

Factors associated with adherence to antiretroviral therapy among HIV-infected children in Pokhara, Nepal: a cross-sectional study

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Abstract

Introduction: Children below the age of 15 years account for the majority of acquired immunodeficiency syndrome (AIDS)-related deaths in Nepal. Antiretroviral therapy (ART) improves health and prolongs lives of people with human immunodeficiency virus (HIV). Poor adherence to ART provides clue to a sub-therapeutic level of antiretroviral drug, which can facilitate multi-drug resistance of similar regimen, leading to treatment failure and death. The objective of this study was to determine the level of adherence to ART and its associated factors among HIV-infected children aged 0-14 years in Pokhara Academy of Health Sciences (PoAHS), Pokhara, Nepal.

Material and methods: This cross-sectional study was conducted between September 15th, 2020 and February 15th, 2021, and included 57 HIV-infected children. Caregivers of the children were questioned with a pre-tested, semi-structured questionnaire, which was later translated verbally to Nepali. Trained doctors took the interviews. Acquired data was entered using SPSS version 17 software for analysis. Level of significance was set at $p < 0.05$.

Results: Caregiver's forgetfulness was the main reason for missing ART doses (60%; 6/10). Other reasons were side effects of drug-related fear (30%; 3/10), followed by transportation problems (10%; 1/10). Older children (range, 11-14 years) adhered more to ART than younger ones (aged 0-5 and 6-10 years), with COR = 4.80 and 1.16, and 95% CI: 0.81-28.15% and 0.19-6.88%, respectively. Caregivers who knew their HIV status had their children more adherent to ART than those with unknown HIV status (COR = 27.94, 95% CI: 1.23-634.62%). A significant proportion of children in ART unit of PoAHS (17.54%; 10/57) missed ART doses within the previous week.

Conclusions: The level of non-adherence to antiretroviral therapy in children was found to be 17.54%. Caregiver's forgetfulness, side effects of drug-related fear, and transportation problems were the most common causes of non-adherence. Encouraging caregivers to know their HIV status, providing medicines via nearby ART clinics with coordination of community-based support, and using clues as a reminder to provide the child with drugs at the same time of the day, increase ART adherence in pediatric HIV-positive patients.

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Key words: ART, adherence, children, HIV, Nepal.

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Introduction

According to the World Health Organization (WHO), 34 million people are living with HIV in the world, out of which 3.3 million are children below the age of 15 years [1]. Among them 31,020 people are currently living with HIV in Nepal [2]. Antiretroviral therapy (ART) improves health and prolongs lives of HIV-positive individuals, and is provided free of cost by the government of Nepal [3]. Children below 15 years of age account for 7.5% of those who receive ART in Nepal, and among all AIDS-related deaths, children comprise of 2.52% [2]. ART reduces plasma HIV RNA levels and boosts immunity by increasing CD4 counts, thus decreasing the incidence of opportunistic infections and improve the growth and development of children [4]. Better adherence is accompanied by better socio-economic status and well-accepted regimens. Poor adherence to ART among children leads to a sub-therapeutic level of antiretroviral drugs, which further facilitate multi-drug resistance or cross-resistance in the same regimen, leading to treatment failure and death [5, 6]. By maintaining the optional adherence to ART, treatment success can be achieved [7, 8].

Reluctance to medicate their children in front of others may be a substantial interpersonal fence to adherence, and the age of caregivers and their forgetfulness need different strategies as reminders to administer medications on time by maintaining written records of medications administered and carrying extra medications when traveling [9]. Children on old regimens, i.e., zidovudine-based regimens, may experience ART-related adverse effects, such as anemia, leading to sub-optimal adherence [10]. Health system-related factors, including running out of medications, inconvenient visiting clinic hours, difficulty paying for transportation to the clinic, and finding it physically tiring to reach the clinic, are the potential restraints to adherence [11]. Previously, no adequate research was performed to investigate the cause behind high mortality among children on antiretroviral therapy in Nepal. Therefore, the current study was done to assess the level of adherence and its associated factors among HIV-infected children aged 10-14 years receiving ART in Pokhara Academy of Health Sciences (PoAHS), Pokhara, Nepal. This study can encourage the provincial government in policy-making to combat the burden of HIV in children by improving ART adherence among HIV-infected children in Nepal.

Material and methods

A cross-sectional study was performed from September 15th, 2020 to February 15th, 2021 in PoAHS hospital. All patients were diagnosed with HIV at PoAHS during this period, and were included in this study. This study was conducted in line with the principles of the Declaration of Helsinki. Ethical clearance was obtained from Institutional Review Board (IRB) of Pokhara Academy of Health Sciences (approval No: 12.077/088). Written informed consent was taken from caregivers, and verbal consent was obtained from children. Consent for publication was not applicable.

Availability of data and materials

Datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request. Ethical clearance was obtained before data collection from IRB, PoAHS, Pokhara. This study adhered to STROBE guidelines, and sample size was determined by using the following formula for estimating sample sizes in prevalence studies.

