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Systematic review and meta-analysis of seroprevalence of HIV serological markers among pregnant women in Africa, 1984-2020

HIV in pregnant women in Africa

Abstract**BACKGROUND**

HIV is a major public health concern, particularly in Africa where HIV rates remain substantial. Pregnant women are at an increased risk of acquiring HIV, which has a significant impact on both maternal and child health.

AIM

This systematic review summarizes HIV seroprevalence among pregnant women in Africa. It also identifies regional and clinical characteristics that contribute to study-specific estimates variation.

METHODS

The study included pregnant women from any African country or region, irrespective of their symptoms, and any study design conducted in any setting. Using electronic literature searches, articles published until February 2023 were reviewed. The quality of the included studies was evaluated using the Hoy *et al*, tool. The DerSimonian and Laird random-effects model was applied to determine HIV pooled seroprevalence among pregnant women in Africa. Subgroup and sensitivity analyses were conducted to identify potential sources of heterogeneity. Heterogeneity was assessed with Cochran's Q test and I² statistics, and publication bias was assessed with Egger's test.

RESULTS

A total of 248 studies conducted between 1984 and 2020 were included in the quantitative synthesis (meta-analysis). Out of the total studies, 146 (58.9%) had a low risk of bias and 102 (41.1%) had a moderate risk of bias. No HIV-positive pregnant women died in the included studies. The overall HIV seroprevalence in pregnant women was estimated to be 9.3% (95%CI: 8.3-10.3). The subgroup analysis showed statistically significant heterogeneity across subgroups ($P < 0.001$), with the highest seroprevalence observed in Southern Africa (29.4%, 95%CI: 26.5-32.4) and the lowest seroprevalence observed in Northern Africa (0.7%, 95%CI: 0.3-1.3).

CONCLUSION

The review found that HIV seroprevalence among pregnant women in African countries remains significant, particularly in Southern African countries. This review can inform the development of targeted public health interventions to address high HIV seroprevalence in pregnant women in African countries.

Key Words: HIV; Pregnant women; Africa

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Core Tip: A meta-analysis reveals a 9.3% HIV seroprevalence among pregnant women in Africa, with regional variations. Southern Africa reports the highest rates at 29.4%, whereas Northern Africa shows the lowest at 0.7%. These findings underscore the need

for targeted public health interventions to tackle high HIV seroprevalence in pregnant women, especially in Southern African countries.

INTRODUCTION

HIV treatment guidelines, increased use of testing and counselling have resulted in a significant decrease in HIV rates in the general population during the 2010s, including in Africa [1-4]. The impact of these interventions on pregnant women is less clear. A meta-analysis of participants recruited from 1984 to 2012 showed that HIV acquisition during pregnancy and postpartum was estimated at 3.8 [95%CI: 3.0, 4.6] per 100 person-years [5]. HIV incidence was higher during pregnancy and in Africa. A more recent meta-analysis revealed HIV incidence among pregnant women in sub-Saharan Africa remained significant at 3.6 [95%CI: 1.2, 11.1] [6]. HIV causes maternal deaths between 5.9% and 17.9% [7-9]. HIV-positive pregnant and postpartum women are more likely to die than those without HIV. Moreover, the study estimated that 994 deaths per 100 000 were caused by HIV in pregnant and postpartum women [10]. A more rapid progression of HIV-related illness or obstetric complications may contribute to this higher morbidity in HIV-positive pregnant women [11-13]. Besides health risks for mothers, HIV infection also increases the risks of mother-to-child transmission. HIV transmission from mother to child is also increased during pregnancy and after delivery [5,6]. A study has shown that the risk of mother-to-child HIV transmission during pregnancy is higher than that of chronic infections during pregnancy and postpartum [5]. A separate study found that mothers infected with HIV who don't receive antiretroviral therapy have an increased chance of having a preterm birth, a low birth weight, a small for gestational age, and a stillbirth in sub-Saharan Africa [14]. Several studies have explored the HIV seroprevalence among pregnant women in Africa, but a comprehensive review is needed. A meta-analysis of 15 studies found that 5.74% (95%CI 3.96-7.53%) of pregnant women in Ethiopia had HIV with a high level of regional heterogeneity [15]. To guide future research and policy, it is essential to better understand the characteristics contributing to variations in HIV estimates among pregnant women. Furthermore, it is

vital to develop effective strategies to reduce horizontal and vertical transmission of HIV during pregnancy and breastfeeding. We have summarized estimates of HIV seroprevalence among pregnant women in Africa and identified regional and clinical characteristics that contribute to variation in study-specific estimates.

MATERIALS AND METHODS

Study design

This study complied with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (Supplementary Table 1) ^[16]. Study protocol was registered in PROSPERO (CRD42021272440). The registered protocol specifies objectives, inclusion and exclusion criteria, search strategy, data extraction, and statistical analysis plan.

