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Authors

Das, Aritra

Detels, Roger

Afifi, Abdelmonem A

et al.

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Health-related quality of life (HRQoL) and its correlates among community-recruited children living with HIV and uninfected children born to HIV-infected parents in West Bengal, India

Aritra Das, MBBS, MS, PhD[1], **Roger Detels, MD, MS**[2] **[Professor of Epidemiology and Infectious Diseases]**, **Abdelmonem A. Afifi, MS, PhD**[2] **[Professor of Biostatistics]**, **Marjan Javanbakht, MPH, PhD**[2] **[Associate Professor of Epidemiology]**, **Frank J. Sorvillo, MPH, PhD**[2] **[Professor of Epidemiology]**, and **Samiran Panda, MBBS, MD, DTMandH, FRSPH**[3] **[Senior Deputy Director and Scientist-F]**

[1]CARE India Solutions for Sustainable Development H No. 14, Patliputra Colony. Patna, Bihar, India. PIN Code – 800013

[2]Department of Epidemiology UCLA Fielding School of Public Health University of California, Los Angeles Los Angeles CA 90095-1772, United States

[3]National Institute of Cholera and Enteric Diseases (NICED/ICMR) P-33, CIT Road, Scheme-XM, Beliaghata Kolkata, West Bengal, India PIN-700010

Abstract

Purpose—Helping children living with HIV (CLH) to attain an optimum quality of life is an important goal for HIV programs around the world. Our principal objectives were to determine the association of HIV infection with different domains of health-related quality of life (HRQoL) among 8- to 15-year-old CLH in India and to compare the HRQoL parameters between CLH and HIV-negative children born to HIV-infected parents ("HIV-affected"). We also assessed whether anti-retroviral therapy (ART) and CD4 lymphocyte counts were associated with HRQoL among CLH.

Methods—Using the "Quality of Life (health-related) of Children Living with HIV/AIDS in India (QOL-CHAI)" instrument, we interviewed 199 CLH and 194 HIV-affected children from three districts of West Bengal, India. Participants were asked to quantify the difficulties faced by them in six HRQoL domains: physical, emotional, social, school functioning, symptoms, and discrimination.

Results—The mean age of the participants was 11.6 (SD±2.5) years. CLH, compared to HIV-affected children, had poorer scores on all HRQoL domains except 'discrimination'. Among CLH, there were no significant differences in HRQoL domain scores (except in the 'discrimination'

Correspondence to: Roger Detels.

Compliance with Ethical Standards

Conflict of Interest: All authors declare that they have no conflict of interest.

Ethical approval: All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from the caregivers of all participating children. Additionally, verbal assent was obtained from each of the participating children.

domain) between ART-treated and -untreated groups. CD4 lymphocyte count was found to be a significant positive predictor of the ‘symptom’ scale score.

Conclusions—In India, interventions for CLH mostly focus on biological disease. However, the current study revealed that HRQoL among CLH was much poorer than that of a socio-demographically comparable group. Culturally and developmentally appropriate psychosocial support measures for Indian CLH are urgently needed. Health-related quality of life (HRQoL) and its correlates among community-recruited children living with HIV and uninfected children born to HIV-infected parents in West Bengal, India

Keywords

HIV; quality of life; children; reliability; validation study

Introduction

Access to combination antiretroviral therapy (ART) has led to reduction of incidence of opportunistic infections and other AIDS-defining illnesses among the HIV-infected. This has resulted in delayed, often to an indefinite period, progression to AIDS and, in turn, has prolonged lifespans of the infected. However, existing therapies do not eliminate latently infected T-cells, and are therefore not successful in completely eliminating the virus or curing patients [1]. As complete cure is not possible, helping infected adults and children achieve optimum quality of life remains a fundamental goal of HIV programs around the world [2].

Children and adolescents living with HIV are among the most affected by the current HIV epidemic globally, and therefore must be a key target population for future epidemic control [3,4]. Worldwide, in 2015, 2.6 million children and adolescents younger than 15 years were living with HIV, and about 140,000 of them were in India [5,6]. Review of the published literature reveals that these children, due to the chronic nature of their disease, often face biological, cognitive, and social developmental challenges, as well as low self-esteem resulting from HIV-related stigma [7–9]. Moreover, the epidemic also affects the lives of many other children who have been orphaned by parental deaths from HIV [10]. Thus, the tremendous impact of HIV/AIDS at the family level invariably trickles down to the most susceptible population – children – regardless of their own HIV status [7].

