

Factors associated with the risk of HIV infection among HIV-exposed infants in Malawi: 2013–2020

Wingston Felix Ng'ambi ^{1,2,3}, Fatma Aziza Merzouki,^{1,3} Janne Estill,^{1,3} Erol Orel,^{1,3} Tiwonge Chimpandule,⁴ Rose Nyirenda,⁴ Olivia Keiser^{1,3}

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¹GRAPH Network, University of Geneva, Geneva, Switzerland

²Epidemiology and Biostatistics, Kamuzu University of Health Sciences, Lilongwe, Central Region, Malawi

³Global Health, University of Geneva, Geneva, Switzerland

⁴Department of HIV/AIDS, Ministry of Health, Lilongwe, Malawi

Correspondence to

Wingston Felix Ng'ambi;
wingston.ngambi@gmail.com

ABSTRACT

Background Despite the availability of individual-level data of infants accessing HIV DNA-PCR testing service, there has been little in-depth analysis of such data. Therefore, we describe trends in risk of HIV infection among Malawi's HIV-exposed infants (HEI) with DNA-PCR HIV test result from 2013 to 2020.

Methods This is an implementation study using routinely collected patient-level HIV DNA-PCR test result data extracted from the national Laboratory Management Information System database managed by the Department of HIV/AIDS between 1 January 2013 and 30 June 2020. We calculated frequencies, proportions and odds ratio (OR) with their associated 95% CI. We performed a random-effects logistic regression to determine the risk factors associated with HIV infection in infants, controlling for the spatial autocorrelation between districts and adjusting for other variables.

Results We evaluated 255 229 HEI across 750 facilities in 28 districts. The HIV DNA-PCR test was performed within 2 months in 57% of the children. The overall HIV prevalence among all tested HEI between 2013 and 2020 was 7.2% (95% CI 7.1% to 7.3%). We observed a decreasing trend in the proportion of HEI that tested HIV positive from 7.0% (95% CI 6.6% to 7.4%) in 2013 to 5.7% (95% CI 5.4% to 5.9%) in 2015 followed by an increase to 9.9% (95% CI 9.6% to 10.2%) in 2017 and thereafter a decreasing trend between 2017 (i.e. 9.72% (95%CI: 9.43-10.01)) and 2020 (i.e. 3.86% (95%CI: 3.34-4.37)). The HIV prevalence increased by age of the HEI. There was spatial heterogeneity of HIV prevalence between districts of Malawi. The prevalence of HIV was higher among the HEI from the Northern region of Malawi.

Conclusion The main findings of the study are that the DNA test is performed within 2 months only in 57% of the children, that the decreasing trend of HIV prevalence among HEI observed up to 2015 was followed by an increase up to 2017 and a decrease afterwards, and that the risk of HIV infection increased with age at HIV testing. We summarised spatial and temporal trends of risk of HIV infection among HEI in Malawi between 2013 and 2020. There is need to ensure that all the HEI are enrolled in HIV care by 8 weeks of age in order to further reduce the risk of HIV in this population.

INTRODUCTION

Of the estimated 38.0 million people living with HIV worldwide in 2020, 2.8 million were

What is known about the subject?

- ▶ Malawi has implemented the early infant diagnosis (EID) since 2009 and studies on EID in Malawi have focused on just one or two health facilities.

What this study adds?

- ▶ Our study has shown that there is spatial and temporal heterogeneity in risk of HIV infection amongst the HIV-exposed infants in Malawi between 2013 and 2020.

children aged 0–19.¹ Globally, most of the children living with HIV are found in Africa. Sub-Saharan Africa has the largest burden of paediatric HIV in the world.^{2,3} In Malawi, the HIV estimates from the Spectrum software indicate approximately 2500 children living with HIV and 1800 AIDS deaths among children aged below 15 years in 2020.⁴

Although countries in sub-Saharan Africa have registered very high uptake of prevention of mother to child transmission (PMTCT) services, the uptake of services for HIV-exposed infants (HEIs) have been suboptimal for various reasons in most low-income and middle-income countries.^{5,6} Diagnosis of paediatric HIV has been one of the major challenges in resource-limited settings leading to lower proportion of children living with HIV who start antiretroviral therapy (ART) compared with adults.⁷ HIV ascertainment among HEI is critical in facilitating provision of life-saving treatment for those infected with the virus and enables access to HIV prevention information and support for those testing negative. The WHO guidelines recommend that all infants exposed to HIV during pregnancy, labour, delivery and breast feeding have HIV status ascertainment by the age of 6 weeks with follow-up tests at 12 and 24 months.⁷