Eligibility criteria

This systematic review and meta-analysis assessed the seroprevalence of HIV serological markers among pregnant women in Africa up to 2023. The study included pregnant women from any African country or region, irrespective of their symptoms, and any study design (cross-sectional, cohort, clinical trial, or case-control) conducted in any setting (hospital-based, antenatal clinics, or community-based). All laboratory diagnostic methods using any sample type to detect HIV serological markers were eligible. Studies with a sample size greater than 10, with enough data available, written in English and French were included. When overlapping data appeared in different articles, the most recent or complete study was used. Review articles, comments, case reports, and studies with inaccessible full-text or abstracts were excluded from the study.

Article search strategy

Using Pubmed and Web of Science, African Index Medicus, and African Journal online, we reviewed the electronic bibliography for articles published till February 2023. Search terms related to HIV, pregnant women, and Africa were used (Supplementary Table 2).

The reference lists of all relevant articles were reviewed to complete searches in the bibliographic database and identify possible additional data sources.

Article selection

Two investigators (JETB and SK) independently screened titles and abstracts of articles retrieved from electronic literature searches, and full texts of those eligible were obtained and assessed further for final inclusion. A PRISMA flow diagram was used to document the screening process. Consensus was reached between reviewers to resolve disagreements.

Data extraction from the included articles.

Data extraction for this systematic review was conducted using a Google form by 14 study authors and verified by JETB. The extracted data included information on the first author's name, year of publication, and participants' inclusion period. We also collected information about the study design and countries. A number of websites were used to obtain the WHO region, United Nations region, and World Bank income group from country information [17,18]. Other extracted information included single HIV diagnostic methods or algorithms of diagnostic methods, parity, gravidity, gestational age, educational level, sample size, HIV positive number, and type of HIV. In studies reporting results with undetermined HIV status, we excluded these patients from our estimations. In cases where detection algorithms were used, we considered the number of positives from the group of detection methods constituting the algorithm, not the results of the individual detection methods. Discrepancies encountered during data extraction were resolved through discussion and consensus among the authors.

Assessment of study quality

The risk of bias assessment was conducted using the Hoy *et al*, tool, which is designed to assess the risk of bias in prevalence studies (Supplementary Table 3) [19]. This tool includes ten items related to the study's external and internal validity. Each item is scored as either low risk, high risk, or unclear risk of bias. Scores range from 0 to 10, with higher scores indicating lower bias risk. Each study included in the review was

assessed for bias using the tool, with disagreements resolved through discussion and consensus.

Statistical analysis

This meta-analysis used the DerSimonian and Laird random-effects model to determine pooled HIV seroprevalence among pregnant women in Africa [20]. This was done by inputting numerators (HIV positive) and denominators (HIV tested) extracted from selected studies. Using the Clopper-Pearson method, we calculated 95% confidence intervals (95%CI) for individual studies. The results of individual studies were summarized using forest plots. The analysis was conducted with the 'meta' package in R v4.0.3 (R Foundation for Statistical Computing, Vienna, Austria), and the 'metaprop' function was applied to conduct the meta-analysis of single proportions to obtain HIV pooled seroprevalence [21, 22].

Sub-group and sensitivity analyses

A subgroup meta-analysis was conducted to identify potential sources of heterogeneity. Several covariates were considered, including: (i) regional characteristics such as countries, UN regions, WHO regions, and World Bank Income Groups; (ii) HIV characteristics such as type of HIV and HIV diagnostic method; and (iv) participant characteristics such as gestational age, parity, gravidity, and educational level. Only covariates with at least three data points were considered in the subgroup analyses. Furthermore, only cross-sectional studies and those with low bias risks were included in the sensitivity analyses.

Heterogeneity and publication bias

Heterogeneity was assessed using Cochran's Q test and I^2 statistics [23]. A statistically significant Cochran's Q test ($p < 0.05$) was indicative of true heterogeneity of effect sizes between studies. The I^2 statistic was calculated as an estimate of between-studies variance using the maximum likelihood method. I^2 values of 50% or higher indicate substantial heterogeneity. Publication bias was assessed with Egger's test, with a statistical significance ($p < 0.05$) suggesting evidence of funnel plot asymmetry [24].

RESULTS

Selection of included articles.

A comprehensive search was conducted using relevant databases to identify studies investigating HIV seroprevalence and case fatality rates in pregnant women. The search yielded 26538 records (Figure 1). After removing duplicates, 16348 records were screened, and 15729 records were excluded based on title and abstract. The remaining 619 full-text articles were assessed for eligibility, and 371 articles were excluded based on predefined inclusion and exclusion criteria. Reasons for exclusion included no data on HIV prevalence or case fatality rate in pregnant women (293), full text or abstract not found (27), duplicates (17), reviews (17), study outside Africa (13), article not in English or French (2), Sample size < or = 10 participants (1), and comment on an article (1). Finally, 248 articles met the inclusion criteria and were included in the quantitative synthesis (meta-analysis) [25-272].

