Biomedical Statistics and Informatics
2021; 6(4): 76-83
http://www.sciencepublishinggroup.com/j/bsi
doi: 10.11648/j.bsi.20210604.12
ISSN: 2578-871X (Print); ISSN: 2578-8728 (Online)

Factors Affecting Anti-retroviral Therapy Adherence Among HIV Positive Children Attending Wollega University Referral Hospital, ART, Nekemte, West Ethiopia, 2019

Edosa Amente Gutema[1], Gemechu Kejela[2], Zelalem Keba Babure[3]

[1]Ethiopian Public Health Institute, Addis Ababa. Ethiopia

[2]Institute of Public Health, Wollega University, Nekemte, Ethiopia

[3]East Wollega Zonal Health Department, Nekemte, Ethiopia

Email address:
idoamante07@gmail.com (E. A. Gutema), gemechukejela86@gmail.com (G. Kejela)

To cite this article:
Edosa Amente Gutema, Gemechu Kejela, Zelalem Keba Babure. Factors Affecting Anti-retroviral Therapy Adherence Among HIV Positive Children Attending Wollega University Referral Hospital, ART, Nekemte, West Ethiopia, 2019. *Biomedical Statistics and Informatics*. Vol. 6, No. 4, 2021, pp. 76-83. doi: 10.11648/j.bsi.20210604.12

Received: November 8, 2021; **Accepted**: December 15, 2021; **Published**: December 24, 2021

Abstract: Since the introduction of Antiretroviral Treatments, morbidity and mortality due to HIV/AIDS have been significantly reduced. Through successful prevention of mother-to-child transmission programs, developed countries face few new cases of infant HIV infection annually; however, as a result of successful ART use, children are surviving into adolescence and struggling with many adherence challenges associated with long-term therapy. This study aims to assess factors affecting child antiretroviral treatment adherence at WollegaUniversity Medical Center anti-retroviral therapy clinic. To assess factors that affect child ART adherence among HIV positive children attending Wollega University Referral hospital ART clinic, Nekemte, West Ethiopia, 2019. Cross sectional study design was conducted from March to May/2019 among HIV positive children on ART who have follow-up at Wollega University medical anti-retroviral therapy clinic. Data was collected by interviewing of the care givers of the child using a structured questionnaire. The collected data wascleaned, coded, and analyzed by manual and calculator, and the results found wascompared with findings in the area and aboard, then appropriate conclusions and recommendations wasgiven. Among the 80 study participants, 30 (37.5%) took medications other than ARD. Out of this, 20 (25%) of them took one other tablet per day and the rest were taking two to four other tablets per day. The study showed that the majority (96.3%) of the children had a near perfect (>95%) adherence rate. There were limited researches done in the study area on adherence rate and no research was found describing the national adherence rate.

Keywords: Adherence, ART, Wollega University Referral Hospital

1. Introduction

The United Nations Joint Program on AIDS (UNAIDS) estimates that over 2 million children under the age of 15 years are living with HIV/AIDS in the world, with nearly 80% of these children living in sub-Saharan Africa [1]. High levels of antiretroviral therapy (ART) adherence are critical for viral suppression and reduced morbidity and mortality among HIV-infected children [2, 3].

Through successful prevention of mother-to-child transmission programs, developed countries face few new cases of infant HIV infection annually; however, as a result of successful ART use, children are surviving into adolescence and struggling with many adherence challenges associated with long-term therapy [4]. Developing countries are confronting different challenges for achieving and maintaining ART adherence as they scale up pediatric ART programs [5].

Health care resources are typically constrained, and the burden of co-morbid disease is high. In a recent systematic review of pediatric ART adherence studies in middle- and low-income countries, Vreeman et al. [6] found that estimates of ART adherence levels ranged from 49% to 100%, with 76% of articles reporting greater than 75% adherence. The authors contrasted these values with reports from high-income countries, as summarized in another recent systematic review

by Simoni et al. [7].

Estimates of pediatric adherence levels in high-income countries ranged even more widely, from 20% to 100%, and 33 of 55 studies reported ART adherence less than 75%. The initial high levels of adherence in developing countries are encouraging; however, adherence failures may become increasingly common as healthier children gain access and confront the long-term challenges of adherence to ART. Even with early success, resistance levels among some children are unacceptably high [8].