The Malawi government started the early infant diagnosis (EID) programme in 2009 following a recommendation by the WHO so that all infants exposed to HIV during pregnancy, labour, delivery and breast feeding have HIV status ascertainment by the age of 6 weeks with follow-up HIV tests at 12 and 24 months.⁸ HIV ascertainment among HEI is critical in facilitating provision of life-saving treatment for those infected with the virus and enables access to HIV prevention information and support for those testing negative. Currently over 690 facilities are providing EID services in Malawi.⁹ The Malawi Ministry of Health (MOH) as well as the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) supported programmes track HIV prevalence among HEI. Since the introduction of this programme no in-depth analyses have been done to assess the trends of HIV prevalence among the DNA-PCR tested HEI at a national level. However, in-depth analyses are necessary for a greater understanding of HIV prevalence for EID programme quality improvement and to assess the effectiveness of PMTCT strategies in Malawi and other similar settings. Furthermore, in-depth analyses of the EID programme are necessary in tracking the first and second steps of the UNAIDS 95-95-95 target for ending HIV/AIDS by 2030. This study therefore aims to describe HIV prevalence trends and assess the factors associated with the risk of HIV infection of HEI tested with DNA-PCR in Malawi between 2013 and 2020.

METHODS

Study design

This is an implementation study involving a retrospective review of patient-level HIV DNA-PCR data obtained from the National Laboratory Information Management Systems (LIMS) national database containing data collected between 2013 and 2020 in Malawi.¹⁰ The LIMS database is managed by MOH Diagnostics in the Department of Technical and Support Services (HTSS). The LIMS database contains individual level DNA-PCR data for HIV ascertainment among the HEI aged 24 months and below. Data across all the districts and facilities are included. The database has inbuilt tools for performing data quality assessment like range checks and other associated validation rules. The data are entered at the DNA-PCR laboratories in Malawi. By 30 June 2020, there were 10 laboratories performing DNA-PCR HIV testing for HEI in Malawi: Dream laboratory in Blantyre, Dream Laboratory in Balaka, Kamuzu Central Hospital, Mzimba District Hospital, Mzuzu central Hospital, Nsanje District Hospital, Partners in Hope, Queen Elizabeth Central Hospital, Thyolo District Hospital and Zomba Central Hospital.

Management of HEI in Malawi

The management of HEI is based on the Malawi ART/PMTCT guidelines.⁸ The HEIs are registered in the EID Programme at 6 weeks after birth, and a HIV DNA-PCR test is conducted during the registration into the EID

programme. In addition, HEI are put on Cotrimoxazole Preventive Therapy to prevent certain opportunistic infections.⁸ Rapid HIV diagnostic tests are done at 12 months and 24 months or as necessary.⁸

Statistical analysis and data management

The data were managed in Stata V.16.0 (StataCorp). The response variable was HIV infection status. The independent variables were: age (in months) at sample collection, year sample collected, sex, facility location (rural/urban) and region (north/centre/south). A descriptive analysis was first performed detailing the characteristics of the study population. We also fitted bivariate analysis of each of the independent variable and HIV status. We fitted a multivariable logistic regression model of HIV infection, with HIV clustered by district, using a forward stepwise selection method, with age and sex entered as a priori variables. Since HIV prevalence varies by district, we controlled for random clustering effect of the district when conducting logistic regression of the independent variables on HIV infection. We presented both crude and adjusted OR of HIV infection of each independent variable. Multiple imputation chained equations, with five imputation rounds and 5000 permutations, were used to impute missing data of the following covariables: age category when sample was taken, HIV status, child's sex and year of sample collection. The analysis produced the within district variation (τ) and between district variation (σ) of the risk of HIV infection due to controlling for clustering effect of the district. We presented the annual the prevalence of HIV for all the districts of Malawi using a forest plot of the pooled prevalence of HIV by districts in order to get the degree of heterogeneity of the HIV prevalence by districts. Statistical significance was set at $p < 0.05$.