In developing countries, treatment policies on pediatric HIV have primarily depended on biological disease markers such as the CD4 lymphocyte count for assessment of infected children and for disbursement of health services. However, in view of the multitude of psychosocial challenges faced by children living with HIV (CLH), such clinical markers often fail to provide a complete picture of the disease impact [11]. Therefore, to comprehensively assess the overall impact of HIV infection on the lives of CLH and to better inform policy-makers regarding the various needs of this population, health-related quality of life (HRQoL) measures are being increasingly preferred as more efficient alternatives to traditional clinical assessments of health [12,13]. There has been no unanimous agreement on the beneficial effects of ART on HRQoL [14]. Some published studies have reported little change or even decline in HRQoL of patients following initiation

of ART, possibly due to drug-related adverse events [15–17]. Therefore, it is important to assess the association of ART with HRQoL, especially among CLH, to inform programmatic interventions. While the majority of studies on HRQoL of pediatric HIV-infected populations have been conducted in developed country settings [12], implications of such studies are no less important for resource-constrained nations where basic amenities and social support are often found wanting, even for healthy children. Similar to many other developing nations, improving the quality of life of the children suffering from this stigmatizing infection has not been a priority for India's national HIV program, and HRQoL is yet to be accepted widely as an outcome measure for planned interventions [18,19].

Prior Indian studies on determinants of HRQoL among children and adults living with HIV have mostly recruited patients and control groups from treatment settings [19–21], which probably led to assessment of HRQoL among participants with poorer health status. Thus, their responses might have been influenced by treatment setting-associated stigma [22]. In this setting, the current study set out to assess and compare the HRQoL of community-recruited CLH and children born to HIV-infected parents but not infected ("HIV-affected"). The objectives of the present study were four-fold: a) to describe and compare the socio-demographic characteristics and common disease symptoms among CLH and HIV-affected children; b) to identify association of HIV infection status with different HRQoL domains; c) to compare HRQoL scores between ART-treated and -untreated CLH; and d) to determine whether CD4 lymphocyte count, the most widely used clinical parameter for HIV in India, can predict HRQoL among CLH.

Methods

Study setting and participant recruitment

The present study was conducted in West Bengal, an eastern Indian state which is middling in terms of economic and health indicators (compared to the national average) [23]. Participants in this study were a convenience sample of 8- to 15-year-old CLH and HIV-affected children residing in three districts of the state - Purba Medinipur, Paschim Medinipur, and Kolkata. To facilitate participant recruitment, we collaborated with a community-based organization (CBO), 'Society for Positive Atmosphere and Related Support to HIV/AIDS' (SPARSHA). Since 2000, SPARSHA was comprised of and managed by people living with HIV and their friends, and has been working with children and adults living with HIV in rural and urban settings of West Bengal. The various services offered by SPARSHA include facilitating access to ART, conducting community awareness programs, HIV stigma reduction activities, and HIV/AIDS counseling services. As part of its activities, SPARSHA prepared a roster of its service recipients and their families residing in the study districts. CLH and HIV-affected children meeting the inclusion criteria were identified from the roster, and their parents or primary caregivers were contacted by outreach workers from SPARSHA regarding participation of their children. Parents/caregivers who expressed preliminary approval for participation of their children in the study were invited to bring their children to the nearby SPARSHA field office for an interview. If the child or his/her caregiver wanted the interview to be conducted at their home, an interview team

visited their home on appointment. Each interview was preceded by obtaining informed consent from the respective parent/caregiver, followed by verbal assent from the child.

Eligibility criteria for participating CLH were: 1) being diagnosed with HIV at a center approved by the West Bengal State AIDS Prevention & Control Society; 2) aged 8–15 years; 3) not previously diagnosed with a disorder that would prevent the participating child from responding rationally to the questionnaire (such as psychiatric, neurologic or developmental disorders, but not limited to them); 4) consent from the accompanying caregiver to participate; and 5) verbal assent from the child. In terms of recruitment to the HIV-affected group, an eligible child must be born to HIV-infected parents and have tested negative for HIV antibody at or after 18 months of age. Other than having an HIV diagnosis, the rest of the eligibility criteria for the HIV-affected group were the same as for the CLH group. For CLH and HIV-affected children, the HIV status of their biological parents was obtained from their medical records. However, medical records for parents were not available in few instances where the parents died long ago or abandoned the family. In such cases, we depended on the information recorded in SPARSHA's register on people living with HIV (PLH).

