Immunization for Children Living With HIV: A Scoping Review

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1. Background

- Immunosuppression secondary to human immunodeficiency virus (HIV) increases the risk of vaccine- preventable diseases in children living with HIV (CLWH).
- Vaccines are cost-effective interventions.
- CLHIV are more likely to benefit from vaccination because of an increased frequency and severity of Vaccine Preventable Diseases (VPDs)
- Vaccine efficacy, immunogenicity, safety, and persistence of post-vaccination immunity in CLWH receiving antiretroviral therapy (ART) is unclear.
- Vaccine-induced immunity wanes more rapidly among CLWH compared to their HIV-exposed uninfected (HEU) and HIV-unexposed uninfected (HUU) counterparts, independent of ART status
- Aimed to identify existing scientific evidence on immunization of CLWH generated in the last 10 years in order to identify the need for a systematic review.

2. Methods

Two independent authors (S. B. and L. K.) conducted the review.

- A broad search strategy was designed combining terms using keywords and Medical Subject Headings (MeSH) terms including HIV, immunity, immunisation, vaccination, vaccines, antiretroviral agents, immunogenicity.
- There was no limit on study de- sign, study setting, or geographic location. Only studies written in English and published between January 2012 and February 2019 were considered.
- S. B. conducted the search using MEDLINE (via PubMed), EMBASE databases, the Cochrane library, and screened abstracts from the International AIDS Society (IAS) and the Conference on Retroviruses and Opportunistic Infections (CROI) conferences.
- Results from the search were combined in the EndNote Library Software, and after removing duplicates.
- S. B. and L. K. independently screened the titles and abstracts to identify relevant papers.
- A screening form was developed, based on eligibility criteria, to standardize the screening

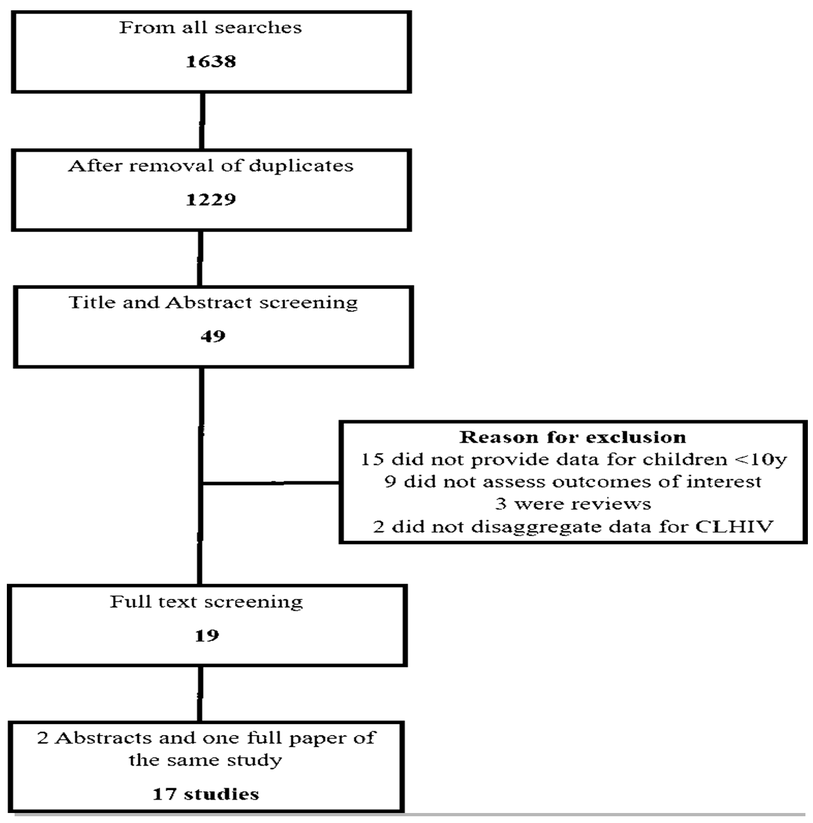

Fig 1 PRISMA flow diagram: searched and screening items and reason for exclusion at full-text screening.

3. Methods

Immunogenicity was measured by comparing post-vaccination antibodies to pre-vaccination levels using:

- Anti-Hib polyribosylribitol phosphate (PRP)
- Hemagglutination inhibition (HAI) titers
- Antibodies to DPT and filamentous hemagglutinin (FHA)
- Serum bactericidal antibody (Ab)
- Rubella and mumps immunoglobulin G
- GMC and increase in Ab concentrations
- Serum anti-rotavirus neutralizing Ab and IgA levels
- Anti-TT levels

4. Results

Rotavirus Vaccine (RTV)

- Majority (81%) of CLWH achieved an appropriate post-pentavalent RTV antibody response; significantly higher than the placebo group ($P < .001$).
- There was no difference in vaccine safety between CLWH and control groups, either HEU or HUU.

5. Results

Pneumococcal Conjugate Vaccine (PCV)

- no differences in seroprotective antibody levels (≥0.35 μg/mL) and safety profiles between CLWH and HUU.
- CLWH reached the same seroprotective antibody level as the HUU after the second dose of PCV 7 in a 3-dose primary series, independent of ART status at the time of vaccination
- Lower post-vaccination naso- pharyngeal colonization with pneumococcus in CLHIV com- pared to HUU
- There was no significant difference in safety between CLWH, HUU, HEU children

Measles, Mumps, and Rubella (MMR) Vaccine

- Rubella seroprotection and mumps seropositivity was significantly lower in CLWH compared to HEUs in perinatally infected children aged 7-15 years.
- MMR seropositivity waned faster in CLWH vs HEU.
- A greater number of vaccine doses while receiving ART was associated with higher seroprotection

Haemophilus influenzae Type b (Hib) Vaccine

- 32.4% (95% CI: 17.4%-50.2%) of CLHW reached the optimum threshold of Ab for seroprotection against Hib carriage
- No difference in seroprotective Ab levels between 6 and 12-week-old HUU children and CLHIV who initiated ART immediately in infancy
- >90% of the infants achieved seroprotective Ab levels measured 1 month after a 3-dose primary series of diphtheria toxoid, TT; whole-cell pertussis and Hib conjugate vaccines and given at 6, 10, and 14 weeks with no differences across groups

6. Results

Diphtheria, Pertussis, and Tetanus (DPT) Vaccine

- The post-vaccination antibody response was significantly lower among CLWH irrespective of the timing of ART initiation compared to HEU and HUU children for the diphtheria and pertussis components.
- For the diphtheria component, the proportion of children achieving protective titers was similar between HEU and CLWH that started ART immediately.
- Of the CLWH with non-protective levels, a significantly higher proportion (89%; $P = .03$) had moderate to severe disease than those with protective levels.
- 10 months following vaccination, antibody levels were higher in CLWH vs HUU.
- The majority (71%) of CLWH who received booster doses developed protective levels following 1 booster dose

7. Conclusion

1. Most studies found that CLWH and HUU children achieved similar post-vaccination antibody levels for most vaccines except the pertussis vaccine and OPV.
2. There was significant variability in time points of post-vaccination serological testing across studies.
3. Except for HAV, post-vaccine immunity waned more rapidly among CLWH compared to HUU following MMR and tetanus vaccination.
4. No significant difference in vaccine safety between CLWH and HUU children
5. A more uniform approach to sampling and follow-up would make the comparison of different studies and interpretation of results more robust.

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