Sample size (n) = $z^2 p (1 - p) / d^2 = 1.96^2 \times 0.03842 \times (1 - 0.03842) / 0.05^2 = 3.8416 \times 0.03842 \times 0.96158 / 0.0025 = 0.14192 / 0.0025 = 56.7$, where $z = 1.96$ (standard), $p = 0.03842$ prevalence of pediatric HIV patients below 15 years old [12], and $d =$ tolerated margin error within 5%.

Caregivers were interviewed using a pre-tested, semi-structured questionnaire translated verbally into the predominant local language, Nepali. Interviews were conducted by trained doctors. This study assessed several factors that were suspected to influence ART adherence. The factors pertaining to the caregiver included caregiver's relationship with the child, stress and depression, age, sex, occupation, highest level of education attained, and duration as the child's caregiver. Drug regimen of each child was documented along with other factors, such as ART side effects, drug dosing, and tolerability. Moreover, caregiver's forgetfulness to remind their HIV-infected child on ART to take their medication on time was assessed, as it has been found to affect child's adherence. Measurement of adherence was based on the number of missed ART doses in the last 7 days prior to the interview. Three days recall was also applied to assess adherence, which was characterized as optimal adherence versus poor adherence. Children, whose caregivers reported no missed doses were considered to have optimal adherence to ART, while those reported missing one or more doses were considered with poor adherence. The percentage of children with good adherence was calculated by dividing the number of caregivers, who reported that their children did not miss any dose within the last 7 days. After completion of the study, data were entered into Microsoft Excel Sheet version 2007 and analyzed with Statistical Package for Social Sciences (SPSS version 11.5). Descriptive statistics including mean, median, percentage, standard deviations, and interquartile range were computed. Odds ratio was calculated using MedCalc odds ratio calculator, and the level of significance was set at $p < 0.05$.

Ethics' approval and consent to participate

This study was performed in line with the principles of the Declaration of Helsinki. Ethical clearance was obtained from Institutional Review Board (IRB) of Pokhara Academy of Health Sciences (approval No.: 12.077/078). Written informed consent was taken from the caregivers and verbal assent was obtained from the children.

Results

All the 57 caregivers agreed to participate in the study and were interviewed in PoAHS, Pokhara. Most of the care-

Table 1. Socio-demographic characteristics of caregivers and children on antiretroviral therapy, Pokhara Academy of Health Sciences, Pokhara

Characteristic	Frequency (n = 57)	Percentage (%)
Age of child (years)		
0-5	7	12.28
6-10	13	22.80
11-14	37	64.91
Sex of child		
Female	31	54.38
Male	26	45.61
Age of caregiver		
< 31	4	7.01
31-40	11	19.29
> 40	42	73.68
Sex of caregiver		
Female	15	26.31
Male	42	73.68
Level of education of caregiver		
None	2	3.50
Primary (1-8 class)	18	31.57
Secondary (9-12 class)	32	56.14
Tertiary (post-secondary education)	5	8.77
Occupation of caregiver		
Agriculture	48	84.21
Small local business	5	8.77
Civil servant	1	1.75
Other ^a	3	5.26
Caregiver's relationship with child		
Biological parent	39	68.42
Other relative	14	24.56
Not related	4	7.01

^aOther (students, housewives)

Table 2. Reasons for missing antiretroviral therapy (ART) doses and side effects of ART among HIV-infected children on ART, Pokhara Academy of Health Sciences, Pokhara

Reasons for missing dose	Frequency (n = 10)	Percentage (%)
Caregiver's forgetfulness	6	60.0
Transportation problems	1	10.0
Side effects of drug	3	30.0
Drug run out	0	0.0

givers were older than 40 years (73.68%; 42/57) and were males (73.68%; 42/57). Among them, 31.57% (18/57) had a primary level of education. Most of the caregivers (84.21%; 48/57) were involved in farming. Moreover, 68.42% (39) children had their biological parents as caregivers (Table 1).

Level of adherence to ART

Overall, 82.45% (47/57) of the children did not miss any ART doses over the past 7 days. Ten children (17.54%) missed at least one dose within a period of 7 days. The commonest reason was forgetfulness of the caregivers (60%). Only one (10%) had a transportation problem getting medicine from the hospital. Three (30%) caregivers reported various side effects of ART, including vomiting, dizziness, stomach pain, rashes, headache, and fever as the cause of missed dose (Table 2). Drugs' delivery was properly managed by the concerned authority; therefore, nobody was out of ART during the study. Female caregiver, a caregiver with no formal education, a caregiver who did not know HIV status of children, and children with side effects experienced during ART were significantly associated with non-adherence (Table 3).

Discussion

Factors associated with adherence to antiretroviral therapy

Along with the age of the child, duration of ART, knowledge about HIV status, age of caregivers, and their level of education and relationship with the child were found to have significant associations with adherence.

Older children (range, 11-14 years) showed more adherence to ART than the younger ones (0-5 and 6-10 years). A study done in northern Ethiopia reported a similar result among older children (range, 11-14 years) showing good adherence due to better awareness and knowledge of negative effects of poor ART adherence, especially when their HIV status had been disclosed to them [12]. Therefore, service providers should pay more attention to younger children and offer support to their caregivers to bridge these gaps. The children of caregivers, who knew their HIV status had more adherence to ART than the children of caregivers who did not know their HIV status. This implies that all caregivers of HIV-infected children should be advised to know their HIV status, which promotes adherence to ART.