Patient and public involvement statement

To determine the risk of HIV infection in HEI data on HIV status need to be collected in the implementations of the EID programme in Malawi. This risk ascertainment begins with the enrolment of HEI into the EID programme. Every mother of HEI undergoes a counselling session in order to be sensitised on the follow-up of her child in the EID programme. The mothers of HEI ensures that the HEI get enrolled and followed up in the EID programme. All follow-up processes conform to the national HIV treatment guidelines. The results of this study will be shared with the HIV programme managers across health facilities of Malawi. This will ensure that the results inform practice at both facility and national levels.

RESULTS

Characteristics of HEI who had DNA-PCR HIV test

The characteristics of HEI with HIV DNA-PCR testing are shown in [table 1](#). We evaluated 255 229 HEI with DNA-PCR results. Of these, 145 622 (57%) had HIV DNA-PCR testing done before 2 months after birth. The numbers

Table 1 Characteristics of HIV-exposed Infants with DNA-PCR HIV test results between 2013 and 2020 in Malawi

Patient characteristics	n (%)
Total	255 229 (100.0)
Gender	
Male	122 610 (48.0)
Female	125 275 (49.1)
Missing	7344 (2.9)
Location	
Rural	168 258 (65.9)
Urban	86 971 (34.1)
Age at sample draw (in months)	
0–1	145 622 (57.1)
2–5	74 707 (29.3)
6–11	21 307 (8.4)
12–17	3337 (1.3)
18–24	1902 (0.8)
Missing	8354 (3.3)
Region	
Northern	22 897 (9.0)
Central	72 633 (28.5)
Southern	159 699 (62.6)
Year sample drawn	
2013	16 308 (6.4)
2014	25 858 (10.1)
2015	41 271 (16.2)
2016	41 178 (16.1)
2017	42 252 (16.6)
2018	43 370 (17.0)
2019	36 372 (14.3)
2020*	7741 (3.0)
Missing	879 (0.3)

*The data are from January to June.

of males and females tested for HIV were similar, 159 699 (63%) were from the southern region while 22 897 (9%) were from the northern region (table 1). We observed an increasing trend in the number of HEI tested for HIV from 16 308 (6%) in 2013 to 43,370 (17.0%) in 2018 and a decrease in 2019 (table 1). The proportion of missing data ranged from 2.9% (7344 of 255 229) for sex of the child to 3.3% (8354 of 255 229) for age at sample draw.

Factors associated to HIV prevalence among HEI with HIV DNA-PCR test

A total of 235 774 (92%) children had complete data on location and region. We observed that 16 936 (7.2%, 95% CI 7.1% to 7.3%) of the 235 774 HEI had positive HIV DNA-PCR results. The factors associated with the risk of HIV infection are shown in table 2. The adjusted odds of HIV infection among female HEI were 1.07 (95%

CI 1.03% to 1.10%, $p < 0.001$) times those of male HEI. There was increasing odds of HIV infection by age at HIV testing (AOR 3.47; 95% CI 3.33 to 3.62 and AOR 36.24; 95% CI 32.69 to 40.17) among those aged 2–5 and 18–24 months, respectively, compared with those aged less than 2 months at HIV DNA-PCR sample collection). Infants residing in urban areas had higher odds of HIV infection compared with those living in rural areas. After adjusting for age, sex, location and region, the infants that were tested between 2016 and 2019 were more likely to be HIV positive compared with those tested in 2013 (see table 2). The data for the year 2020 is from January to June.

