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ORIGINAL ARTICLE

Predictors of Unsuppressed Viral Load Among Children Below Five Years of Age Living with Human Immunodeficiency Virus Infection in Mwanza, Tanzania

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ABSTRACT

Background: Children below five years of age have increased risk of unsuppressed viral load due to various socio-demographic and clinical factors. This study investigated the prevalence and predictors of unsuppressed viral load among HIV infected children below five years of age in Mwanza, Tanzania.

Methods: A cross sectional study involving 279 children below five years of age who were on antiretroviral therapy (ART) for at least six months was conducted in the care and treatment clinics (CTC), from December 2020 to April 2021.

Results: A total, 20 (7.2%, 95% CI; 4.2-10.2) had unsuppressed HIV viral load. The duration on ARVs less than 24 months (AOR 3.8, 95% CI: 1.2-12.0; *P=.026*), poor ARVs adherence in the past six months (AOR 5.7; 95% CI: 1.6-18.6; *P=.004*), severe or moderate malnutrition (AOR 3.3, 95% CI: 1.2-8.9; *P=.020*) and caregivers with no home supporters (AOR 4.4, 95% CI: 1.5-13.3; *P=.008*) independently predicted unsuppressed HIV viral load among children below five years of age.

Conclusions: More than 90% of children below the age of five years on ART had suppressed viral load. Short time on ARVs, moderate and severe malnutrition, poor ARV adherence and economic constrain among caregivers were found to predict unsuppressed viral load. These factors should be used to identify children at risk of unsuppressed viral load and provide tailored support.

BACKGROUND

Human Immunodeficiency Virus (HIV)/AIDS is among the leading cause of morbidity and mortality globally and 1.7 million children are living with HIV, of these, two thirds are in Africa and the majority in sub-Saharan Africa.[1] In Sub-Sahara region HIV/AIDS is among the top ten cause of deaths among children below five years of age.[2,3] In the region, Tanzania is among countries with high mortality rate of children below-five years of age with HIV/AIDS being among the top ten diseases which causes death in this particular population.[4, 5]

Treatment of HIV using ART reduces morbidity and mortality however its effectiveness depends on sustained suppression of plasma viral replication.[(6)] Viral load suppression(VLS) is defined as less than 1000 copies of HIV ribonucleotides copies per milliliter after being on antiretroviral (ARVs) medication for at least six months.[(7)]The suppressed viral load is critical in reducing HIV/AIDS associated child morbidity and mortality.[8] Children receiving ART are at increased risk of lower rates of viral suppression and would delay the achievement of this target if not given special consideration.[(9, 10)]In Tanzania, a previous report showed that children below fourteen years of age who were on ARV treatment, 81.6% did not attain viral suppression[11] while 87.5% of adolescents above 15 years attained viral load suppression showing the worse problem in children under 15 years.[(1)]It is important that children achieve viral suppression during lifelong ART use, to mitigate the exceptionally high mortality associated with unsuccessful HIV treatment.[12]

Previous studies in different settings have documented that poor adherence, drug resistance, toxicity of ARVs, young age and caregiver knowledge are some of primary factors of unsuppressed viral load in LMIC.[13-15] Literatures have documented that children below five years have poor viral load suppression compared to other groups due to their low body immunity, variability in children's weight, variability in

antiretroviral pharmacokinetics, pretreatment HIV drug resistance due to prior exposure to drugs as part of prevention of mother-to-child transmission (PMTCT) interventions,[16] and adherence problems due to poor palatability of drugs or dependence on caregivers.[1,11,17] In Tanzania all children who are diagnosed with HIV are prompt initiated ARV treatment,[7] despite early initiation of ARV there is still unsuppressed viral load among this population.

Prolonged unsuppressed viral load without intervention often results into drug resistance, increase in the burden of HIV/AIDS related illness leading to poor growth and development and increase in mortality.[19, 20] In this age group, morbidity and mortality can be reduced by early detection of children with unsuppressed viral load and prompt interventions.[21] The purpose of this study was to determine the prevalence and factors associated with unsuppressed viral load among children below five years of age living with HIV in Mwanza, Tanzania.

MATERIALS AND METHODS

Study Design, Duration and Study area

This was a cross sectional study conducted from December 2020 to April 2021 in four Care and Treatment Clinics (CTCs) in Mwanza region namely: Baylor pediatric HIV clinic, Sengerema Designated District Hospital, Misungwi District Hospital, and Magu District Hospital. These clinics attend children on monthly bases. Baylor pediatric HIV clinic have a total of 210 children, Magu District Hospital CTC 46 children, Sengerema Hospital CTC 44 children, Misungwi District Hospital CTC 40 children. The clinics were chosen purposefully to represent both rural and urban setting of Mwanza Region.