During the interviews, 12 out of 47 adherent children (25.5%) looked unhealthy due to their late visits to health facility, which represents the actual burden of HIV in the community. Male caregivers were providing more assistance in our study. However, in a research done in Uganda, female caregivers were more involved [13].

The level of education of a caregiver also played a key role in adherence to drugs. The more the educated caregiver, the higher the adherence level [14]. The children of caregivers with a tertiary level of education presented 100% adherence level.

Table 3. Factors associated with non-adherence to antiretroviral therapy among HIV-infected children on antiretroviral therapy, Pokhara Academy of Health Sciences, Pokhara (*n* = 57)

Variable	Adherence				p-value
	Yes (<i>n</i> = 47)	No (<i>n</i> = 10)	OR	95% CI	
Age of child (years)					
0-5	4	3	4.80	0.81-28.15	0.08
6-10	11	2	1.16	0.19-6.88	0.86
11-14 years	32	5	Ref.	–	–
Sex of child					
Female	23	8	4.17	0.80-21.77	0.09
Male	24	2	Ref.	–	–
Duration on ART					
0-4 years	29	3	Ref.	–	–
5 years and above	18	7	3.75	0.86-16.42	0.07
Child's health appearance					
Looking healthy during interview	35	8	Ref.	–	–
Looking unhealthy during interview	12	2	0.72	0.13-3.92	0.71
Sex of caregiver					
Female	9	6	Ref.	–	–
Male	38	4	0.15	0.03-0.67	0.01*
Age of caregiver					
< 31 years	2	2	Ref.	–	–
31-40 years	8	3	0.37	0.03-3.99	0.4167
> 40 years	37	5	0.13	0.01-1.18	0.07
Level of education of caregiver					
None	0	6	Ref.	–	–
Primary (1-8 class)	10	2	0.01	0.0008-0.44	0.01*
Secondary (9-12 class)	30	2	0.006	0.0003-0.14	0.001*
Tertiary (post-secondary)	7	0	0.005	0.0001-0.29	0.01*
Occupation of caregiver					
Agriculture	37	9	0.76	0.02-20.17	0.86
Small local business	6	0	0.23	0.003-17.06	0.50
Civil servant	1	0	Ref.	–	–
Others	3	1	1.28	0.03-53.51	0.89
Caregiver relationship with child					
Biological parent	39	7	Ref.	–	–
Other relative	4	3	4.17	0.76-22.86	0.09
Not related	4	0	0.58	0.02-12.04	0.72
Caregiver knowledge of HIV status					
Known HIV status	47	8	Ref.	–	–
Not known HIV status	0	2	27.94	1.23-634.62	0.03*
Drug tolerability					
Child does not find swallowing the drug a problem	45	8	Ref.	–	–
Child finds swallowing the drug a problem	2	2	5.62	0.68-45.90	0.10

Table 3. Cont.

Variable	Adherence				p-value
	Yes (n = 47)	No (n = 10)	OR	95% CI	
Drug dosage complexity					
Child find dose easy to take	26	3	Ref.	–	–
Child find dose not easy to take	21	7	2.88	0.66-12.56	0.15
Side effects of ART					
Child has never experienced drug side effects	44	7	Ref.	–	–
Child has experienced a side effect due to ART	3	3	6.28	1.05-37.57	0.04*

OR – odds ratio, CI – confidence interval, * – statistically significant

In the current research, caregiver's forgetfulness was the major (60%) reason for missing child's ART doses, which can be improved by proper counselling on giving the medicines regularly at the same convenient time of the day, or by using clues to remind about the application of the child's drugs [15]. Other causes for non-adherence included the fear of side effects (30%) and transportation problems to ART center (10%). Transportation constraint was also a limiting factor to reach ART center. Similar findings were found in a study from Zambia and Nepal [16, 17]. Nepal's unique geographical and altitudinal variation combined with a limited number of ART sites were considered to have a negative effect on adherence in that study, which is in line with the current research.

Drug run out was not considered a problem in our study. Community-based support for stable patients was shown to relieve drug run out, and also improved efficiency of service delivery [18, 19].

Limitations of the study

In the present study, the major limitation was the small sample size that gave rise to very wide confidence intervals. The caregivers due to emotional reasons were unlikely to report all missed doses, so there could be an overestimation of adherence.

Conclusions

In the study, poor adherence to ART was found to be 17.54%. The main reasons for missed doses were caregiver's forgetfulness and transportation issues. Education level of the caregivers, knowledge/ information on their HIV status, and the perceived side effects of ART drugs were associated with adherence to ART. It is recommended to find out HIV status of caregivers and address physical access to ART facilities to improve the adherence to ART. There is a need to integrate efforts to encourage caregivers to know their HIV status along with community-based support for stable patients facing transportation and distance challenges to improve efficiency of service delivery. Also, policy-makers should develop suitable strategy in social policies to promote adherence among ART recommended patients.

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Conflict of interests

The authors declare no conflict of interest.

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