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Loss to follow-up among children in pre-ART care under the National AIDS Programme, Tamil Nadu, South India

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Setting: Children aged <15 years constitute 7% of all people living with the human immunodeficiency virus (HIV) in India. A previous study from an antiretroviral therapy (ART) centre in south India reported 82% loss to follow-up (LTFU) among children in pre-ART care (2006–2011).

Objective: To assess the proportion of LTFU within 1 year of registration among HIV-infected children (aged < 15 years) registered in all 43 ART centres in the state of Tamil Nadu, India, during the year 2012.

Design: This was a retrospective cohort study involving a review of programme records.

Results: Of 656 children registered for HIV care, 20 (3%) were not assessed for ART eligibility. Of those remaining, 226 (36%) were not ART eligible and entered pre-ART care. Among these, at 1 year of registration, 50 (22%) were LTFU, 40 (18%) were transferred out and 136 (60%) were retained in care at the same centre. The child's age, sex, World Health Organization stage or occurrence of opportunistic infection were not associated with LTFU.

Conclusion: One in five children registered under pre-ART care were lost to follow-up. Stronger measures to prevent LTFU and reinforce retrieval actions are necessary in the existing National HIV Programme.

India has the third highest estimated number of people living with the human immunodeficiency virus (PLHIV) in the world, estimated at 0.21 million in 2015. Children aged <15 years accounted for 7%, while about 40% were females.[1]

Pre-antiretroviral therapy (ART) care involves providing comprehensive care and regular monitoring of HIV-infected children and adults who are not yet eligible for ART per national guidelines.[2] Pre-ART care is essential to maintain a positive, healthy living status until those affected require antiretroviral therapy. Several studies in adults and children living with HIV have reported high attrition rates in pre-ART care.[3–6]

In a previous study, we found that 82% of the children living with HIV/AIDS (acquired-immune deficiency syndrome) (CLHIV) who were registered for pre-ART care between 2006 and 2011 in Madurai district of Tamil Nadu in South India were lost to follow-up within 1 year of registration.[7] This study was from one ART centre, however, and the findings were not generalisable to the entire state of Tamil Nadu. Furthermore, the study period, 2006–2011, did not reflect the most recent situation. Although the monthly reporting format used by the ART centres now reviews and captures details of children's care, priority has been given to periodic assessments and follow-up of PLHIV initiated on ART.

There is no published information on pre-ART care among children managed in public sector ART centres at state level in India. In this study we therefore aimed to assess the proportion of children on pre-ART care who were lost to follow-up within 1 year of registration, and associated sociodemographic and clinical characteristics, in a cohort of HIV-infected children registered for HIV care at ART centres in 2012 in the state of Tamil Nadu, South India.

METHODS

Study design

This was a retrospective cohort study of HIV-infected children using routinely collected programme data.

Study setting and population

The study was planned in 2014 as a 1-year project. It included all HIV-infected children registered at all 43 ART centres between 1 January and 31 December 2012 across all 32 districts of Tamil Nadu.

The National Paediatric HIV/AIDS initiative was launched in India in 2006. As of March 2014, ~100 000 CLHIV were registered for HIV care at ART centres, of whom 42 015 were receiving free ART while the remainder were on pre-ART care.[8] The functions of the ART centres include registering and providing care, support and treatment services to all PLHIV. This includes periodically assessing those in pre-ART care for ART eligibility and initiating them on ART in a timely manner per the National AIDS Control Organisation (NACO) guidelines. Children in pre-ART care are treated symptomatically for their opportunistic infections (OI) and are prescribed multivitamin supplements.

HIV prevalence among adults (aged 15–49 years) in the state of Tamil Nadu was 0.38% in 2007, and declined to 0.28% in 2011.[8] The free ART initiative was launched in Tamil Nadu on 1 April 2004. A total of 4068 children had been started on ART in Tamil Nadu as of March 2014.[8]

Children found to be eligible were initiated on ART based on national clinical criteria, i.e., World Health Organization (WHO) clinical stages 3 or 4 or immunological criteria (CD4 cell count <1500 cells/μl or <25% in children aged <12 months, CD4 count <750 cells/μl or <20% in those aged 12–35 months, CD4 count

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KEY WORDS
HIV; attrition; retention; India; operational research

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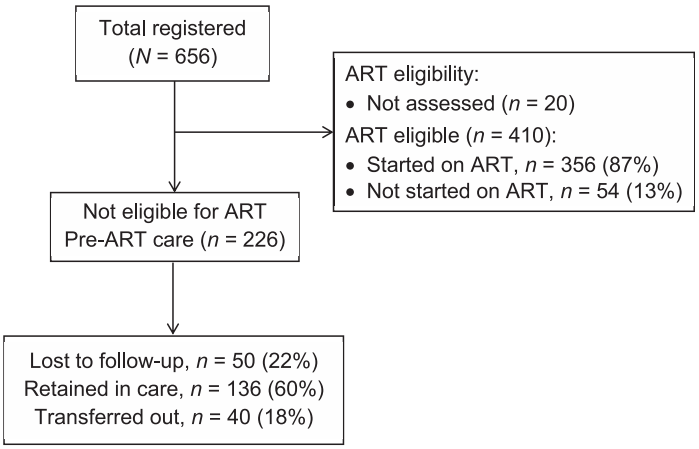