Sample Size Estimation and Sampling Technique

A total of 279 children below the age of five years on ART for at least six months and with documented recent viral load were enrolled. Those below five years of age with missed important information in the files were excluded. A sample size was estimated by the Kish Leslie formula,[22] using previous prevalence of 23% among children with unsuppressed VL in Kenya[23]

$$N = Z^2 \times P\frac{(1-P)}{d^2}$$

Where N = Sample size

Z = Standard normal variate (at 5% type 1 error (P<.05) it is 1.96.

D = Absolute error or precision is set at 5%

P = Prevalence which in this case was 23%

N = 272.13 ~ 272 participants

A minimum sample size for associated factors was calculated from Double Proportional formula. Poor adherence among unsuppressed (53.9%) and suppressed (31.3%) children from a previous study conducted in Dodoma, Tanzania was used to determine sample size of associated factors. Thus,

$$N = (Z_{\alpha/2} + Z_{\beta})^2 \left(\frac{P_1(1-P_1) + P_2(1-P_2)}{(P_1 - P_2)^2}\right)$$

Where,
For ARV adherence

N = number of participants

= Standard normal variate (at 5% type 1 error (P<.05) it is 1.96

= Standard normal variate for power for 80% power it is 0.84

P_1 = Prevalence of poor adherence among unsuppressed children is 53.9%

P_2 = Prevalence of poor adherence among suppressed children is 31.3%

Therefore, the minimum sample size were 279 participants.

The minimum sample size represented 60% of children below the age of five years attending the selected Care and Treatment clinics.

Study Population and Data Collection

Sociodemographic characteristics of caregiver (age of the caregiver, relationship with the child, marital status residency, education information and income, economic and wealth information) were collected using structured questionnaire. While children's clinical information (age, sex, height, weight, duration on ART, regimen of ARVs, tuberculosis infection history, adherence, HIV RNA viral load) were extracted from client file using a checklist.

Nutrition status and growth status were evaluated using WHO standards charts for weight for age, weight for length/height and length/height for age of children below five years of age and interpreted accordingly.[24] Unsuppressed HIV RNA viral load was defined according to WHO and Tanzania HIV/AIDS guidelines as more than 1000 copies/mL of HIV ribonucleotides copies after a child being on ART for at least six months.[7,25]

Data Management and Data Analysis

Data were collected using pretested questionnaire and analyzed by STATA Version 15. All continuous variables were summarized as means with standard deviation and categorical variables were expressed as proportions. Univariate and multivariate logistic regression analysis were done to establish factors associated with unsuppressed viral load. Backwards regression analysis was done whereby all factors with P value of less than 0.2 on univariate analysis were subjected into multivariate analysis. P value of less than <.05 at 95% confidence interval was considered as statistically significant.

Institutional Review Board Statement

The ethical clearance to conduct this study was sought by the joint Catholic University of Health and Allied Sciences and Bugando Medical Center research ethics and review committee and provided with ethical certificate number CREC/454/2020. A written informed consent was

requested from parents/guardians after explaining the importance of the study. Any refusal to participate did not affect the patient to get services from the corresponding CTC. Confidentiality was maintained throughout the study.

RESULTS

Sociodemographic Characteristics of Children and Their Caregivers

A total of 279 children below five years of age living with HIV were enrolled and analyzed in the study (Figure 1) with mean age of 41.3 ± 12.7 months. The mean duration on ART was 27.4 ± 12.3 months and 50% (141) were in HIV WHO stage 1 and 2 (Table 1). Enrolled children were kept in a combination of either Abacavir (ABC) or Zidovudine (AZT) with Lamivudine (3TC) and Lopinavir/Ritonavir (LPV/r).

More than two thirds of caregivers were biological mothers 194 (69.5%) and the mean age of caregivers was 37.1 ± 12.4 years (Table 2).

Prevalence of Unsuppressed Viral Load among Children below Five Years of Age Living with HIV

Overall, 20 (7.2%, 95% CI 4.2-10.2) of enrolled children had unsuppressed viral load (≥1000 copies of HIV RNA copies/ml). Misungwi District Hospital CTC had higher prevalence of 8.3% of children with unsuppressed viral load compared to other CTCs (Figure 2).