Temporal and spatial distribution of the HIV prevalence

The trend in HIV prevalence across the regions is shown in figure 1. The overall HIV prevalence dropped from 7.0% (95% CI 6.6% to 7.4%) in 2013 to 5.7% (95% CI 5.4% to 5.9%) in 2015 followed by an increase to 9.9% (95% CI 9.6% to 10.2%) in 2017 and then a decreasing trend to 4.2% (95% CI 3.71% to 4.63%) in 2020. Between 2015 and 2017, the northern, central and southern regions experienced an increase in the trend of risk of HIV infection (see figure 1). There was a strong association between HIV infection and district of residence ($p < 0.01$). Within each district, the HIV prevalence varied by 0.78% (95% CI 0.42% to 1.44%) over the 2013–2020 time period. There was variation in HIV prevalence across the districts ($\sigma = 16.13\%$; 95% CI 11.88% to 21.90%; $p < 0.001$). Some districts had the HIV prevalence as high as 9.9% while in others it was as low as 4.6% between 2013 and 2020 as shown in figure 2. The six districts with the highest risk of HIV infection among HEI were Lilongwe, Likoma, Nkhonkhotakota, Chitipa, Karonga and Nkhata Bay while the lowest risk of HIV infection was observed in Neno, Chiradzulu, Phalombe, Thyolo, Mulanje and Dedza.

DISCUSSION

This is a national analysis of HIV DNA-PCR data obtained from the laboratory management information system (LIMS) in Malawi. The overall HIV prevalence among the DNA-PCR tests was high implying the need to strengthen the MTCT programme. We observed increasing trend in probability of HIV infection by age at sample collection. There was a decreasing trend in HIV prevalence in the first years of the analysis and the observed increase in 2017–2018. HIV prevalence differed across the districts of origin of the HEI, and the highest risk of HIV infection were observed among the HEI from the Northern region. Furthermore, the odds of HIV infection were higher in urban than in rural areas.

The prevalence of HIV acquisition among infants exposed to HIV in our study was almost two times higher than that observed in South Africa^{11 12} but similar to other studies conducted in Malawi and India.^{13–15} Consistent with other studies, the prevalence of HIV infection of the HEI was higher with older age at DNA-PCR sample

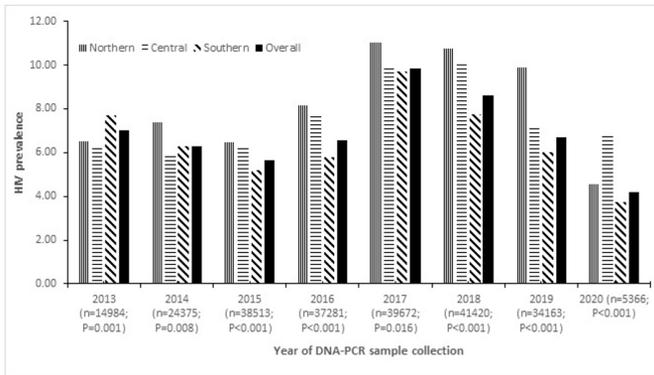


Figure 1 : Temporal Trend in HIV prevalence amongst HIV exposed infants in Malawi across the Northern, Central and Southern Regions between 2013 and 2020

collection.¹⁶ With the high prevalence of HIV infection being observed among EID in the Northern Region of Malawi, it is imperative to consider the northern region with quality improvement projects aimed at bringing down the HIV infection risk among HEI. The northern region does not have as many HIV implementing partners as the other regions due to funding prioritisation; among the general population HIV infection risk is substantially higher in the southern and central regions than the northern region.¹⁷ Similar to other studies showing higher HIV prevalence among the females than the males,¹⁷ we also observed higher prevalence of HIV by female than male children.

Our findings also demonstrate considerable heterogeneity in prevalence of HIV among the HEI in Malawi. Several spatial epidemiological studies indicate spatial variation of diseases which could be attributed to social