FIGURE Retention of HIV-infected children in pre-ART care in Tamil Nadu ART centres, Tamil Nadu, South India, 2012. ART = antiretroviral therapy; HIV = human immunodeficiency virus.

<350 cells/μl or <15% in those aged 36–59 months and CD4 count < 200 cells/μl in those aged >59 months).[2] If a patient was documented as 'ART eligible' in the records and started on ART, even though there was no full documentation of CD4 count and/or WHO clinical staging, we considered such patients to be eligible for ART for this analysis.

A child registered under pre-ART care is scheduled to visit the ART centre at least once every 6 months for clinical follow-up and CD4 count. During this visit, the child and the care giver are counselled on positive healthy living, family and social support, risk reduction behaviour, substance abuse and its side-effects, proper dietary intake/nutritional counselling, accessing appropriate health care services when required and appropriate psychosocial support. If children do not attend on the scheduled date, measures to trace them are initiated immediately, which include contacting the care givers by telephone and informing the outreach workers of the community care centres for help in tracing the patients and having them return to care.

For the purpose of this study, all children on pre-ART care were assessed for their status at 1 year after registration up to 31 December 2013 to see whether they were on care or lost to follow-up. If a child had not visited an ART centre within 1 year of registration, she or he was considered as 'lost to follow-up'; if the child visited at least once within 1 year, she or he was considered as 'retained in care'. Children who transferred out to other ART centres in the programme were considered as 'retained in care' for the purpose of this analysis.

Data collection and analysis

Data were extracted from the patient treatment cards and the registers available at the centre by the data entry operators or staff at the respective ART centres. The variables collected included baseline sociodemographic data (age at registration in completed years, date of registration and HIV diagnosis, sex, and HIV status of parents), clinical information (opportunistic infections, WHO clinical staging, CD4 cell count), ART eligibility, ART initiation, and pre-ART outcome from the pre-ART and ART registers and treatment cards (white cards).

The data were entered into Excel spreadsheets (Microsoft Corp, Redmond, WA, USA). The databases were checked for inconsistencies or discrepancies that were resolved by referring to the individual patient treatment cards kept at the ART centres. After removing personal identifiers, a duplicate version of the final database was used for statistical analysis using EpiData analysis software v. 2.2.2.182 (EpiData Association, Odense, Denmark). Proportions were used to summarise the baseline demographic and clinical characteristics. To assess the relationship of demographic and clinical characteristics with loss to follow-up (LTFU), undajusted relative risks (RR) with 95% confidence intervals (CI) were calculated and the χ^2 test was used. A P value of $\leqslant 0.05$ was considered statistically significant. We used an exploratory approach for the analysis and did not have any a priori hypothesis.

Ethics approval

The study was approved by the Ethics Committees of NACO, New Delhi, India, and the National Institute for Research in Tuberculosis, Chennai, India. As this was a retrospective study using programme data, informed consent from individual patients was not obtained. The ethics committees waived the need for individual informed consent.

RESULTS

Of 656 children registered for HIV care in 2012, 20 (3%) were not assessed for ART eligibility. Of those remaining, 410 (64%) were found to be ART-eligible at baseline, while 226 (36%) were not eligible and entered pre-ART care. Of the 410 ART-eligible children, 356 (87%) were started on ART.

Of the 226 children who were enrolled into pre-ART care, 110 (49%) were females and 160 (71%) were in the 5–14 years age group. The median age (interquartile range, IQR) of the children was 7 (IQR 4–10) years. Only 20 (9%) of the cohort were documented to have had any OI, of whom 10 (50%) had acute respiratory infection. None of the children were documented to be suffering from tuberculosis.

At 1 year of registration, 50 children (22%) were lost to follow-up, 40 (18%) were transferred out and 136 (60%) were retained in care (Figure). Among the 136 children retained in care, 11 subsequently became eligible for ART, and of these, 9 were started on ART. The median (IQR) CD4 count at the time of the follow-up visit was 798 (593–1100) cells/μl, and 97% were in WHO clinical stages 1 or 2. In an unadjusted analysis, none of the demographic and clinical characteristics were found to be associated with LTFU (Table). As no variables were associated in the unadjusted analysis, we did not perform an adjusted analysis.