The United Nations Joint Program on AIDS (UNAIDS) estimates that over 2million children under the age of 15 years are living with HIV/AIDS in the world, with nearly 80% of these children living in sub-Saharan Africa [1]. Developing countries are confronting different challenges for achieving and maintaining ART adherence as they scale up pediatric ART programs. Health care resources are typically constrained, and the burden of co morbid disease is high [6].

In countries with an HIV prevalence of above 5%, child mortality rates have not fallen in line with global trends. This is most probably due to the high risk of mortality associated with untreated HIV infection in young children [11].

If there is poor adherence, then there is a higher risk that drug resistance will develop, which will result in the need for second line drug treatment. This can be more difficult to administer, and the cost implications are considerable. If people living with HIV require second-line treatment, it can be ten times more expensive than first-line drugs. The long-term implications for the sustainability of ART in resource poor countries are considerable, as WHO states, ”Drug resistance may result in the failure of immense global and national efforts to provide hope to peopleliving with HIV”[12].

A key challenge in HIV clinical management is facilitating ART adherence. According to research studies, a 95 percent adherence rate is associated with controlling HIV replication, which allows an optimal therapeutic response to medications. Suboptimal adherence to ART regimens results in:

1) Incomplete suppression of HIV replication
2) Emergence of resistance to ARVs

ARV resistance may increase the potential for regimen failure, compromise future treatment options, and lead to an increased risk of mortality. Children with ART and their caregivers face particular challenges:

1) Disclosing the HIV infection when the child is able to understand and using language and concepts appropriate to the child’s age and developmental stage.
2) The need to take a liquid drug formulation if an infant or child is unable to swallow a pill.
3) Infants or children may resist taking drugs, whether in liquid or pill form, because of the bad taste or frustration in having to take medicine several times a day, day after day [13].

Ninety percent of the 2.3 million HIV-infected children in the world live in sub-Saharan Africa. Understanding children's adherence in resource-limited countries presents a critical challenge, because they have limited options if viral resistance develops [14].

WHO recognizes the need to strengthen health systems with a view to maximizing the quality and long-term benefits of ART. Improved access to HIV diagnostic testing for infants and children is necessary to save lives. The inability to diagnose HIV infection as early as possible in infants and children severely limits access to ART and its timely initiation. Reliable access to immunological assays for assessing CD4 levels in children is crucial for guiding the initiation of treatment and for optimizing the maintenance of ART [15].

Despite an increase in children accessing treatment, the overall coverage for children remains extremely low. Kenyan children living with HIV who need treatment do not have access to it. A child’s access to treatment can sometimes be inhibited by reasons other than the reach of treatment services. According to Human Rights Watch, the reasons for this include: neglect on the part of the child’s caregivers; a lack of accurate information about medical care for children; and the stigma and guilt associated with HIV and AIDS [16].

The sharp increase in ART uptake in 2006 is largely due to the rapid increase in the provision of free treatment at more sites. The marked variation in ART utilization patterns between urban and rural communities and between zones and regions requires further studies [17].

Adherence to HAART in children in Addis Ababa/2008was higher than other similar set-ups. However, there are still significant numbers of children who are non-adherent to HAART [18].

Many factors have been cited as reasons for non-adherence in studies of Western countries. In African settings, patients have achieved excellent rates of adherence with subsidized ART. Reasons reported for non-adherence in African studies include forgetting, travel, fear of disclosure, shortage of pills, difficult schedules, cost, lack of access and privacy. In two studies in Addis Ababa, being too busy/forgetting, travels, depression, drug adverse effects, treatment fitting to daily routine, relationship with health care providers, patients’ perceptions of their doctors’ capacities, perceived access to support from their ART unit, and reliable pharmacies, keeping clinical appointments, using memory aids, and educational levels were associated with ART adherence [19].

Since the introduction of ART, there is a substantial reduction in the mortality and morbidity of PLWHA. Such achievements always needs near total adherence to ART. And adherence is one of the few potentially alterable factors in determining outcomes for in PLWHA.

In Ethiopia, many researches which determine factors affecting child ART drug adherence are not done. This study will therefore, help to determine the adherence status of patients on ART and the factors related to decreased adherence. It will thus help improve the care of patients living with HIV and lay ground for further studies to be performed in the area.