FIGURE 1: Flow Chart of Study Participants

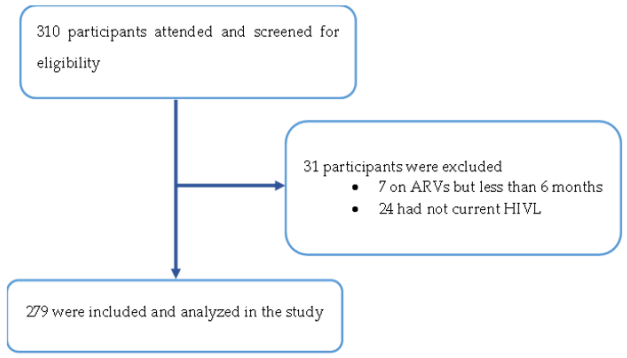


TABLE 1: Socio-demographic and clinical Characteristics of Children Below Five-year of Age Living with HIV (N=279)

Characteristics	Number	Percentage/ mean(s)
Age – Months	279	41.3 ± 12.7
Sex		
Male	135	48.4
Female	144	51.6

Continue

TABLE 1: Continued

Characteristics	Number	Percentage/ mean(s)
Duration on ART- Months (279)	279	27.4 ± 12.3
Child who ever used Isoniazid Preventive Therapy (IPT) (279)		
Yes	256	91.6
No	23	8.4
Children who ever treated Tuberculosis (279)		
Yes	48	17.2
No	231	82.8
WHO stages (279)		
Stage 1 & 2	141	50.5
Stage 3 & 4	138	49.5
Growth stunted (height for age, Z-score) (279)		
Yes	163	58.4
No	116	41.6
Malnutrition (height for length, Z-score) (279)		
Yes	82	29.6
No	195	70.4
Scalp Infection in the past 6 months (279)		
Yes	115	41.4
No	163	58.6
Diarrhea in the past 6 months (279)		
Yes	71	25.8
No	204	78.2

TABLE 2: Social Demographic Characteristics of the Care Giver of Children Below Five Years of Age Living With HIV (N=271)

Characteristics	Number (n)	Percentage
Age of the caregiver (271) ++		
≤35 Years	141	50.5
≥35 Years	138	49.5
Size of the family (271)	1.7	4.6
Relationship with children (279)		
Mother	194	69.5
Guardian	85	30.5
Occupation (271)		
Employed	19	7.1
Not Employed	250	92.9
Education Level (271)		
Not complete primary	83	30.7
Complete primary and above	188	69.3
Residence (279)		
Urban	151	54.1
Rural	128	45.9
Mother of the child alive (271)		
Yes	223	82.3
No	48	17.7

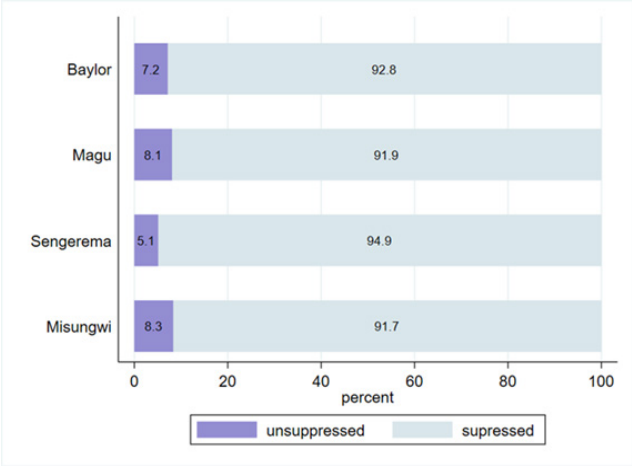
Continue

TABLE 2: Continued

Characteristics	Number (n)	Percentage
Father of the child alive (269)		
Yes	224	83.27
No	45	16.7
Marital status (269)		
Married	154	57.3
Not married	53	19.7
Devoiced	62	23.1
Caregiver possesses phone (271)		
Yes	218	80.4
No	53	19.6

++Some children were from Orphanage centers so had no specific caregiver

FIGURE 2: Prevalence of Unsuppressed Viral Load Among Children Below Five-Years of Age Living with HIV On the Selected CTC



Factors Associated With Unsuppressed Viral Load Among Children Below The Age of Five Year

On univariate logistic regression analysis, duration on ART less than 24 months (OR 5.5, 95% CI: 1.8-16.8, *P*=.003), moderate or severe malnutrition (OR 4.0, 95% CI: 1.6-10.2, *P*=.004) and poor ARV's adherence in past 6 months (OR 6.9; 95% CI: 2.3-20.6, *P*=.001) (Table 4) were significantly associated with unsuppressed HIV viral load. On multivariate logistic regression analysis, short duration of ARV use (≤ 24 months) (AOR 3.8, 95% CI: 1.2-12.0; *P*=.026), and poor ARVs adherence in past six months (AOR 5.7; 95% CI: 1.6-18.6; *P*= .004), severe or moderate malnutrition (AOR 3.3, 95% CI: 1.2-8.9; *P*=.020), remained significant children's factors associated with unsuppressed HIV viral load (Table 3).

