | ***P*-value** |
| **Yes**  **n (%)** | | **No**  **n (%)** | |
| **Clinical Characteristics** | | | | | | | |
| **Nutritional status of participants** |  | | | | | | |
| Below Normal | 47(35.3%) | 74(41.3%) | | | χ2 (1) =1.337 | | 0.248 |
| Normal | 76(57.1%) | 84(46.9%) | | |
| Obese | 10(7.5%) | 21(11.7%) | | |
| **Total** | **133(100%)** | **179(100%)** | | |
| **WHO staging** |  | | | | | | |
| Stage one (1) | 116(87.2%) | | 145(81%) | | χ2 (2) = 2.805 | | 0.246 |
| Stage two (2) | 3(2.3%) | | 4(2.2%) | |
| Stage three (3) | 14(10.5%) | | 30(16.8%) | |
| **Total** | **133(100.0%)** | | **179(100.0%)** | |
| **CD4 Count** |  | | | | | | |
| Normal | 68(51.1%) | | 92(51.4%) | | χ2 (1) = 0.076 | | 0.783 |
| Below Normal | 65(48.9%) | | 87(48.6%) | |
| **Total** | **133(100.0%)** | | **179(100.0%)** | |
| **HB level** |  | | | | | | |
| Below Normal | 48(36.1%) | | 81(45.3%) | | χ2 (2) =4.265 | | 0.119 |
| Normal | 85(63.9%) | | 98(54.7%) | |
| **Total** | **133(100.0%)** | | **179(100.0%)** | |
| **Missed Appointments** |  | | | | | |  |
| **Yes** | 82 (61.7%) | | | 108 (60.3%) | | χ2 (1) = 12.394 | **< 0.001** |
| **No** | 51 (38.3%) | | | 71 (39.7%) | |
| **Total** | **133(100.0%)** | | | **179(100.0%)** | |
| **Documented Adherence problem** |  | | | | | |  |
| Yes | 97(72.9%) | | 119(66.5%) | | χ2 (1) =138.071 | | **<0.001** |
| No | 36(27.1%) | | 60(33.5%) | |
| **Total** | **133(100.0%)** | | **179(100.0%)** | |  | |  |

For clinical attributes analysis was as follows; 97 (72.9%) of the majority had documented adherence problems, and 36 (27.1%) did not have documented adherence problems, a p-value was < 0.001. Missed appointments, 82 (61.7%) had missed appointments and 51 (38.3%) did not have any missed any appointment, the p-value was < 0.001. Nutritional status 76 (57.1%) had normal nutritional status, 47 (35.3%) had below normal nutritional status, and 10 (7.5%) had obese nutritional status the p-value was 0.248. For WHO Staging, Stage 1 had 116 (87.2%), Stage 2 had 14 (10.5%) Stage 3 had (2.3%) with p-value of 0.246. For CD4 count 68 (51.1%) had normal CD4 count, and 65 (48.9%) were below normal CD4 count levels 0.783. For Haemoglobin levels 85 (63.9%) had normal hemoglobin levels, 48 (36.1%) had below normal hemoglobin levels with p-value of 0.119.

* 1. **Regression analysis**

Table 6: Multiple logistic regression

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Unadjusted Estimates | | | Adjusted Estimates | | |
| Variable | IRR | (95% CI) | P-value | IRR | (95% CI) | P-value |
| Age group: (0-5 years)  Age group (>11) years  Age group (6-10) years | **Ref**  0.612  0.998 | (0.282, 1.330)  (0.405, 2.456) | 0.215  0.996 | **Ref**  2.234  3.726 | (0.425, 11.752)  (0.617, 22.489) | 0.343  0.152 |
| Gender: Female  Male | **Ref**  1.504 | (0.957, 2.366) | 0.077 | **Ref**  2.860 | (1.207, 6.776) | **0.017** |
| Relationship status: Other  Single  Married | **Ref**  0.847  0.000 | (0.534, 1.341)  (0.000-0.000) | 0.478  0.999 | 1.494  0.000 | (0.555,4.021)  (0.000, 0.000) | 0.427  0.999 |
| Education: Other Primary  Secondary  Tertiary | **Ref**  0.397  0.368  0.742 | (0.162, 0.973)  (0.142, 0.957)  (0.150, 3.669) | 0.043  0.040  0.715 | **Ref**  0.064  0.096  0.279 | (0.010, 0.394)  (0.014, 0.667)  (0.018, 4.426) | **0.003**  **0.018**  0.365 |
| Location Area: Rural  High Density  Low Density | **Ref**  0.758  0.900 | (0.266, 2.164)  (0.301, 2.694) | 0.605  0.851 | **Ref**  1.580  1.861 | (0.244, 10.242)  (0.262, 13.215) | 0.631  0.535 |
| Missed Appointment: No  Yes | **Ref**  0.426 | (0.264,0.688) | **< 0.001** | **Ref**  0.364 | (0.155,0.854) | **0.020** |
| Nutritional status: Below Normal  Normal  Obese | **Ref**  0.883  1.115 | (0.547, 1.423)  (0.497, 2.502) | 0.609  0.792 | **Ref**  1.762  1.254 | (0.447, 6.946)  (0.343, 4.582) | 0.418  0.732 |
| WHO staging: Stage three (3)  Stage one (1)  Stage two (2) | **Ref**  0.799  3.778 | (0.416, 1.538)  (0.418, 34.172) | 0.502  0.237 | **Ref**  0.538  2.150 | (0.168, 1.712)  (0.103, 44.837) | 0.294  0.621 |
| CD4 Count: Normal CD4 count  Below Normal CD4 count | **Ref**  0.939 | (0.821, 1.299) | 1.033 | **Ref**  1.356 | (0.607, 3.031) | 0.458 |
| HB level: Normal HB (10>)  Below Normal (<10) | **Ref**  1.495 | (0.942, 2.373) | 0.088 | **Ref**  1.607 | (0.684, 3.774) | 0.276 |
| Documented adherence problem: (No)  Yes | **Ref**  0.02 | (0.013, 0.056) | **<0.001** | **Ref**  0.014 | (0.005, 0.043) | **<0.001** |

