A systematic review on the safety and immunogenicity of vaccines used in pregnant women living with HIV

Citation

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Review question

How safe and immunogenic are vaccines in pregnant women living with HIV compared to pregnant women without HIV, considering published randomized clinical trials, cohort studies, observational studies, and population-based registries?

Searches [1 change]

Databases:

PubMed/MEDLINE

Embase

Cochrane data base

Web of Science

Virtual Health Library (VHL Regional Portal)

Searches will be run on 11th and 12th November 2021.

Searches will be run in English with no date restrictions. Results written in English, Spanish, and Portuguese will be included.

Types of study to be included

Include: Randomized Clinical Trials, Cohort studies, Observational studies, and Population-based registries.

Exclude: case reports, systematic reviews

Condition or domain being studied

HIV infection among pregnant women remains relatively high in many African countries especially Sub-Saharan Africa. The advances in Ante Retro Viral Therapy(ART) and early initiation of treatment with linkage to holistic care has enabled a number of children born with HIV to reach their reproductive age group and now have families of their own.

Pregnant women living with HIV are generally known to have lower pre-vaccination antibodies. Despite the advances in the Prevention of Mother to Child Transmission of HIV (PMTCT) which have resulted in a significant reduction of babies born with HIV, HIV-exposed uninfected infants (HEU) remain more susceptible to infection in the first six months of life, especially in the first two months before completion of their primary infant vaccination schedules. The immunogenicity of vaccines given to pregnant women living with HIV has been reported to be poorer than their non-infected counterparts, and recommendations have been made for alternate vaccination strategies including higher antigen doses in the vaccine, two or more doses, and use of adjuvanted vaccines.

Participants/population

Include: pregnant women living with HIV who have received vaccines in their current pregnancy.

Exclude: non-pregnant women receiving vaccines and pregnant women who are vaccinated outside of pregnancy.

Intervention(s), exposure(s)

Include: Vaccination against infectious diseases given during pregnancy

Exclude: Vaccination designed to boost antibodies against HIV

Comparator(s)/control

Pregnant women who are not HIV infected and received vaccines during pregnancy.

Main outcome(s) [1 change]

Safety and immunogenicity:

Maternal outcome- Hospital admission with life threatening complications (Diagnosis at admission), maternal deaths

Fetal outcome- intra-uterine fetal deaths, admission to NICU

Measures of effect

Odds ratio or risk ratios

Additional outcome(s) [1 change]

Maternal Outcome- Preterm delivery, chorioamnionitis, pre-eclampsia, premature rupture of membranes

Fetal Outcome- miscarriage, intra-uterine growth restriction, small for gestational age at birth

Measures of effect

Odds ratio or risk ratios

Data extraction (selection and coding) [1 change]

Search results titles and/or abstracts will initially be screened independently by two reviewers using the following criteria:

Inclusion: Studies which are Randomized Clinical Trials, Cohort studies, Observational studies, or Population-based registries, investigating vaccination of pregnant women living with HIV.

Exclusion: Case reports, systematic reviews, studies investigating vaccination aiming to boost antibodies against HIV.

Decisions will be recorded on Rayyan blinded.

Studies included based on title / abstract will be re-screened by two reviewers based on the full text.

Data will then be extracted independently by two authors into a pilot-tested standardized form in Excel. Data extracted will include:

- Study design and setting

- Intervention details

- Study outcomes

- Population details

- Monitoring details

- Maternal and fetal adverse events

- Follow up information

- Conclusion

Any discrepancies at any point will be reviewed by a third reviewer, and agreement reached on discussion.

Risk of bias (quality) assessment

Two reviewers will assess the risk of bias and quality for each defined outcome using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) framework. The ROBINS-I quality assessment tool for assessing the risk of bias will be used in the case of non-randomized studies. A third reviewer will participate in case of discrepancies. All data will be gathered and recorded at the GRADEpro GDT online tool following the GRADEpro Guideline Development Tool. The risk of bias assessment will include the analysis per outcome for low, unclear or high risk of bias for selection bias, deviation from intended analysis from the original cohort or clinical trial (for sub-analysis), residual confounding and how outcomes were measured. Each study will be evaluated according to the risk of the total outcomes assessed in this systematic review. The quality assessment included the risk of bias, inconsistency, indirectness and imprecision of each outcome.

Strategy for data synthesis [1 change]

We will undertake a systematic review of the literature, but as our primary outcome is safety, we will report results as a narrative. The analyzed data obtained will be evaluated for the safety of patients.

Data will be synthesised as a narrative synthesis, to describe overall trends that may appear as well as to highlight areas where data may be lacking. Anticipated groups for synthesis include type of vaccine/pathogen target, demography (age, socioeconomic factors, antiretroviral therapy) as well as which countries/areas collect the most data on the topic. A minimum of three studies will be required for synthesis.

We will investigate heterogeneity by defining a set of clinical covariates from the participant level and intervention including reporting of key variables around HIV infection such as CD4 count, viral load and antiretroviral regimen, as well as the use of placebo or alternative vaccine in the trials.

Uncertainty will be addressed by evaluation of the bias and heterogeneity between studies and the number of participants for each outcome.

The data will be summarized in tables and figures

Analysis of subgroups or subsets

We will undertake sensitivity analysis to determine the effect of variables below on our primary outcomes:

Country of study/GDP

Population

Pathogen

Other co-infections or co-morbidities (e.g. malaria, TB, syphilis)

HIV status (CD4 and VL)

Contact details for further information

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Organisational affiliation of the review

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Collaborators

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Type and method of review [1 change]

Narrative synthesis, Systematic review

Anticipated or actual start date

08 November 2021

Anticipated completion date

28 January 2022

Funding sources/sponsors

Medical Research Council (London)

Grant number(s)

State the funder, grant or award number and the date of award

MRC/UKRI

Number MR/T004983/1

Awarded Jan 2020

Conflicts of interest

Language

English

Country

England, Uganda

Stage of review

Review Ongoing

Subject index terms status

Subject indexing assigned by CRD

Subject index terms

Female; HIV Infections; Humans; Influenza Vaccines; Pregnancy; Pregnant Women

Date of registration in PROSPERO

29 November 2021

Date of first submission

10 November 2021

Stage of review at time of this submission

Stage	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	Yes	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

The record owner confirms that the information they have supplied for this submission is accurate and complete and they understand that deliberate provision of inaccurate information or omission of data may be construed as scientific misconduct.

The record owner confirms that they will update the status of the review when it is completed and will add publication details in due course.

Versions

29 November 2021