HIV-affected children were chosen as a comparison group for CLH, as these two groups were similar in many socio-demographic aspects, such as socio-economic background, receiving services from the same CBO, and geographic location, as well as parental HIV status. Therefore, as HIV infection status was apparently the only differentiating factor between these two groups of children, any differences between the groups in HRQoL could be assumed to be sequelae of the infection.

Data collection

Between November, 2014 and February, 2015, caregivers of 217 CLH and 232 HIV-affected children were approached for participation, of whom we interviewed 199 (92%) CLH and 194 (84%) HIV-affected children. Following informed consent from caregivers about interviewing their child and assessing treatment records, socio-demographic information was obtained from the respective caregivers about the children and their families. Treatment-related information, including CD4 cell count and ART intake, was recorded from ART cards issued by their treatment centers. The children giving verbal assent were requested to complete the "Quality of life (health-related) of children living with HIV/AIDS in India (QOL-CHAI)" [24,25] study instrument, with assistance from a trained interviewer.

Measures

The QOL-CHAI is a 45-item instrument comprised of six domains. The first four domains – physical (eight items), emotional (five items), social (five items) and school (five items) functioning - were adapted from the "Pediatric Quality of Life Inventory (PedsQL)" generic core scale [26,27]. The other two domains contain questions regarding disease symptoms (18 items) and experiences of discriminating behavior (four items). Participants were required to answer how much of a problem they faced during the past month from each item in the instrument, except for the 'discrimination' domain, which covered the past year. Frequency of the problems associated with each item were classified as: never (0), almost

never (1), sometimes (2), often (3), and almost always (4). Interviews with children took approximately 15 minutes to complete. The QOL-CHAI instrument had been validated in the present study setting and showed good internal consistency (Cronbach's α ranging from 0.69 to 0.85 for different domains), convergent validity with clinical parameter (symptoms domain with CD4) and discriminant property between HIV-infected and -affected children [24]. To aid interpretation of and comparison between different domains, we reverse-coded each item and then linearly transformed them to a score ranging 0–100 (higher scores indicated better HRQoL) [26]. The summary score for each domain was computed by adding together the scores on items constituting the domain and dividing by the number of items. The overall summary score was also converted to a scale of 0 to 100 by adding together the scores on all 45 items and dividing by 45.

In addition to recording participants' responses on the QOL-CHAI scale items, we collected information on participants' age, gender, school class (attending grade/standard in school), primary caregiver, survival status of parents, parental education, number of family members, family income, ART intake, ART initiation date, and CD4 cell count at the time of ART initiation and at last measurement. To estimate prevalence of the reported symptoms during the past month, we dichotomized the 'symptom' scale into: i) no symptoms (score 0); and ii) some occurrence of symptoms (scores 1–4). Parental status of children was categorized into: both parents alive, one parent alive, and neither parent alive. Per capita income of the children's family was categorized into quartiles.

Statistical analysis

Descriptive analyses were carried out to determine the distribution of socio-demographic characteristics of the study participants and to determine whether any differences existed between CLH and HIV-affected children. Also, bivariate analysis was used to compare the prevalence of common symptoms between CLH and HIV-affected children. To evaluate the magnitude and direction of associations between HIV infection status and QOL-CHAI scale scores, we employed simple and multiple linear regression models. The multiple regression model was adjusted for age, gender, parental status (parents alive or not), and per-capita family income. In the sub-sample consisting only of CLH, we compared the socio-demographic characteristics and symptom prevalence between ART-treated and -untreated CLH. Among CLH, the associations of ART regimen and CD4 lymphocyte count with QOL-CHAI scores were determined using separate unadjusted and adjusted linear regression models. The multiple regression models for the CLH sub-sample were adjusted for the same covariates as the model for assessing the association between HIV status and QOL-CHAI score. Model fit was assessed by adjusted R^2 statistic and residual plots. All statistical analyses were performed using SAS 9.4.

Ethical approval

Ethical approval for this study was obtained from the institutional review board of the University of California, Los Angeles and the Institutional Ethics Committee of the National Institute of Cholera and Enteric Diseases (under the Indian Council of Medical Research), the collaborating research institute located in Kolkata, West Bengal.