Caregiver Factors Associated With Unsuppressed Viral Load Among Children Below the Age of Five Years Living With HIV in Mwanza, Tanzania.

On univariate logistic regression analysis, caregivers with no home care supporter (OR 2.8, 95% CI: 1.0-8.0; *P*=.052) and caregivers who attended CTC by feet (OR 3.0, 95% CI: 0.8-9.7; *P*=.074) had borderline significant association with unsuppressed viral load. On multivariate logistic regression analysis, caregivers with no home supporter (AOR 4.4, 95% CI: 1.5-13.3; *P*=.008) and caregivers who attended CTC by feet (AOR 4.0, 95% CI: 1.1 – 15.2; *P*=.037) were significantly associated with unsuppressed viral load (Table 4).

TABLE 3: Children's Factors Associated with Unsuppressed Viral Load Among Children Below Five-Year of Age Living With HIV

Characteristics	HIV Viral load Suppressed N (%)	HIV Viral load Unsuppressed N (%)	OR (95% CI,)	P-value	AOR (95% CI)	P-value
Age						
≥24 Months	31(93.9)	2(6.1)				
≤24 Months	228(92.7)	18(7.3)	1.2(0.3-5.5)	.793	-	
Duration on ART						
≥24 Months	149(97.4)	4(2.6)				
≤24 Months	109(87.2)	16(12.8)	5.5(1.8-16.8)	.003	3.8(1.2-12.0)	.026
Diarrhea in past six 6 months						
Yes	61(89.7)	7(10.3)				
No	194(93.7)	13(6.3)	0.6(0.2-1.5)	.273	-	

Continue

TABLE 3: Continued

Characteristics	HIV Viral load Suppressed N (%)	HIV Viral load Unsuppressed N (%)	OR (95% CI,)	P-value	AOR (95% CI)	P-value
AIDS's WHO stages						
Stage 1	95(96.0)	4(4.0)				
Stage 2	32(82.1)	7(17.9)	5.2(1.4-18.9)	.012	-	
Stage 3	50(94.3)	3(5.7)	1.4(0.3-6.6)	.651	-	
Stage 4	82(93.2)	6(6.8)	1.7(0.5- 6.4)	.404	-	
Any poor ARVs adherence in past 6 months						
Yes	242(94.5)	14(5.5)				
No	15(71.4)	6(28.6)	6.9(2.3-20.6)	.001	5.7(1.6-18.6)	.004
Child ever treated TB						
Yes	47(97.9)	1(2.1)				
No	212(91.8)	19(8.2)	4.2(0.6-32.2)	.166	2.5(0.3-19.9)	.394
Malnutrition (Weight for Age, Z-score)						
No	187(95.9)	8(4.1)				
Yes	70(85.4)	12(14.6)	4.0(1.6-10.2)	.004	3.3(1.2-8.9)	.020

TABLE 4: Caregiver's Factors Associated with Unsuppressed Viral Load Among Children Below Five Years of Age Living With HIV

Characteristics	HIV Viral load Suppressed N (%)	HIV Viral load Unsuppressed N (%)	OR (95% CI,)	P-value	AOR (95% CI)	P-value
Age						
≤35 Years	127(90.1)	14(9.9)				
≥35 Years	132(95.6)	6(4.4)	0.4(0.2-1.1)	.079	0.5(0.2-1.5)	.228
Caregiver Relationship						
Mother	177(91.2)	17(8.8)				
Non-Mother	82(96.5)	3(3.5)	0.4(0.1-1.3)	.132	0.4(0.1-1.7)	.223
Home caregiver supporter						
Present	122(96.1)	5(3.9)				
Absent	130(89.7)	15(10.3)	2.8(1.0-8.0)	.052	4.4(1.5-13.3)	.008
Measure of transport to attend CTC						
Non-feet	225(93.4)	16(6.6)				
Feet	19(82.6)	4(17.4)	3.0(0.8-9.7)	.074	4.0(1.1-5.2)	.037
Possession of Radio at home						
Yes	114(95.0)	6(5.0)				
No	136(90.7)	14(9.3)	2.0(0.7-5.2)	.183	2.1(0.8-6.0)	.148