DISCUSSION

This first statewide study from India on pre-ART care among children showed that 20% of children were lost to follow-up within 1 year of registration. LTFU remained similar across the subcategories of demographic and clinical variables. While not statistically significant, there was a trend towards lower CD4 counts being associated with a higher chance of LTFU. Children with lower CD4 counts could thus be prioritised for close follow-up and enhanced monitoring.

Possible reasons for LTFU may be unaccounted for deaths, given the rapid progression of HIV among children,[12] 'silent' transfers to other ART centres in the public or private sector, healthy children whose care givers do not perceive the need to visit the ART centre regularly[13] and a lack of incentive for patients to visit ART centres regularly, as cotrimoxazole preventive therapy and isonozid preventive therapy were not routinely provided under pre-ART care. The high turnover of medical officers managing

TABLE Demographic and clinical characteristics of HIV-infected children lost to follow-up in pre-ART care in the state of Tamil Nadu, South India, 2012 (n = 226)

Characteristics*	Total	LTFU *n* (%)	RR (95%CI)	*P* value
Total	226	50 (22)	–	
Sex				
Male	116	25 (22)	1	0.83
Female	110	25 (23)	1.1 (0.7–1.7)	
Age, years				
<5	66	18 (27)	1.4 (0.8–2.3)	0.23
⩾5	160	32 (20)	1	
HIV status of father (*n* = 158)				
HIV-positive	136	26 (19)	0.7 (0.3–1.5)	0.38
HIV-negative	22	6 (27)	1	
HIV status of mother (*n* = 183)				
HIV-positive	176	36 (20)	0.5 (0.2–1.2)	0.15
HIV-negative	7	3 (43)	1	
CD4 cell count, mm^3 (*n* = 219)				
⩽500	22	8 (36)	2.0 (1.0–4.1)	0.06
501–1000	108	24 (22)	1.2 (0.7–2.2)	0.46
>1000	89	16 (18)	1	
WHO staging (*n* = 210)				
Stage I	144	27 (19)	1	
Stage II	66	14 (21)	1.1 (0.6–2.1)	0.68
Opportunistic infection (*n* = 225)				
Yes	20	2 (10)	1	0.18
No	205	47 (23)	2.3 (0.6–8.7)	

*Information missing: HIV status of father for 68 children, HIV status of mother for 43 children, CD4 cell count for 7 children, WHO staging for 16 children, opportunistic infection for 1 child.
HIV = human immunodeficiency virus; ART = antiretroviral therapy; LTFU = loss to follow-up; RR = risk ratio; CI = confidence interval; WHO = World Health Organization.

the ART centres, deficiencies in tracing children recorded as LTFU and returning them to care may be other reasons.

Although not entirely comparable, this might be viewed as a considerable improvement over the LTFU rate of 82% reported in our previous study from a single ART centre in the same study setting.[7] It is still, however, suboptimal. The decrease in LTFU could be attributed to several factors. First, following the previous operational research study, the high findings of LTFU among children were shared with the district programme managers in the state, who were sensitised to carefully monitor this issue. The counsellors at the ART centres were asked to document the correct addresses and telephone numbers of the clients while registering, and to verify the accuracy of telephone numbers by test-calling during the counselling session. The telephone number of the ART centre was given to the clients to contact if required. The lists of LTFU clients were shared with the outreach workers and volunteers from non-governmental organisation partners to enable the tracing and retreival of clients back into care. Second, the national guidelines changed in 2013 to include an indicator for pre-ART LTFU in the ART centre monthly reports, followed by intensive training of all ART staff in monitoring and evaluation, thus enabling better monitoring. Third, the revised national guidelines for ART initiation (2012) would have increased the overall numbers of children eligible for ART, i.e., ART for all children aged <24 months with confirmed HIV infection and for children aged >24 months of age with CD4 viral load of <25%, thereby reducing the number of children enrolled in pre-ART care.

Several studies have reported high LTFU in pre-ART care among children. Studies from Cambodia and sub-Saharan Africa reported even higher rates of attrition of respectively 22% and 37%.[6,9–11] A study from a non-governmental setting from a neighbouring state in south India reported an LTFU rate of 15% among children.[5] Due to differences in the availability and quality of counselling and testing (CD4 cell count) services and ART initiation guidelines, it is difficult to compare LTFU across different study settings.