Results

In total, we interviewed 393 children (199 CLH and 194 HIV-affected), of whom 59% were males (65% among CLH and 52% among HIV-affected). Socio-demographic and disease-related characteristics of participating children are presented in Table 1. The overall mean age of participants was 11.6 years (standard deviation (SD) ±2.5 years), with CLH being slightly younger (11.3 years, SD±2.5 years) than HIV-affected (11.9 years, SD±2.5 years). Mothers were the primary caregivers for the majority of participants (CLH 77% and HIV-affected 95%). A significantly higher proportion of CLH (36%) studied at a school class/standard lower than that recommended for their age compared to HIV-affected children (19%) [$p < 0.01$]. The proportions of both-parent orphans (11%) and single-parent orphans (43%) were much higher among CLH than the HIV-affected group (both parents 2% and single parent 32%, $p < 0.01$). One hundred and thirty CLH (65%) had been taking ART for at least six months prior to the date of interview. Among those taking ART, 71% of CLH had CD4 cell counts above 500/mm^3 (i.e., non-significant immunosuppression) [28] compared to 45% of the CLH group not taking ART (including those taking it for less than six months) [$p < 0.01$].

Prevalence of symptoms among CLH and HIV-affected children and p-values from the significance tests comparing the prevalence in these two groups of children are presented in Table 2. The most reported symptom among both study groups was common colds, with 73% CLH and 55% HIV-affected children reporting at least a single occurrence during the previous month. Other commonly reported symptoms occurring in the past month were pain in the limbs (CLH 56%, HIV-affected 39%), loss of appetite (CLH 52%, HIV-affected 37%), headache (CLH 45%, HIV-affected 34%), and tingling/numbness in the limbs (CLH 38%, HIV-affected 37%). Compared to HIV-affected children, prevalence of most of these physical symptoms were significantly higher among CLH, except for abdominal pain, yellowish discoloration of eyes, and tingling/numbness in the limbs.

As can be seen in Table 3, the overall QOL-CHAI mean score and mean scores in each HRQoL domain were lower among CLH than HIV-affected children. In simple linear regression analysis, HIV infection was found to be associated with lower mean scores on all HRQoL domains except ‘discrimination’. The overall QOL-CHAI score was also significantly lower for CLH than HIV-affected children (parameter estimate (β): 7.2, 95% confidence interval (CI): −8.6, −5.7). The findings were similar for multiple linear regression models that adjusted for children’s ages, gender, parental status, and per capita family income. With all covariates being equal, it was observed that HIV infection was significantly associated with poorer HRQoL scores in individual domains (except discrimination) and total score.

Mean HRQoL domain scores for CLH who had been taking ART for at least six months and those who had not started ART (or had taken it for less than six months) are shown in Table 4. From findings of unadjusted linear regression, we could see that ART intake was associated with significantly poorer scores in the discrimination domain (β: −5.6, 95% CI: −9.9, −1.4). Even after adjusting for covariates, ART intake (β: −4.7, 95% CI: −9.1, −0.3) remained a significant negative predictor of discrimination scale scores. In other HRQoL

domains and in terms of overall scores, there were no significant differences between ART-treated and -untreated groups in both unadjusted and adjusted analyses.

Linear regression of HRQoL domain scores on last reported CD4 cell counts revealed that CD4 cell count was a significant positive predictor of the ‘symptom’ scale score (Table 5). From unadjusted analyses we could see that every 100-unit increase in CD4 cell count was associated with a mean increase of 0.5 units on the symptom scale scores (β: 0.5, 95% CI: 0.2, 0.9). In multiple linear regression analyses, every 100-unit rise in CD4 cell count led to a 0.6-unit increase in mean scores on the symptom scale (β: 0.6, 95% CI: 0.2, 0.9). CD4 cell count did not have significant associations with the other HRQoL domains and overall QOL-CHAI score.

Discussion

The current study aimed to provide insights into an often neglected aspect of HIV care for children – quality of life. In developing countries such as India, the HIV programs for children are primarily focused on clinical parameters, whereas ensuring optimum HRQoL of children infected with or affected by HIV is given little emphasis [12]. To attain our study objectives, we used convenience sampling to recruit 8- to 15-year-old children residing in the state of West Bengal, India to compare HRQoL between CLH and children who were born to HIV-infected parents but were not infected with HIV (“HIV-affected”), and also between ART-treated and -untreated CLH.