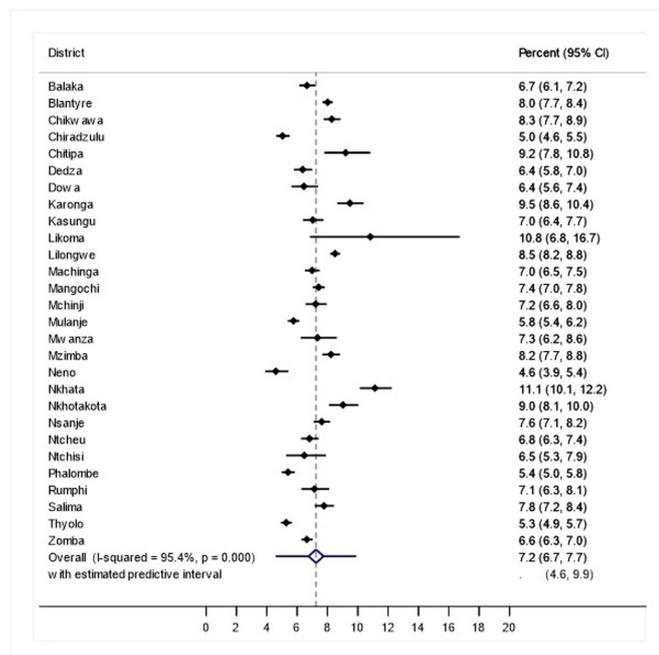


Figure 2 : Pooled HIV Prevalence among the HIV Exposed Infants with HIV-DNA PCR Tests in Malawi between 2013 and 2020

and cultural factors.^{15 18 19} Generally, studies of HIV epidemiology in Malawi have been highly predominant in the districts in the southern region, followed by the central and northern regions.^{17 20} The spatial pattern of the risk of HIV infection would imply the need to target PMTCT interventions in the districts with high risk of paediatric HIV acquisition in order to improve the health of the children and the women.¹⁷

There has been a temporal trend in HIV prevalence by year. This is consistent with many studies and surveys conducted in Malawi that have shown a downward trend in the risk of HIV infection.¹⁷ The upward increase in the risk of HIV infection of the HEI may have occurred as a result of a weaker implementation of PMTCT services especially with regard to follow up of HEI which has been reported in Malawi.¹³ This is also consistent with what has been observed in sub-Saharan African settings with the general decreasing trend in HIV infection among the HEI. Possible explanations to the downward trend in HIV infections include successful implementation of PMTCT programmes and the high ART coverage in general.^{21 22} However, the data do not show any significant decrease in the prevalence of HIV and there is need to further reduce the risk of HIV among the HEI if much improvement is to be achieved in reducing paediatric HIV infection in Malawi.

The major strength of this study is the large sample size and being conducted within a routine programme setting, which has the potential to improve the EID programmes in Malawi and similar settings. The major limitation of this study is that the data in LIMS only cover baseline data with no follow-up tests conducted with rapid HIV diagnostic tests at 12 and 24 months. The Department of HIV/AIDS of the Malawi MOH and Population should make an attempt to have all HIV laboratory tests of the HEI recorded in the LIMS. Such data should be managed in a way that it would be possible to track the HEI throughout the 24 months of follow-up in the EID programme. Another limitation is that the data are not linked to data on ART initiation among the HEI that were found to be HIV positive. Furthermore, the maternal information was not captured in LIMS hence we could not include such information in this analysis. Having such data would provide more information on the risk factors for HIV infection on HEI.

CONCLUSION

In conclusion, this study has shown that there is spatial and temporal heterogeneity in risk of HIV infection among the HEI in Malawi between 2013 and 2020. There is a need for further strengthening the EID programme to ensure that all the HEI are enrolled in care by 8 weeks of age. As this study only looks at HIV DNA-PCR test results, there is a need for a follow-up study examining risk of HIV infection in the entire 24 months of follow-up in order not to underestimate or overestimate the true risk of HIV infection. Access to HIV DNA-PCR testing will

ensure that 95% of the HEI with HIV will have known HIV status hence supporting the way towards reaching the 95-95-95 target HIV strategy by 2030 in Malawi.²²

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Contributors WFN led the manuscript writing, conducted data management and analysis; FAM advised on the data analysis and policy insights on the paper; JE advised on data analysis and policy insights on the paper; EO advised on data analysis and policy insights on the paper and OK advised on the analysis and policy insights on the paper. All authors read and approved the final manuscript. OK was responsible for the full conduct of the study. Prof Olivia Keiser acts as the guarantor for the work.

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Patient consent for publication Not applicable.