Figure 1: Study selection

Included article characteristics.

We conducted a systematic review of studies published from 1987 to 2023 and reviewed 248 studies. There were no cases reported of HIV-positive pregnant women dying in the included studies, which only reported HIV seroprevalence among pregnant women. Included studies recruited participants between 1984 and 2020, with unclear inclusion periods in 25 studies (Supplementary Table 4). The studies were conducted in several African countries, with the majority being from Nigeria (23.0%), followed by Tanzania (8.5%), Ethiopia (7.3%), and South Africa (7.3%). The studies were mostly conducted in Lower-middle-income countries (58.5%), followed by Low-income countries (32.3%) and Upper-middle-income countries (8.9%). Most studies were hospital-based (99.2%), with only one community-based study. The HIV diagnostic methods used in the studies varied, with the most common methods being algorithm of rapid antibody tests (29.0%), single rapid antibody test (14.9%), and indirect Enzyme-Linked ImmunoSorbent Assay (ELISA) (11.7%).

Risk of bias in the included studies.

Out of the total number of studies included in the review (248), 146 (58.9%) were deemed to have a low risk of bias, while 102 (41.1%) were categorized as having a moderate risk of bias (Supplementary Table 5).

Meta-Analysis.

A meta-analysis was performed to estimate the overall HIV seroprevalence in pregnant women, as well as the seroprevalence among cross-sectional studies and those with a low risk of bias (Table 1). The overall HIV seroprevalence in pregnant women was estimated to be 9.3% (95%CI: 8.3-10.3). The seroprevalence among cross-sectional studies was slightly lower at 8.8% (95%CI: 7.7-9.8), while the seroprevalence among studies with a low risk of bias was also 8.8% (95%CI: 7.5-10.2). All three analyses exhibited high heterogeneity ($p < 0.001$). The analysis of publication bias using the Egger test indicated evidence of significant publication bias ($p < 0.001$) in the meta-analysis (Supplementary Figure 1).

Metanalysis by UN regions

Subgroup analysis was conducted to explore the difference in seroprevalence among different UN regions (Figure 2). The results showed statistically significant heterogeneity across subgroups ($P < 0.001$). The seroprevalence of the disease varied across different regions with the highest observed in Southern Africa (29.4%, 95%CI: 26.5-32.4) and the lowest in Northern Africa (0.7%, 95%CI: 0.3-1.3). Eastern Africa had a relatively high seroprevalence (11.7%, 95%CI: 10.2-13.2), while that in Western Africa was relatively low (6.2%, 95%CI: 5.2-7.3). Middle Africa had a moderate seroprevalence (4.8%, 95%CI: 4-5.8). The difference in seroprevalence between UN regions was statistically significant ($P < 0.001$).

Fig. 2: HIV seroprevalence among pregnant African women according to UN regions from 1984 to 2020

Meta-analysis of other regional categories

HIV seroprevalence in pregnant women varied among different countries (Supplementary Table 6). The highest seroprevalence was reported in South Africa (29.9%, 95%CI: 26.7-33.2), followed by Zimbabwe (25.7%, 95%CI: 16.4-36.3) and Malawi

(18.7%, 95%CI: 14.2-23.8) (Figure 3). The lowest seroprevalence was reported in Sudan (1.0%, 95%CI: 0.4-1.7) and Senegal (0.7%, 95%CI: 0.5-0.9). The difference was statistically significant ($p < 0.001$). HIV seroprevalence in pregnant women varied significantly among WHO regions ($P < 0.001$) (9.5%, 95%CI: 8.4-10.6 in Africa *vs* 1.4%, 95%CI: 0.6-2.4 in Eastern Mediterranean) (Supplementary Table 6). HIV seroprevalence during pregnancy was significantly different among World Bank Income Groups ($p < 0.001$) (Supplementary Table 6). The highest seroprevalence was observed in upper-middle-income countries (24%, 95%CI: 19.9-28.3), followed by low-income countries (8.4%, 95%CI: 6.9-10.1) and lower-middle-income countries (8.1%, 95%CI: 7.2-9.1).

Figure 3: Map of the distribution of HIV (A), HIV-1 (B), and HIV-2 (C) data among pregnant women in Africa. ³ The base map was taken from (<https://www.naturalearthdata.com/>) and modified with Qgis software.