We found that HIV infection was associated with poorer scores in all HRQoL domains except ‘discrimination’. This was in accordance with multiple prior published studies, which reported that HIV infection significantly compromised HRQoL in children [20,29,30]. In the Indian context, HIV-related discrimination is often not limited to the infected individual, and social ostracism frequently involves the entire family [31]. As having HIV-infected parents was a common characteristic of both CLH and HIV-affected children, it was likely that any discrimination directed at parents/family members might have also affected the children. Also, a low proportion of participants reported experiencing any discriminatory behavior during the previous year, as evidenced from very high mean scores for the ‘discrimination’ domain. This might have reduced the statistical power of finding significant differences in the ‘discrimination’ scores between the two study groups. Fewer discrimination experiences might have resulted from the fact that participating children and their family members were likely to conceal their HIV diagnosis to avoid stigma [31–33].

Among CLH, we found that ART intake was not associated with any of the HRQoL domains except ‘discrimination’. This finding was in contrast to that reported from prior studies conducted in India [19] and developed countries [30,34]. However, as mentioned earlier, there has been no consensus on the beneficial effects of ART on HRQoL [14,15]. ART initiation in India depends on immunological status (CD4 cell count). Therefore, the probable poorer immunological status of ART-treated CLH at baseline compared to the ART-untreated CLH probably negated any potential benefits provided by ART. Because of our cross-sectional study design, we could not determine whether ART intake led to improvements in HRQoL among the recipients over time. Being on ART was found to be

associated with poorer scores in the ‘discrimination’ domain. A possible explanation could be that the ART-treated CLH and their family members found it difficult to conceal their HIV diagnosis because of poorer overall health status and frequent visits to health facilities/ART centers, which might have resulted in experiencing discrimination. Adverse effects associated with antiretroviral medications perhaps also contributed to HIV status disclosure and increased likelihood of discrimination against ART-treated CLH [33].

Interestingly, higher CD4 cell count, the most commonly used disease marker in the Indian context, was not found to be associated with better HRQoL scores in any of the domains other than ‘symptoms’. As reported by Punpanich et al. [35], clinical parameters related to disease progression may not always successfully capture an individual’s perception about his/her well-being and overall quality of life. Previous studies on HRQoL of patients with HIV and other chronic diseases have also noted that clinical indices did not always consistently predict performance on self-reported HRQoL parameters [36–38].

Regarding the socio-demographic profile, we observed that the proportion of single-parent and both-parent orphans were higher among CLH than the HIV-affected group. We hypothesize that married PLH who presented to the health system early and received treatment and/or behavioral interventions were not only more likely to have better survival, but also had less likelihood of transmitting the infection to others (including vertical transmission). Thus, it was possible that, although both groups of children were born to HIV-infected parents, a higher proportion of parents of HIV-affected children received treatment and other associated services for themselves (leading to longer life) and also received pregnancy-related interventions that reduced their likelihood of giving birth to a HIV-positive child [39]. We further observed that a significantly higher proportion of school-going CLH, compared to the HIV-affected group, had a study lag (i.e., they attended a class/standard lower than that recommended for their age). This was not surprising, as a number of prior studies have documented cognitive difficulties and poor school performance among CLH [40–42]. Interestingly, among CLH, the ART-treated children were not only more likely to have a study lag, but also had a higher proportion of school drop-out compared to the ART-untreated children. As previously mentioned, children on ART probably had a poorer overall health status at baseline (prior to ART initiation) compared to the ART-untreated group and, as a result, had more difficulty keeping up in school or even continuing to attend. Furthermore, prior studies have suggested that neurocognitive decline due to HIV infection among school-going children may not be reversed by ART [43–45].

Being an observational study, our results had a few limitations. First, because of the cross-sectional design, lack of temporality prevented us from drawing any causal inferences. The time sequences of predictors were often unclear, such as whether ART intake affected perceptions about health status or already poor health status led to initiation of ART. Second, we employed convenience sampling to recruit participants from the contact list of a CBO that mostly serves low- and lower-middle-income families. The fact that most study participants belonged to lower socio-economic strata was evident from low family income and low parental educational levels of study participants. Therefore, generalizability of our study findings to different socio-economic groups, populations, and other Indian states may be inappropriate. Third, the fact that most of our data was self-reported raises concerns about