To assess factors affecting child ART adherence among HIV positive children on ART in WURH, ART clinic, Nekemte, Oromia, West Ethiopia, 2019.

2. Methods and Materials

2.1. Study Area and Period

The study was conducted in Wollega University Referral Hospital (WURH), ART clinic from March- May/2019.

2.2. Study Design

A cross-sectional study design was used and child care givers were interviewed by using a structured questionnaire to assess social demographic characteristics, number of doses missed, and reasons for missing, and the other relationship between ART drug adherence and associated factors.

2.3. Sample

2.3.1. Source Population

All children with HIV/AIDS who attended WURH ART clinic for ARVD refill during the study period.

2.3.2. Study Population

All children with HIV/AIDS who attended WURH ART clinic for ARVD refill during the study period.

2.3.3. Sample Size

By assuming that 31.5% of the proportion of Utilization of antiretroviral treatment in Ethiopia [6].

P=22.8%=0.228 [9].

q=1-p=0.772

z=1.96 for 95% confidence interval

d=0.05 (5% margin of error)

$$n = \frac{(Z\frac{\alpha}{2})^2 p(1-p)}{d^2}$$

$$= \frac{(1.96)^2.0.228\,(1-0.228)}{(0.05)^2}$$

$$= \frac{0.65}{0.0025} = 276$$

With 5% nonresponse rate, the final sample size of this research is about 290 children attending ART clinic at WURH

2.3.4. Sampling Technique

Caregivers of all children with HIV/AIDS and on ART who come for follow-up and refill during the two weeks study period was interviewed

2.4. Study Variables

2.4.1. Independent Variables

1. Age of the child
2. Marital status of caregiver
3. Occupational statusof caregiver
4. Educational status of caregiver
5. Monthly income of the care givers
6. Religion of the care giver
7. Residency of care giver
8. HIV status of caregiver

2.4.2. Dependent Variables

1) Missed pills
2) Level of adherence

2.5. Data Collection

2.5.1. Data Collection Instruments

Structured questionnaire which contains information about socio-demographic characteristics, ART, and child ART adherence.

2.5.2. Data Collectors

Data was collected by ART providers who assigned to ART clinic.

2.5.3. Data Collection Method

Data was collected by interviewing child care givers.

2.6. Data Processing and Analysis

Data was cleaned, checked, and analyzed manually and by a calculator. Results were expressed in tables and graphs after analysis.

2.7. Ethical Considerations

1) Verbal consent was obtained from every respondent.
2) Name of the care givers will not be included to preserve the privacy of the respondents.

2.8. Data Quality Assurance

Questionnaires werechecked for completeness and consistence.

2.9. Operational Definitions

Measurement of adherence index was calculated

$$\text{Adherence Index} = \frac{Total\ number\ of\ drugs\ taken}{\text{Total number of drugs prescribed}} \times 100$$

Children with more than 95% of adherence wasconsidered as having high adherence and those with less than 95% were considered as having low adherence.

Adherence is defined as caregivers and child's ability to follow a treatment plan, take medications at prescribed times and frequencies, and follow restrictions regarding food and other medications.

Infants < 1 year age, toddlers 1-2 year's age group, preschool 2-5 years age group, school age group 6-12 years, and adolescent 13-18 years.

3. Result

A total of 80 HIV positive children on ART in WURH ART clinic who were coming for follow-up during the study period was included in the study with 1.1:1 boy to girl ratio. The age of the children ranged from 6 weeks to14 years. Most of them were below 9 years and came from urban areas. Among the care givers, most were married and had attended 1-8th grade. (Table 1)

Among the 80 study participants, 30 (37.5%) took medications other than ARD. Out of this, 20 (25%) of them took one other tablet per day and the rest were taking two to four other tablets per day.