DISCUSSION

Achievement of sustained virological suppression in children living with HIV is vital in ensuring long-term survival and reducing HIV-related morbidity and mortality. In the current study we report a low prevalence of virological treatment failure, seven out of 100 children below the five years in the selected health facilities on ARTs were not HIV virally suppressed. Compared to previous studies in the rural and urban areas of Tanzania[6, 26-28] and elsewhere,[29] the current prevalence of unsuppressed viral load is significantly low. The low prevalence in the current study can be due to number of factors including increased number of trained CTC health workers, retaining social workers in the hospital settings, enhanced adherence and counseling (AEC), availability of various modes of retaining clients on ART, availability of ARTs with high efficacy and early ART initiation in children regardless of immunological and clinical stages.[30-32] Several factors have been documented in literatures that contribute to different rates of unsuppressed viral load including, HIV prevalence in a region, definition of virological treatment failure, and socioeconomic factors related to HIV/AIDS care access and adherence.[6,33,34] No significant differences in virological failure were observed among selected health facilities, signifying that there is uniformly acceptable

care of HIV infected children in health facilities, making Tanzania being in a right direction of meeting the UNSAIDS goals of ending up HIV epidemic by 2030.

As documented in previous studies,[35-38] the current study found that children with less than two years on ART duration have more than 3.5 odds to have unsuppressed viral load compared to those with more than two years duration on ART. Unsuppressed viral load observed in children, below 2 years duration on ART are contributed to a combination factors including: adherence difficulties, drug dosing and viral resistance.[16,18,35]

Poor adherence was found to be associated with unsuppressed viral load in this study, this is in line with the previous study in Dodoma, Tanzania whereby poor adherence was associated with unsuppressed viral load among children below 14 years of age.[36] Several other studies in Africa have reported similar findings.[17,37,38] Poor adherence is the most common cause of treatment failure leading to increased risk of clinical progression of AIDS.[39,40]

As reported elsewhere in Africa,[45-48] the current study observed that low weight for age, less than -2 z-square was significantly associated with unsuppressed HIV viral load among children below 5 years of age. These studies further reported, children with undernutrition had significantly higher mortality than children with normal weight. Similar findings were reported in a systematic review and meta-analysis of 17 studies on 4891 children with severe acute malnutrition in sub-Saharan Africa, revealed that children with HIV infection were three times likely to die than those with severe acute malnutrition and not infected with HIV.[41] Malnutrition increases susceptibility to infection by causing immune dysfunction in many fold ways. The depressed immune status due to undernutrition can amplify HIV replication and accelerate progression of HIV disease to AIDS.[42] On the other hand, infections and low-grade chronic inflammation caused by HIV infection suppress appetite, increase catabolism of muscles and push patients towards malnutrition.[43] Therefore, HIV/AIDS and malnutrition form a deadly duo with each one fueling the other, this needs a prompt intervention to prevent rapid HIV progression and mortality.

The study observed that the chance of a child to have unsuppressed viral load was four times higher if the main caregiver had no supporter at home. Absence of home supporter creates an economic gap and resulting to economic constrains such as failure to attend CTC, lack of balanced diet to the child.[44-46]

Balance diet has been found to be an important factor in successful management of AIDS patient[47] and for optimisation of health outcomes and prevention of future chronic complications.[48] Attending at CTC by feet was significantly associated with unsuppressed viral load, this may reflect the economic constrains to the caregiver. These findings are in line with a previous study conducted in South Africa which reported that lack of money for transport affected attendance to CTC as well as HIV care and treatment of the children[49] Caregiver socioeconomic constrains impact adherence and overall child's growth and development. Therefore, further qualitative studies are recommended on caregiver social economic constrain and their impact of child HIV management and for possible sustainable intervention that we achieve the ambitious 95-95-95 strategy aiming to end the AIDS epidemic by 2030.

Limitations

Due to the fact that some questions involved events occurred in the past 6 months, there is a potential of recall bias which is intentional or unintentional that would affect the validity of responses in relation to clinical outcome. This could have contributed to lack of association of these factors with outcome.

CONCLUSIONS

The prevalence of unsuppressed viral load among children below five years of age in Mwanza was low and in line with UNAIDS's 90-90-90 global targets that set to be met at 2020 and it's a good beginning to attain ambitious strategy 95-95-95 by 2030. Majority of unsuppressed viral load were due to short time on ARVs, moderate or severe malnutrition, poor ARV adherence and an economic constrain factors among caregivers. Therefore, we recommend larger studies on social economic constrains and their impact of child's HIV management for possible sustainable interventions that so that we achieve the ambitious 95-95-95 strategy that is aiming to end the AIDS epidemic by 2030. In addition, there is a need of routine HIV resistance testing that will be used to guide appropriate treatment.

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