social desirability bias, which could potentially introduce outcome misclassifications in our analyses, especially for the ‘social functioning’, ‘school functioning’ and ‘discrimination’ domains. Fourth, as we recruited children from community settings and not from treatment facilities, participants in this study were mostly ambulatory and not severely ill. This was reflected by the fact that the majority of study participants reported no or very few problems in most HRQoL domains. Therefore, our findings could differ if the QOL-CHAI had been administered to HIV-infected or -affected children with poorer general health. Moreover, although HIV-affected children constituted a reasonable comparison group for CLH, differences in HRQoL parameters for CLH possibly would be more pronounced if compared to a general population control group (as opposed to HIV-affected children). Also, because of unavailability of medical records, we could not verify the parental HIV status from medical records in few instances, and we had to rely on the information recorded in SPARSHA’s PLH register. However, given SPARSHA’s close association with the HIV-specific healthcare providers in the study area, we expect the information to be accurate. Finally, in the current study, we relied on CD4 lymphocyte counts as a marker of disease progression. Plasma viral load (PVL), alone or in combination with other markers, is generally considered superior to CD4 count in predicting clinical outcomes of PLH [46,47]. However, in India, due to cost considerations, PVL assessment is not offered routinely under the national HIV program. As all CLH participants in this study attended state-run HIV clinics that did not have PVL evaluation and/or did not recommend it as part of standard treatment protocol, almost none of the participants ever had his/her PVL measured. Therefore, despite recognizing its relevance, we could not determine whether PVL status had an important bearing on HRQoL of participating CLH.

Nationwide scale-up of the ART program has made it possible for an increasing number of pediatric HIV patients in India to survive into adolescence and adulthood. However, as the presently available treatments are unsuccessful in completely eliminating the virus [1], the patients must continue medications indefinitely, and suffer from associated drug-related adverse effects. Therefore, as with other chronic diseases, ensuring an adequate level of quality of life for CLH remains a challenge for policy-makers and health care providers. Poor HRQoL status of Indian CLH revealed in the current study calls for culturally and developmentally appropriate psychosocial support measures to address the multitude of challenges faced by these children. As recommended by Amzel et al [48], in order to be comprehensive, such support measures should involve individual, family, and community-level components, and utilize existing support networks in communities, schools, and treatment facilities. Further insights into the problems faced by this population might be gained through follow-up studies designed to monitor changes in HRQoL with disease course. Such studies could also help in assessing effectiveness and feasibility of planned medical and/or socio-behavioral interventions targeted to CLH and children affected by HIV.

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Table 1

Socio-demographic and disease related characteristics of study participants (n=393)

Characteristic	Children living with HIV (n=199)				HIV-affected children (n=194)	*p*- value[3]
	On ART[2] (n=130)	Not on ART (n=69)	*p*- value[4]	Total	Frequency (%)[1]	
	Frequency (%)[1]	Frequency (%)[1]		Frequency (%)[1]		
Mean age in years (SD)	11.8 (2.5)	10.6 (2.4)	<0.01 *	11.3 (2.5)	11.9 (2.5)	0.02 *
Gender						
Male	88 (67.7)	42 (60.9)	0.34	130 (65.3)	101 (52.1)	<0.01 *
Female	42 (32.3)	27 (39.1)		69 (34.7)	93 (47.9)	
Residential district						
Paschim Medinipur	58 (44.6)	32 (46.4)		90 (45.2)	133 (68.6)	
Purba Medinipur	13 (10)	11 (15.9)	0.37	24 (12.1)	31 (16)	<0.01 *
Kolkata	59 (45.4)	26 (37.7)		85 (42.7)	30 (15.5)	
Primary caregiver						
Mother	98 (75.4)	56 (81.2)		154 (77.4)	185 (95.4)	
Father	5 (3.9)	1 (1.5)	0.52	6 (3)	1 (0.5)	<0.01 *
Other	27 (20.8)	12 (17.4)		39 (19.6)	8 (4.1)	
Parent status						
Both parents alive	54 (41.5)	37 (53.6)		91 (45.7)	129 (66.5)	
Single-parent orphan	58 (44.6)	28 (40.6)	0.12	86 (43.2)	62 (32)	<0.01 *
Both-parent orphan	18 (13.9)	4 (5.8)		22 (11.1)	3 (1.6)	
School drop-out						
Yes	11 (8.5)	1 (1.5)	0.04 *	12 (6)	7 (3.6)	0.26
No	119 (91.5)	68 (98.6)		187 (94)	187 (96.4)	
Studying at a class/standard lower than recommended for age						
Yes	55 (42.3)	16 (23.2)	<0.01 *	71 (35.7)	36 (18.6)	<0.01 *
No	75 (57.7)	53 (76.8)		128 (64.3)	158 (81.4)	
Mother's education						
Did not attend school	34 (26.2)	23 (33.3)	0.85	57 (28.6)	27 (13.9)	<0.01 *