Table 1. *Socio-demographic characteristics of care givers and children on ART at WURH ART clinic, 2019.*

Socio demographic characteristics		Number	Percent
Age	<3	19	23.8
	3-5	32	40
	6-8	18	22.5
	>=9	11	13.8
Sex	Boy	42	52.5
	Girl	38	47.5
Address of care givers	Rural	11	13.8
	Urban	69	86.3
Religion of care givers	Muslim	50	62.5
	Orthodox	14	17.5
	Protestant	14	17.5
	Catholic	2	2.5
Marital status of care givers	Single	7	8.8
	Married	52	65
	Divorced	16	20
	Widowed	5	6.3
Educational status of care givers	Illiterate	20	25
	Read and write	14	17.5
	1-8 grade	26	32.5
	8-12 grade	12	15
	>12	8	10
Occupation of care givers	Farmer	6	7.5
	Merchant	28	35
	Government employee	8	10
	Daily laborer	18	22.5
	House wife	20	25
Monthly total household income of care givers	<250 birr	8	10
	250-1000 birr	37	46.3
	>1000 birr	35	43.8

Table 2. *Self report adherence rate among children on ART at WURH ART clinic, 2019.*

Level of adherence	Number	Percent
100%	67	83.8
95-99%	10	12.5
81-94%	3	3.8
<80%	0	0%

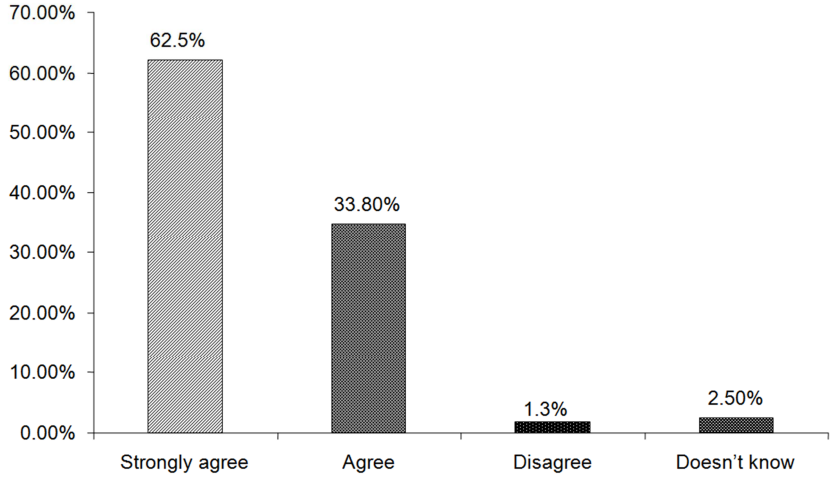

Figure 1. *Attitude towards the importance of ART for PLWH among care givers who attended WURH ART clinic from March- May/2019.*

Among the study groups, 22 (27.5%) had known their HIV status. Most of the care givers were helped by other family members in remembering to give pills to the child [45 (56.3%)] some time and 10 (12.5%) most of the times, the rest 25 (31.3) were remembered and give the pills to the child by themselves].

Table 3. *Reasons for missing doses among HIV positive children on ART in WURH ART clinic, 2019.*

Reasons for missing drugs	Number	Percent
Care giver was busy with other things	8	10
Care giver felt asleep	1	1.3
Ran out of medication	0	0
Became disgusted to give the pills	0	0
Thought that the pills have no use	1	1.3
Care giver was away from home	0	0
Due to adverse effects	0	0
Simply forgot	3	16.3
Others/specify	0	0

Among the 80 study participants, 13 (16.3%) of them had missed at least 1 dose of their ARTDS in the month before the interview and among them most [10 (76.9%)] had missed only one dose (95-99% adherence rate). In most children, the main reason for missing pills was being the care giver was busy with other things.

Most of the children (96.3%) had greater than 95% adherence rate, among which83.8% had a 100% adherence rate.

Table 4. *Following specific drug time schedule among HIV positive children on ART in WURH ART clinic, 2019.*

Following specific drug time schedule	Number	Percent
All of the times	42	52.5
Most of the Times	30	37.5
Some of the times	7	8.8
Never	1	1.3

Majority of the study participants (52.5%) followed the specific drug time schedule in all times.

