Challenges in setting up the antiretroviral paediatric registry in South Africa: Lessons learned from Free State Province clinics

Despite the remarkable progress towards achieving the UNAIDS 95-95-95 (United Nations Programme on HIV and AIDS) targets in South African (SA) adults, progress in the paediatric population seems to be lagging.[1,2] Owing to their vulnerability, differentiated approaches to care are necessary for these groups of patients to attain the UNAIDS 95-95-95 targets. Notably, SA boasts the world's largest paediatric HIV care and treatment programme.[3] Statistical data from the year 2021 demonstrated that 270 000 SA children were living with HIV. This figure has been projected to increase to more than 300 000 in 2023.[4] The SA data from the latest global Joint UNAIDS estimates show that ~79% of children living with HIV know their status. Out of these, only 47% are on treatment, and only about 34% of those on treatment are virally suppressed.[4] Globally, only 4% of people living with HIV are children. However, they account for 15% of all AIDS-related deaths.[5] In SA, HIV/AIDS remains a major factor in the morbidity and mortality of children.[6] A recent study in a SA paediatric cohort reported a high rate of loss to follow-up and virological non-suppression in HIV-infected children on antiretrovial therapy (ART), indicating an urgent need for improved quality of care for children on ART.[2] Therefore, there is a need to institute a mechanism of safety monitoring.

The antiretroviral paediatric registry is a system that collects and updates information on children who receive ART in Free State Province. The registry aims to cover selected clinics that provide ART for children in the province. The registry will play a significant role in improving the quality of care for these children by allowing for timely interventions, providing detailed information about possible adverse drug reactions (ADRs) and monitoring the effectiveness and safety of ART. Focusing on important key indicators and context-relevant tools, the registry helps collect central data on baseline characteristics of paediatric patients (aged 0 - 13 years) at the initiation of ART and follow-up on treatment, including tolerability and adherence to different ART and associated ADRs as well as spontaneous ADR reporting. The ARV paediatric registry will achieve the following four major objectives:

(*i*) detect ADRs/events as soon as they occur and promptly report to healthcare providers to enable successful drug therapy
(*ii*) determine the long-term burden of *in-utero* fetal exposure to ARV and TB drugs by identifying possible congenital and neurodevelopmental problems
(*iii*) determine the burden of ARV and TB drug-related morbidity and mortality in paediatric patients on both therapies
(*iv*) provide an early warning signal of the potential risk to assist clinicians in weighing the potential risks/benefits of ARV and TB drugs in *in-utero* fetal exposure and paediatric exposure.

Generally, the register provides real-time accurate information on paediatric ART and comorbidities from all clinics providing care for paediatric patients on ART in Free State Province, making interventions easier. As children living with HIV reach adulthood, the major concerns of clinicians are treatment adherence and the prevention of comorbidities.[7] The programme was initiated in five clinics, and after that, it was rolled out to other selected clinics in Free State Province. However, setting up the registry has encountered some challenges, such as:

- Incomplete patient records: this affects the accuracy and reliability of the data in the registry. For instance, some co-infected patients with medical conditions such as tuberculosis (TB) and epilepsy do not have their medication and dosage information documented, which may interfere with their ART regimen.
- Communication/co-ordination: there is a need for regular and effective communication and co-ordination among healthcare providers and the research/pharmacovigilance team. There have been cases of mismatch between the medication prescribed by doctors/nurses and the medication dispensed by the pharmacy. This confuses the specific ART combination given to the patient.
- Logistics: owing to the distance between clinics, more funds are needed for transportation and other expenses to ensure the completeness and accuracy of the data in the registry.
- Research: the registry can serve as a valuable data source for novel research on the safety and effectiveness of ART for paediatric patients. Despite the development in paediatric ART in the ODYSSEY trial, published in 2022,[8] there is a recent report of drug resistance to dolutegravir, a highly effective ART drug, in a paediatric SA patient.[9] This calls for spontaneous monitoring of ADRs, which can be easily extracted from the registry. The registry can also help isolate the incidence of drug interactions when multiple medicines are combined for co-infection or other medical conditions.
- The ARV paediatric registry is a vital initiative for improving the quality of care for children who receive ART in Free State Province. The registry is currently being implemented, and efforts are being made to address the challenges identified and improve surveillance of ADRs. Successful implementation means that the registry can be extended to other parts of SA.

B R Omotoso
Department of Internal Medicine, Faculty of Health Sciences, University of the Free State, Bloemfontein, South Africa
Omotoso.BR@ufs.ac.za

R Baleni
Department of Internal Medicine, Faculty of Health Sciences, University of the Free State, Bloemfontein, South Africa

M Dheda
Pharmacovigilance Centre for Public Health, National Department of Health, Dr AB Xuma Building, Pretoria, South Africa

T Mofokeng
Department of Internal Medicine, Faculty of Health Sciences, University of the Free State, Bloemfontein, South Africa

Keywords: HIV, paediatric, adverse drug reactions

S Afr Med J 2024;114(7):e2115. https://doi.org/10.7196/SAMJ.2024.v114i7.2115

1. Archary M, Van Zyl R, Sipambo N, Sorour G. Opinion paper: Optimised paediatric antiretroviral treatment to achieve the 95-95-95 goals. South Afr J HIV Med 2021;22(1):a1278. https://doi. org/10.4102/sajhivmed. v22i1.1278
2. UNAIDS. AIDS and the Sustainable Development Goals. Geneva: UNAIDS, 2024. https://www.unaids.org/en/AIDS_SDGs#:~:text=A%20core%20principle%20of%20the,health%20and%20vulnerability%2C%20being%20addressed (accessed 16 June /2024).
3. Van Liere GA, Lilian R, Dunlop J, et al. 2021. High rate of loss to follow-up and virological non-suppression in HIV-infected children on antiretroviral therapy highlights the need to improve quality of care in South Africa. Epidemiol Infect 2021;149:e88. https://doi.org/10.1017/S0950268821000637
4. World Data Atlas 2021. https://www.unaids.org/sites/default/files/media_asset/2020_aids-data-book_en.pdf (accessed 31 March /2024).
5. Joint United Nations Programme on Hiv/Aids (UNAIDS). UNAIDS Data 2023. https://www.unaids.org/en/resources/documents/2024/unaids-data (accessed 30 March 2024).
6. Ngoyi K, Hlabyago K, Ogunbanjo G, Steyn C, Bongongo, T. Prevalent clinical assessments of HIV positive infants in a South African district hospital. Open Public Health J 2024;17(1):E18749445278115. https://doi.org/10.2174/0118749445278115231228054735
7. Escosa-García L, Sainz T. HIV and ART in children. Front Pediatr 2022;10:1074684. https://doi.org/10.3389/fped.2022.1074684
8. Malinga S, Khan A, Archary M. Breaking the unbreakable: A paediatric case of dolutegravir resistance from KwaZulu-Natal. South Afr J HIV Med 2023; 24(1):1458.
9. Amuge P, Lugemwa A. Wynne B, et al. Once-daily dolutegravir-based antiretroviral therapy in infants and children living with HIV from age 4 weeks: results from the below 14 kg cohort in the randomised ODYSSEY trial. The Lancet HIV, 2022;9(9):e638-e648. https://doi.org/10.1016/S2352-3018(22)00163-1