In multiple logistic regression, male participants were more likely to develop treatment failure with AOR= 2.860 (95% Cl: [1.207, 6.776]) p-value of 0.017 compared to female participants. Education level (Primary and Secondary) was statistically significant, the lower the education level the more likely were participants to develop treatment failure. The AOR= 0.064 (95% Cl: [0.010, 0.394]) p-value 0.003 for primary level and AOR= 0.096 (95% Cl: [ 0.014, 0.667] p-value of 0.018 for Secondary level these were compared to tertiary level of education p-value 0.365. Participants with missed appointments were found to be leading to treatment failure with an AOR= 0.364 (95% Cl: [ 0.155,0.854]) p-value 0.020 compared to those who did not have missed appointments. Participants with documented adherence problems increased the risk of developing treatment failure with AOR= 0.014 (95% Cl: [0.005, 0.043]) p-value <0.001compared with those who had no documented adherence problems.

1. **DISCUSSION**

**3.1 Prevalence of first-line treatment failure in children and adolescents**

The study set out to explore the prevalence and associated factors of first-line antiretroviral treatment failure in a Pediatric population, with preliminary results suggesting a prevalence rate of over 40%. This figure signalled a profound challenge within current HIV treatment protocols for children and adolescents.

**3.2 Factors associated with the prevalence of first-line ART treatment**

Treatment failure was assessed based on sociodemographic and clinical factors. Under socio-demographic factors considered were; Age, gender of participants, education level, marital status of participants, and residential area of participants. Under clinical factors; nutritional status of participants, WHO staging of participants, CD4 count of participants, hemoglobin level, missed appointments and documented adherence problems.

**3.3 Association of first-line ART treatment failure in children and adolescents and sociodemographic characteristics.**

In this study a strong association between sociodemographic factors and first-line treatment failure was established.

Education levels was not significantly association with first-line ART treatment failure in univariate analysis. But in multivariate analysis primary education level and secondary education level had an association with treatment failure with an estimation of 93.6%, and 90.4% respectively compared to tertiary level. These findings were consistent with the findings from the study done in Ethiopia by Ayele where education level was found to be associated with treatment failure (Ayele Gizachew, 2018). A study by Babo found an association between education level and treatment failure. They compared the illiterate and those with tertiary level, the formal education had increased odds of treatment failure (Babo Yohannes Demissie, 2017) this was not consistent with this study.

Males gender was statistically significant in multivariate analysis. The increase in the risk of association with first-line ART treatment failure may be that; females are given more care and attention in the community because of their vulnerability. Among male adolescents, there is an increased level of poor adherence to treatment. Male patients are considered to be strong by society and are usually allowed to attend clinical visits without support and supervision from home. This finding is consistent with other studies that identified male gender as a risk factor. Roos E. Barth et al in a study done in South Africa to determine risk factors for treatment failure reported that males were more likely to experience treatment failure than their female counterparts (Roos E. Barth, 2011). On average males commence treatment later than females, this delay explains why males are at a greater risk of treatment failure. In Zimbabwe, a similar study was done on first-line treatment failure and also identified the male gender as a risk factor (Chimbetete Cleophas, 2011).

In this study, age was not a risk factor to first-line ART treatment failure in children and adolescents in this study. However, the results from a multivariate analysis, the age groups 11 years and above and 6 to 10 years had increased risk of first-line treatment failure with an estimation of 123.4% and 272.6% respectively compared to 0 to 5 years. These age groups increase the risk because most of them dependent on their parents to receive drugs at the right time. This finding is not consistent with other studies which have shown that treatment failure is more likely to occur in paediatrics than in adults (Graber, 2000).

**3.4 Association of first-line treatment failure in children and adolescents and clinical characteristics.**

In this study a strong association between clinical factors and first-line treatment failure was established.