Table 5. *Variables association with adherence rate among HIV positive children receiving ARV drugs in WURH ART clinic, 2019.*

Variables		Adherence rate					
		100%		95-99%		81-94%	
		No	%	No	%	No	%
Age of child (yrs)	<3	18	94.7	0	0	1	5.2
	3-5	21	65.6	9	28	2	6.2
	6-8	18	100	0	0	0	0
	>9	10	90.9	1	9.0	0	0
Sex of child	Boy	36	85.7	4	9.5	2	4.7
	Girl	31	73.8	6	14.2	1	2.3
Address of care giver	Rural	9	81.8	1	9.0	1	9.0
	Urban	58	84	9	13	2	2.8
Religion of care giver	Muslim	40	80	8	16	2	4
	Orthodox	12	85.7	1	7.1	1	7.1
	Protestant	13	92.8	1	7.1	0	0
	Catholic	2	100	0	0	0	0
Marital status of care giver	Single	5	71.4	1	14.2	1	14.2
	Married	52	100	0	0	0	0
	Divorced	7	43.7	7	43.7	2	12.5
	Widowed	3	60	2	40	0	0
Educational level of care giver	Illiterate	12	60	5	25	3	15
	Read and write	13	92.8	1	7.1	0	0
	1-8 grade	24	92.3	2	7.6	0	0
	8-12 grade	12	100	0	0	0	0
	>12 grade	6	75	2	25	0	0
Occupation of care giver	Farmer	3	50	2	33.3	1	16.6
	Merchant	28	100	0	0	0	0
	Government employee	8	100	0	0	0	0
	Daily labourer	8	44.4	8	44.4	2	11.1
	House wife	20	100	0	0	0	0
Duration on ART	250-1000 birr	32	86.4	2	5.4	3	8.1
	>1000 birr	28	80	7	20	0	0
	<=1 year	16	61.5	8	30.7	2	7.6
	2-4 years	25	89.2	2	7.1	1	3.5
	>=5 years	26	100	0	0	0	0
Other medications other than ART	Yes	19	63.3	8	26.6	3	10
	No	48	96	2	4	0	0
Disclosure to child	Yes	18	81.8	4	18.1	0	0
	No	49	84.4	6	10.3	3	5.1
Help fromfamily members in remembering to givepills	Most of the times	39	95.1	2	4.8	0	0
	Sometimes	22	88	2	8	1	4
	Never	6	42.8	6	42.8	2	14.2
Agree that ART is important for PLWHA?	Strongly agree	50	100	0	0	0	0
	Agree	17	62.9	7	25.9	3	11.1
	Disagree	0	0	1	100	0	0
	Doesn't know	0	0	2	100	0	0

Toddlers and preschool children were found to be less adherent to ART than infants, school children, and adolescents. Those care givers whose occupations were daily laborers, divorced, and old age child under their care were found to be less adherent. Those care givers, who were educated, married, got help from family members, and had a good attitude toward the importance of ART for PLWHA were found to be more adherent. Children withless pill burden and longer duration of ART use were also more adherent.

However, the adherence status was not affected by sex, economic status of care givers, religion of care givers, residence of care givers, and knew HIV status.

4. Discussion

During the study time, there were a total of 159 HIV positive patients on follow-up at WURH ART clinic, among them, 80 children who had received ART at WURH from March- May/2019 were included in the study. Forty two (42 (52.5%) were boys. The adherence rate was measured based on the recommended number of doses taken in the past one month.

In this study, 96.3% of the participants had greater than 95% adherence rate, of which 83.8% had a 100% adherence rate. This is much higher than the researchers conducted in high-income countries with ART adherence level range 20-100%, ART adherence was less than 75% (8). This value still high when compared with the study conducted in middle and low income countries with ART adherence level ranges 50-100% (7). Still, around 3.7% of the children had < 95% adherence rate which had an increased risk of drug resistance and treatment failure.

In this study, the adherence rate was found to be associated with age, marital status of care givers, educational level of care givers, occupation of care givers, and duration of ART use, number of medications other than ART, help from family members in remembering to give pills to the child, care givers attitude on the importance of ART for their child, relationship of care givers and child and drug time schedule.

No association was found between adherence rate and sex, address, religion, household income of care givers, and awareness of children on their HIV status.

In this study, the adherence rate is less in toddler and preschool age groups. In these age groups, independency and medication refusal can be a challenging condition. Studies in the United States and Africa have shown that adherence levels generally decline with increasing age among HIV-infected children [15–17].

Children whose care givers were married had a higher adherence rate than single, divorced, or widowed care givers. This can be due to the support and advice they got from their spouse and his/her role in reminding to give pills to the child.