The study has some strengths. It is the first statewide report from India providing information on pre-ART LTFU among children, and the findings are therefore generalisable to the whole state. Second, the study was conducted in the routine programme setting, reflecting the true situation in the field. Third, we adhered to international standards in conducting and reporting this study (the Strengthening the Reporting of OBservational studies in Epidemiology [STROBE] guidelines).[14]

The study also has some limtiations. As it was operational research using routinely collected data, errors in documentation or reporting by programme staff could not be ruled out. Also, some variables had a significant proportion of missing information. While we considered 'transfer out' clients to be retained in care for the purpose of analyses, this aspect needs further investigation. It was not clear from the records if the patients who transferred out reached their destination ART centre and continued to receive care. Although a sensitivity analysis (excluding all transfers out) did not make any difference to the factors associated with LTFU, we could not demonstrate statistical significance in

the associations, possibly due to the low numbers in the subgroups. LTFU can occur between the HIV diagnosis and reaching the ART centre, and this study did not capture these pre-registration attritions. We also did not assess the exact reasons for LTFU, and we recommend future qualitative studies to explore this theme.

Providing ART is the biggest incentive to retaining PLHIV in care. Previous studies have shown better patient retention among those who are on ART compared to those in pre-ART care.[5,15] If we adopt the new WHO policy of universal ART,[16] the need for pre-ART care would be limited. In the study setting, this would mean that an additional one third of children will become eligible for ART, which has resource implications. In the meantime, the implementation of cotrimoxazole preventive therapy and isoniazid preventive therapy, instituting a mechanism to actively trace and retreive LTFU patients and the provision of a nutrional and social support system with the active involvement of nongovernmental organisations may help to reduce rates of LTFU.

CONCLUSION

Twenty per cent of children registered under pre-ART care in Tamil Nadu, India, were lost to follow-up at 1 year after registration. Measures to prevent LTFU and reinforce retrieval actions should be strengthened in the existing national HIV programme. The implementation of WHO-recommended universal ART for all persons who test positive for HIV, irrespective of their CD4 cell count, will completely eliminate the need for pre-ART care.

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Contexte : Les enfants âgés de <15 ans constituent 7% de toutes les personnes vivant avec le virus de l'immunodéficience humaine (VIH) en Inde. Une étude précédente émanant d'un centre de thérapie antirétrovirale (TAR) d'Inde du Sud a rapporté 82% de pertes de vue (LTFU) parmi les enfants en soin pré-ART (2006–2011).

Objectif : Evaluer la proportion de LTFU dans l'année suivant l'enregistrement parmi les enfants (âgés de <15 ans) infectés par le VIH enregistrés dans les 43 centres du TAR de l'état du Tamil Nadu, Inde, pendant l'année 2012.

Schéma : Une étude rétrospective de cohorte impliquant une revue des dossiers du programme.

Résultats : Sur 656 enfants enregistrés pour une prise en charge du VIH, 20 (3%) n'ont pas été évalués pour leur éligibilité au TAR. Parmi les autres, 226 (36%) n'ont pas été éligibles au TAR et sont entrés en soins pré-TAR. Parmi eux, à une année de l'enregistrement, 50 (22%) ont été LTFU, 40 (18%) ont été transférés et 136 (60%) sont restés en soins dans le même centre. L'âge de l'enfant, le sexe, le stade de l'Organisation mondiale de la santé et la survenue d'infections opportunistes n'ont pas été associés avec le LTFU.

Conclusion : Un enfant sur cinq enregistré en prise en charge pré-TAR a été LTFU. Les mesures de prévention des LTFU et les efforts de localisation doivent être renforcés au sein du programme national VIH existant.

Marco de referencia: Los niños < l5 años de edad representan el 7% de todas las personas positivas frente al virus de la inmunodeficiencia humana (VIH) en la India. En un estudio anterior realizado en un centro de tratamiento antirretrovírico (TAR) en el sur del país, se notificó una tasa de pérdida durante el seguimiento de 82% en los niños que acudían a la atención pre-TAR (del 2006 al 2011).
Objetivo: Evaluar la proporción de pérdidas durante el seguimiento durante el primer año después del registro de los niños infectados por el VIH (<15 años de edad) en todos los 43 centros de suministro de TAR en el estado de Tamil Nadu, en la India, en el año 2012.
Método: Un estudio retrospectivo de cohortes a partir de los registros del programa.
Resultados: De los 656 niños registrados en la atención de la infección por el VIH, en 20 no se evaluó su aptitud para recibir el TAR (3%). De los niños restantes, 226 no cumplían los requisitos del TAR (36%) y se inscribieron en la atención pre-TAR. De este grupo, un año después del registro, 50 niños se habían perdido durante el seguimiento (22%), 40 se habían transferido a otro centro (18%) y 136 permanecían en la atención en el mismo centro (60%). La edad de los niños, el sexo, el estadio clínico de la enfermedad según la escala de la Organización Mundial de la Salud y la aparición de una infección oportunista no se asociaron con la pérdida durante el seguimiento.
Conclusión: Uno de cada cinco niños registrados en la atención pre-TAR se perdió durante el seguimiento. Es preciso fortalecer las medidas que prevengan estas pérdidas y las intervenciones de recuperación de los pacientes en el programa nacional contra el VIH que existe en el país.

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