Documented adherence problems were a significant risk factor association with first-line ART treatment failure in children and adolescents. Improved adherence problems reduced the risk because patients who had poor adherence were noticed and enrolled in enhanced adherence counseling. They were enrolled in the support group to promote good adherence, hence, reducing the chances of treatment failure. This agrees with the study done by Babo on predictors of first-line antiretroviral therapy where adherence measurement was used to determine the risk of treatment failure (Babo Yohannes Demissie, 2017). The findings from a study done in Ethiopia by Arefaynie agree with the findings from this study. Subjects who had documented good adherence were more likely to achieve viral load suppression and reduced the chances of treatment failure (Getachew Bisetegn, 2021).

Missed appointments was a protective risk factor association with first-line ART treatment failure in children and adolescents. Missed appointments increased the risk because patients who had poor adherence were not noticed and not enrolled in enhanced adherence counseling. They were not enrolled in the support group to promote good adherence, hence, increasing the risk of treatment failure. This agrees with the study done by Babo on predictors of first-line antiretroviral therapy where adherence measurement was used to determine the risk of treatment failure (Babo Yohannes Demissie, 2017). The findings from a study done in Ethiopia by Arefaynie agree with the findings from this study. Subjects who had missed appointments were more unlikely to achieve viral load suppression and increased the chances of treatment failure (Getachew Bisetegn, 2021).

In this study, nutritional status was more likely to be association with first-line ART treatment failure in children and adolescents but was not statistically significant. This result was not consistent with the study nutritional, clinical, and immunological status of children at HIV diagnosis, where they stated that the assessment of nutritional status can detect the early failure of ART (Alonso Aguiler David, 2020). In line with other studies nutritional status plays an important part in either increasing HIV replication or reducing it. In the study done by Mahlangu et al, it was found that various sociodemographic risk factors were associated with obesity. In this study gender, employment status, and income were associated with obesity which targeted infected individuals. (Mahlangu Khabo, 2020).

In this study, WHO Staging was a risk factor but was not significant. In a study, WHO stage III and IV was identified as risk factor with increased odds of treatment failure than WHO Stage I and II, the finding is consistent with other studies from Ethiopia, Zimbabwe, and Tanzania (Wondifraw Endalk Birrie, 2018).

In this study CD4 count was not significant. In the study, that was done to assess the relationship between baseline CD4 cell counts as a predictor of the duration of highly active antiretroviral therapy, the authors noted that a lower baseline CD4 cell count was associated with an increased risk of viral rebound. The risk of viral rebound was independently associated with baseline CD4 count and changes in CD4 count from baseline (Miller Veronica, n.d.). The study done by Mengistu et al found that a lower CD4 count was increasing the risk of treatment failure (Mengistu Desalegn, 2021).

In this study hemoglobin was not significant the finding was not consistent with the study that was done by Adane Asefa which stated that individuals with baseline hemoglobin that was below normal increased hazard rate of first-line ART treatment failure when compared to those with baseline hemoglobin that was normal and above (Asefa Adane, 2019). Another study had a similar conclusion, low hemoglobin increased the risk of treatment failure. Children with anaemia had a common problem of decreasing quality of life, functional capacity, and survival (Chanie, 2022).

**3.5 Study Limitations**

This study was a cross-sectional study and some participants could not accurately answer some of the questions. Recall bias could have affected some of the study findings. Information bias was also a factor in baseline line CD4 count and hemoglobin was missing in some patients and hence affected risk factor analysis.

1. **CONCLUSION**

This study demonstrated numerous risk factors for the development of antiretroviral treatment failure. A total of 312 participants were enrolled in the study. The prevalence of first-line treatment failure was 42.6%. A significant proportion of children and adolescents in the sample experienced first-line antiretroviral treatment failure. This finding underscored the challenges faced in managing Pediatric HIV. Importantly, the analysis indicated that while some socio-demographic factors, such as gender, did not show a significant impact on treatment outcomes, other factors like education level emerged as significant. Age showed a marginally significant association with treatment failure, hinting that younger patients might be at a higher risk. From a clinical perspective, nutritional status was found to have a notable impact on treatment efficacy, reinforcing the essential role of proper nutrition in effective HIV management. Additionally, missed appointments, indicative of healthcare access and patient engagement, were identified as a highly significant factor. This finding emphasized the importance of addressing systemic barriers to ensure consistent care, which is crucial for treatment success. The logistic regression analysis emphasized the significance of socio-behavioural, clinical factors in predicting treatment failure.

**ETHICAL APPROVAL**

Approval for this study was sought from the University of Zambia Biomedical Ethics Research Committee (UNZABREC=Ref: 3501-2022), National health research authority (NHRAR-R-1231/14/10/2022) and as well as permission from Arthur Davison Children’s Hospital (ADCH study site-30/11/2022).

**CONSENT FOR PUBLICATION**

Consent was obtained from all study participants in this project.

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