Those care givers whose educational level was > 8 grades had the highest adherence rate with all of them having > 95% adherence. The lowest were those who were illiterate and can only read and write. This shows that higher level of education has a positive impact on adherence and poor care givers educational level has a negative impact on adherence as found in a research conducted by Romanian [18].

Merchants and government employees had the highest adherence rate unlike daily laborer and farmers. This can be due to the fact that most daily laborers and farmers leave home early in the morning and come late in the evening in which case they were busy all day and get so tired in the evening as a result they may forget or feel asleep before giving the pill to the child [19].

All children who were on ART for > 5 years had a > 95% adherence rate, but those who were on ART for < 1 year had a < 95% adherence rate. This shows that as the duration of ART increases, children became more adherent. This can be due to the longer they are on HAART, the number of times that they contact their health care givers, and the information they get from the health care givers increases. The longer the children on HAART the better the care givers notice the effect of the drug in improving the overall health of the child, since ART would significantly decrease the time of hospitalization and patient visits. This is also found in a research conducted in Saint Vincent Hospital and Medical center [20].

Children who were taking more than one other medication had the lowest adherence rate. Among those who took one other medication, they had < 95% adherence, on the other hand, all of them who took no other medication had > 95% adherence rate. This shows that pill burden and adherence rate have an inverse relationship. A prospective study done by Galin et al. in USA has also shown that patients with more pills per day adhere less [21].

Those care givers who were strongly agreed that ART is important for PLWHA had 100% adherence. However, those who simply agree and disagree had fewer adherences. This result is consistent with that a good level of understanding about the use of ART had a positive impact on adherence [22].

All study participants who closely followed their specific drug time schedule all or most of the times had a > 95% adherence rate. In this study, the major reasons for non-adherence were being busy with other things, felt asleep, and simply forgot [23].

5. Conclusions

The study showed that the majority (96.3%) of the children had a near perfect (>95%) adherence rate. It was also found that good social support (being married, care givers, and getting help from family members), good educational level of care givers, being employed in care givers, longer duration on ART and positive attitude on the importance of ART had a positive impact on adherence. Adherence rate was also found to be affected inversely using other medications than ARTDS.

6. Recommendations

1) Health education should be given by health professionals to increase awareness about the importance of ART for PLWHA and problems of low adherence since there is a direct relationship with adherence rate and the above-mentioned factors.
2) Since most of the reasons for missing a pill were avoidable, health professionals should advise patients to use different reminding techniques (such as an alarm clock).
3) There were limited researches done in the study area on adherence rate and limited researches found describing the national adherence rate. Thus under and post graduate students should be encouraged to do their research on this area and the Ethiopian Ministry Of Health should undergo studies describing the national adherence rate and possible constraints to it.

List of Abbreviations and Acronyms

AIDS: Acquired immune deficiency syndrome, ART: Anti retroviral therapy, ARVD: Anti retroviral drugs

HIV: Human immune deficiency virus, HAART: Highly active antiretroviral therapy

NRTIs: Nucleoside reverse transcriptase inhibitors, NNRTIs: Non nucleoside reverse transcriptase inhibitors, PLWHA: people live with HIV AIDS, WURH: Wollega University Referral Hospital

Acknowledgements

We would also like to thank our data collectors and supervisors and our study participants. We would also like to thank to all staff of WURH Medical Center antiretroviral clinic for providing us information.

References

[1] Joint United Nations Program (UNAIDS) 2015 Report on Global AIDS Epidemic, Global Report 2015.

[2] Havens JF, Mellins CA: Psychiatric aspects of HIV/AIDS. In Rutter's Child andAdolescent Psychiatry, edn 5. Edited by Rutter M, Bishop D, Pine D, et al. Oxford: Blackwell Publishing; 2018: 945–955.

[3] Yogev R: Balancing the upside and downside of antiretroviral therapy in children. JAMA 20011, 293: 2272–2274.

[4] World Health Organization: Scale up of HIV-related prevention, diagnosis, care, and treatment for infants and children. Available at http://www.who.int/hiv/pub/ paediatric/framework, 2011.

[5] Zhang F, Haberer J, Wei H, et al.: Drug resistance in the Chinese National Pediatric Highly Active Antiretroviral Therapy Cohort: implications for paediatric treatment in the developing world. Int J STD AIDS 2013, 20: 406–409.