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ORCID iD

Wingston Felix Ng'ambi <http://orcid.org/0000-0003-3967-905X>

REFERENCES

- 1 Unicef, Global and regional trends, 2021. Available: <https://data.unicef.org/topic/hivaids/global-regional-trends/>
- 2 Remera E, Mugwaneza P, Chammartin F, *et al*. Towards elimination of mother-to-child transmission of HIV in Rwanda: a nested case-control study of risk factors for transmission. *BMC Pregnancy Childbirth* 2021;21:339.
- 3 Ubesie AC. Pediatric HIV/AIDS in sub-Saharan Africa: emerging issues and way forward. *Afr Health Sci* 2012;12:297–304.
- 4 UNAIDS. 2021 Malawi HIV estimates, 2020. Available: <https://www.unaids.org/en/regionscountries/countries> [Accessed 24 Nov 2021].
- 5 Ng'eno B, Rogers B, Mbori-Ngacha D, *et al*. Understanding the uptake of prevention of mother-to-child transmission services among adolescent girls in sub-Saharan Africa: a review of literature. *Int J Adolesc Youth* 2020;25:585–98.
- 6 Ongaki D, Obonyo M, Nyanga N, *et al*. Factors affecting uptake of PMTCT services, Lodwar County referral Hospital, Turkana County, Kenya, 2015 to 2016. *J Int Assoc Provid AIDS Care* 2019;18:232595821983883.
- 7 Lallemand M, Chang S, Cohen R, *et al*. Pediatric HIV—a neglected disease? *N Engl J Med* 2011;365:581–3.
- 8 Government of Malawi- Ministry of Health, . Malawi integrated guidelines for clinical management of HIV/AIDS 2018.
- 9 Malawi Ministry of Health. Government of Malawi Ministry of Health Integrated HIV Program Report April - June 2021 2021:1–37.
- 10 Malawi Ministry of Health. Department HIV/AIDS management information system 2021.
- 11 Sherman GG, Mazanderani AH, Barron P, *et al*. Toward elimination of mother-to-child transmission of HIV in South Africa: how best to monitor early infant infections within the prevention of Mother-to-Child transmission program. *J Glob Health* 2017;7:10701.
- 12 Goga AE, Dinh T-H, Jackson DJ, *et al*. Population-level effectiveness of PMTCT option A on early mother-to-child (MTCT) transmission of HIV in South Africa: implications for eliminating MTCT. *J Glob Health* 2016;6:20405.
- 13 Ng'ambi WF, Ade S, Harries AD, *et al*. Follow-up and programmatic outcomes of HIV-exposed infants registered in a large HIV centre in Lilongwe, Malawi: 2012-2014. *Trop Med Int Health* 2016;21:995–1002.
- 14 Khanam M, Goswami S, Mukhopadhyay P. Effectiveness of early infant diagnosis (EID) in detecting the serostatus of HIV-exposed infants and children. *J Obstet Gynaecol India* 2015;65:315–9.
- 15 Thiabaud A, Triulzi I, Orel E, *et al*. Social, behavioral, and cultural factors of HIV in Malawi: semi-automated systematic review. *J Med Internet Res* 2020;22:e18747.
- 16 Flax VL, Hamela G, Mofolo I, *et al*. Factors influencing postnatal option B+ participation and breastfeeding duration among HIV-positive women in Lilongwe district, Malawi: a qualitative study. *PLoS One* 2017;12:e0175590.
- 17 National Statistical Office. *Malawi demographic and health survey 2015-16*, 2015: 1–658. <http://dhsprogram.com/pubs/pdf/FR319/FR319.pdf>
- 18 Zulu LC, Kalipeni E, Johannes E. Analyzing spatial clustering and the spatiotemporal nature and trends of HIV/AIDS prevalence using GIS: the case of Malawi, 1994-2010. *BMC Infect Dis* 2014;14:285.
- 19 Nutor JJ, Duah HO, Agbadi P, *et al*. Spatial analysis of factors associated with HIV infection in Malawi: indicators for effective prevention. *BMC Public Health* 2020;20:1167.
- 20 Feldacker C, Emch M, Ennett S. The who and where of HIV in rural Malawi: exploring the effects of person and place on individual HIV status. *Health Place* 2010;16:996–1006.
- 21 Kanyerere H, Harries AD, Tayler-Smith K, *et al*. The rise and fall of tuberculosis in Malawi: associations with HIV infection and antiretroviral therapy. *Trop Med Int Health* 2016;21:101–7.
- 22 UNAIDS. Understanding Fast-Track Targets. *Accelerating action to end the AIDS epidemic by 2030*, UNAIDS, 2015: 12. https://www.unaids.org/sites/default/files/media_asset/201506_JC2743_Understanding_FastTrack_en.pdf