Characteristic	Children living with HIV (n=199)				HIV-affected children (n=194)	*p*- value[3]
	On ART[2] (n=130)	Not on ART (n=69)	*p*- value[4]	Total	Frequency (%)[1]	
	Frequency (%)[1]	Frequency (%)[1]		Frequency (%)[1]		
Primary school	18 (13.9)	9 (13)		27 (13.6)	41 (21.1)	
Middle school	68 (52.3)	32 (46.4)		100 (50.3)	122 (62.9)	
High school or above	7 (5.4)	4 (5.8)		11 (5.5)	4 (2)	
Not reported	3 (2.3)	1 (1.5)		4 (2)	-	
Father's education						
Did not attend school	17 (13.1)	20 (29)		37 (18.6)	32 (16.5)	
Primary school	32 (24.6)	12 (17.4)		44 (22.1)	60 (30.9)	
Middle school	64 (49.2)	31 (44.9)	0.09	95 (47.7)	98 (50.5)	0.03*
High school or above	8 (6.2)	3 (4.4)		11 (5.5)	2 (1)	
Not reported	9 (6.9)	3 (4.4)		12 (6)	2 (1)	
Per-capita family income (in INR/month)						
1st quartile (≤375)	34 (26.2)	18 (26.1)		52 (26.1)	50 (25.8)	
2nd quartile (≥400 – ≤600)	30 (23.1)	7 (10.1)	0.11	37 (18.6)	65 (33.5)	<0.01*
3rd quartile (≥625 – ≤1000)	38 (29.2)	22 (31.9)		60 (30.2)	55 (28.4)	
4th quartile (≥1111)	28 (21.5)	22 (31.9)		50 (25.1)	24 (12.4)	
Last measured CD4 cell count(/mm^3)						
<250	12 (9.2)	4 (5.8)		16 (8)	-	
≥250-<500	26 (20)	30 (43.5)	<0.01*	56 (28.1)	-	-
≥500	92 (70.7)	31 (44.9)		123 (61.8)	-	
Not reported	-	4 (5.8)		4 (2)	-	

[1] Values may not sum to 100% due to rounded numbers.

[2] Taking ART for at least past 6 months.

[3] *p*-value of difference between CLH and HIV-affected groups.

[4] *p*-value of difference between ART and non-ART groups.

* Statistically significant ($p \leq 0.05$).

Table 2

Prevalence of reported symptoms among children living with HIV and children exposed to but not infected with HIV (n=393)

Symptoms	Participants reporting at least a single episode during previous month (%)			
	Overall	Living with HIV (n=199)	Exposed but not infected (n=194)	*p*-value[1]
Fever	141 (35.9)	82 (41.2)	59 (3.4)	0.03*
Common cold	252 (64.1)	146 (73.4)	106 (54.6)	<0.01*
Weight loss, emaciation	74 (18.8)	45 (22.6)	29 (15)	0.05*
Diarrhea, loose stools	70 (17.8)	46 (23.1)	24 (12.4)	<0.01*
Pain in limbs	187 (47.6)	111 (55.8)	76 (39.2)	<0.01*
Headache	155 (39.4)	90 (45.2)	65 (33.5)	0.02*
Skin rash, itchy lesions, sores/ulcers	86 (21.9)	63 (31.7)	23 (11.9)	<0.01*
Vomiting, nausea	100 (25.5)	63 (31.7)	37 (19.1)	<0.01*
Ear discharge, hearing difficulties	51 (13)	42 (21.1)	9 (4.6)	<0.01*
Loss of appetite	174 (44.3)	103 (51.8)	71 (36.6)	<0.01*
Abdominal pain	105 (26.7)	60 (30.2)	45 (23.2)	0.12
Yellowish discoloration of eyes/jaundice	7 (1.8)	6 (3)	1 (0.5)	0.06
Dizziness	63 (16)	45 (22.6)	18 (9.3)	<0.01*
Throat swelling, sore throat	73 (18.6)	46 (23.1)	27 (13.9)	0.02*
Abdominal distension	14 (3.6)	9 (4.5)	5 (2.6)	0.3
Shortness of breath, wheezing	52 (13.2)	35 (17.6)	17 (8.8)	<0.01*
Tingling sensation/numbness in limbs	148 (37.7)	76 (38.2)	72 (37.1)	0.83
Oral ulcers	32 (8.1)	27 (13.6)	5 (2.6)	<0.01*