[6] Helmut Kloos, YibeltalAssefa, AynalemAdugna, Mesfin Samuel Mulatu, and Damen Haile Mariam, Utilization of antiretroviral treatment in Ethiopia between February and December 2006: spatial, and demographic patterns, Int J Health Geogr.; 6: 45. 2017.

[7] Centers for Disease Control and Prevention: HIV/AIDS Surveillance Report: HIV Infection and AIDS in the United States. Available http://www.cdc.gov/hiv/topics/surveillance/resources/reports/ 2008report/pdf/2014 SurveillanceReport.pdf.

[8] Wiener L, Mellins CA, Marhefka S, Battles HB: Disclosure ofan HIV diagnosis to children: history, current research, andfuture directions. J DevBehavPediatr 2014, 28: 155–166.

[9] Murphy DA, Belzer M, Durako SJ, et al.: Longitudinalantiretroviral adherence among adolescents infected withhuman immunodeficiency virus. Arch Pediatr Adolesc Med 2010, 159: 764–770. 200 I Behavioral Aspects of HIV Management.

[10] Mellins CA, Brackis-Cott E, Dolezal C, et al.: The role ofpsychosocial and family factors in adherence to antiretroviral treatment in human immunodeficiency virus-infectedchildren. Pediatr Infect Dis J 2012, 23: 1035–1041.

[11] Williams PL, Storm D, Montepiedra G, et al.: Predictors of adherence to antiretroviral medications in children andadolescents with HIV infection. Pediatrics 2016, 118: e1745–e1757.

[12] Brouwer CN, Lok CL, Wolffers I, et al.: Psychosocial andeconomic aspects of HIV/AIDS and counselling of caretakers of HIV-infected children in Uganda. AIDS Care 2010, 12: 535–540.

[13] Nabukeera-Barungi N, Kalyesubula I, Kekitiinwa A, et al.: Adherence to antiretroviral therapy in children attendingMulago Hospital, Kampala. Ann Trop Paediatr 2017, 27: 123–131.

[14] Davies B, Whitsett SF, Bruce A, et al.: A typology of fatigue inchildren with cancer. J PediatrOncolNurs 2012, 19: 12–21.

[15] Ene L, Goetghebuer T, Hainaut M, et al.: Prevalence oflipodystrophy in HIV-infected children: a cross-sectionalstudy. Eur J Pediatr 2017, 166: 13–21.

[16] Adherence to antiretroviral therapy in HIV-infected childrenand adolescents. In Guidelines for the Working Groupon Antiretroviral Therapy and Medical Management ofHIV-Infected Children. Available at http://aidsinfo.nih. gov/Content Files/PediatricGuidelines.pdf. Accessed July 2009.

[17] Feinstein S, Keich R, Becker-Cohen R, et al.: Is noncompliance among adolescent renal transplant recipients inevitable?Pediatrics 2015, 115: 969–973.

[18] Giacomet V, Albano F, Starace F, et al.: Adherence to antiretroviral therapy and its determinants in children with human immunodeficiency virus infection: a multicentre, national study. Act aPaediatr 2013, 92: 1398–1402.

[19] Marhefka SL, VJ, Brown JL, et al.: Caregiver psychosocial characteristics and children's adherence to antiretroviral therapy. AIDS Patient Care STDS 2011, 20: 429–437.

[20] Biadgilign S, Deribew A, Amberbir A, et al.: Adherence tohighly active antiretroviral therapy and its correlates among HIV infected pediatric patients in Ethiopia. BMC Pediatr2017, 8: 53.

[21] Van Dyke RB, Lee S, Johnson GM, et al.: Reported adherenceas a determinant of response to highly active antiretroviral therapy in children who have human immunodeficiency virusinfection. Pediatrics 2012, 109: e61.

[22] Bikaako-Kajura W, Luyirika E, Purcell DW, et al.: Disclosureof HIV status and adherence to daily drug regimens among HIV-infected children in Uganda. AIDS Behav 2016, 10: S85–S93.

[23] Hammami N, Nöstlinger C, Hoerée T, et al.: Integrating adherence to highly active antiretroviral therapy intochildren's daily lives: a qualitative study. Pediatrics 2011, 114.