[1] *p*-value for difference in scale scores between children living with HIV and HIV exposed but not infected children

* Statistically significant ($p \leq 0.05$)

Table 3

Parameter estimates from unadjusted and adjusted linear regression analyses to evaluate the association of HIV infection status with QOL-CHAI scale scores (n=393)[#]

Scale	No. of items	Mean score		Unadjusted analysis		Adjusted analysis[**]	
		Living with HIV (n=199)	Exposed to but not infected with HIV (n=194)	Parameter estimate	95% CI	Parameter estimate	95% CI
Physical functioning	8	80.9	92.5	−10.6[*]	−13.3, −7.8	−11.2[*]	−14.1, −8.4
Emotional functioning	5	73.2	79.7	−5.8[*]	−9.4, −2.2	−6.1[*]	−9.9, −2.3
Social functioning	5	87.9	96.5	−8.1[*]	−11.2, −5.1	−8[*]	−11.2, −4.8
School functioning	5	74.9	87.5	−12.6[*]	−15.8, −9.5	−12.4[*]	−15.7, −9.1
Symptoms	18	86.6	92.2	−5.6[*]	−7, −4.2	−5.7[*]	−7.2, −4.2
Discrimination	4	94.5	96.6	−1.2	−2.9, 0.6	−0.9	−2.7, 0.9
Overall	45	83.1	90.9	−7.2[*]	−8.6, −5.7	−7.3[*]	−8.9, −5.7

[#]Observations with missing values excluded as and where applicable.

Negative parameter estimates indicate that HIV infection is associated with poorer functioning and vice versa.

[*]Statistically significant ($p \leq 0.05$).

[**]Adjusted for child's age, gender, parental status and per capita family income.

Table 4

Parameter estimates from unadjusted and adjusted linear regression analyses to evaluate the association of ART intake (for at least 6 months) with QOL-CHAI scale scores among children living with HIV (n=199)[#]

Scale	Mean score		Unadjusted analysis		Adjusted analysis[**]	
	ART (n=130)	Non-ART (n=69)[^]	Parameter estimate	95% CI	Parameter estimate	95% CI
Physical functioning	79.8	82.9	−3	−8.4, 2.3	−0.9	−6.4, 4.7
Emotional functioning	74	71.7	2.3	−3.7, 8.2	3.6	−2.5, 9.7
Social functioning	86.9	89.9	−3	−8.7, 2.7	−2.4	−8.3, 3.5
School functioning	73.1	78.1	−5	−10.4, 0.4	−4.2	−9.7, 1.3
Symptoms	86.3	86.5	−0.2	−2.7, 2.3	0	−2.6, 2.6
Discrimination	92.5	98.2	−5.6[*]	−9.9, −1.4	−4.7[*]	−9.1, −0.3
Overall	82.3	84.6	−2.3	−5.2, 0.7	−1.2	−4.2, 1.8

[#] Observations with missing values excluded as and where applicable.

[^] Not taking ART or taking ART for < 6 months

Negative parameter estimates indicate that ART intake is associated with poorer functioning and vice versa

[*] Statistically significant ($p \leq 0.05$)

[**] Adjusted for child's age, gender, parental status and per capita family income

Table 5

Parameter estimates from unadjusted and adjusted linear regression analyses to evaluate the association of CD4 count (for every 100 units change in CD4 cells/mm^3) with QOL-CHAI scale scores among children living with HIV (n=199)[#]

Scale	Unadjusted analysis		Adjusted analysis[**]	
	Parameter estimate	95% CI	Parameter estimate	95% CI
Physical functioning	−0.1	−0.8, 0.5	−0.2	−0.9, 0.5
Emotional functioning	0	−0.8, 0.8	0	−0.8, 0.8
Social functioning	0	−0.8, 0.7	0	−0.8, 0.7
School functioning	−0.4	−1.2, 0.3	−0.4	−1.2, 0.3
Symptoms	0.5[*]	0.2, 0.9	0.6[*]	0.2, 0.9
Discrimination	−0.2	−0.6, 0.3	−0.1	−0.6, 0.3
Overall	0.1	−0.2, 0.4	0.1	−0.2, 0.5

[#]Observations with missing values excluded as and where applicable.

Negative parameter estimates indicate that increase in CD4 cell count is associated with poorer functioning and vice versa

[*]Statistically significant ($p \leq 0.05$).

[**]Adjusted for child's age, gender, parental status and per capita family income