Meta-analysis by HIV characteristics

The HIV-1 seroprevalence was 8.7% (95%CI: 7.5-10) with a 95% prediction interval of 0.5-25.4%, while the HIV-2 seroprevalence was 1.2% (95%CI: 0.7-1.9) with a 95% prediction interval of 0-5.2% (Supplementary Table 6). HIV-1 seroprevalence was significantly higher than HIV-2 ($P < 0.001$) (Figure 3). Regarding the HIV diagnostic method, the highest seroprevalence was found in the combination of rapid antibody test and indirect ELISA subgroup (15.9%; 95%CI: 1.3-42.1) (Supplementary Table 6). The lowest seroprevalence was found in the algorithm (rapid antibody test, indirect ELISA, and enzyme immunoassay) subgroup (3.3%; 95%CI: 1.9-4.9). There was a statistically significant difference between subgroups ($P < 0.001$).

Meta-analysis by pregnant women's characteristics

The subgroup analysis by gestational age included 17 studies involving 36,935 participants (Supplementary Table 6). The HIV seroprevalence was highest in the second trimester with 9.6% (95%CI: 5.2-15), followed by the third trimester with 8.7% (95%CI: 5.2-13.1) and the least during the first trimester with a prevalence of 7.3% (95%CI: 3.5-12.2) but without statistical significance ($P = 0.902$). Ten studies were included in the parity subgroup analysis, involving 18,015 participants (Supplementary

Table 6). HIV seroprevalence was 6.7% (95%CI: 4-10) among nulliparous women, 6.5% (95%CI: 4.5-8.8) among multiparous women, and 5% (95%CI: 2.8-7.8) among primiparous women. There was no statistically significant difference between the different categories ($P = 0.690$). The subgroup analysis by gravidity included 17 studies with 53,860 participants (Supplementary Table 6). HIV seroprevalence was 9.2% (95%CI: 5.5-13.7) among multigravidae and 6.5% (95%CI: 4.2-9.2) among primigravidae. HIV seroprevalence was not significantly higher among multigravidae than among primigravidae ($P = 0.276$).

DISCUSSION

Participants were recruited in 248 studies between 1984 and 2020 from 39 African countries, with 1,374,392 participants in total. The overall HIV seroprevalence among pregnant women in Africa was estimated to be 9.3% (95%CI: 8.3-10.3), which suggests that a significant proportion of pregnant women in the region live with HIV. However, it is worth noting that no HIV-positive pregnant women died in any of the included studies. The study also found significant differences in HIV seroprevalence by UN region, WHO region, World Bank income groups, and individual countries. UN regions showed Southern Africa had the highest seroprevalence, followed by Eastern Africa, Western Africa, Middle Africa, and Northern Africa. The WHO region with the greatest seroprevalence was Africa compared to the Eastern Mediterranean. There were significant differences in HIV seroprevalence among World Bank Income Groups, with upper-middle-income countries having the highest seroprevalence, followed by low-income countries, and lower-middle-income countries. The analysis presented data on HIV seroprevalence in different African countries, with South Africa having the highest seroprevalence, followed by Zimbabwe, Malawi, Zambia, and Rwanda. The lowest seroprevalence was observed in Senegal and Sudan. The study found significantly higher HIV-1 seroprevalence (8.2%) than HIV-2 (1.2%). No significant differences were observed in seroprevalence based on gestational age, parity, and gravidity.

It is concerning to find that the overall HIV seroprevalence among pregnant women in Africa was estimated to be 9.3% (95%CI: 8.3-10.3), which indicates that the HIV epidemic continues to have a high impact on the continent. Previous studies show pregnant women in Africa are at higher risk of HIV infection [273, 274]. There have been previous reports of death in African pregnant and postpartum women, primarily in longitudinal studies [275-277]. It is noteworthy that none of the included studies reported the death of HIV-positive pregnant women. As previously reported [278, 279], Southern Africa had the highest HIV seroprevalence among pregnant women, followed by Eastern Africa, Western Africa, Middle Africa, and Northern Africa. This highlights the urgent need for continued efforts to prevent HIV transmission and provide effective care and treatment to HIV-positive pregnant women in these regions. The high HIV seroprevalence in Southern Africa is well documented, with countries like South Africa being among the highest HIV seroprevalence in the world [280, 281]. This can be attributed to a range of factors, including data availability, poverty, violence against women, cultural restrictions promoting intergenerational sex, unprotected sex, multiple sexual partners, political barriers, recreational drug use, stigma, and discrimination [280, 281]. Eastern and Western Africa also have high HIV seroprevalence, with countries like Zimbabwe, Malawi, Zambia, Rwanda, Uganda, and Kenya reporting significant numbers of HIV infections each year [282]. These findings suggest that efforts to prevent HIV transmission and provide care and treatment to HIV-positive pregnant women need to be targeted towards these high-prevalent regions. This may include scaling up prevention interventions such as condom use and pre-exposure prophylaxis, as well as increasing access to HIV testing and treatment services [283-285]. In addition, addressing social and economic factors that contribute to HIV transmission, such as poverty, gender inequality, and stigma, is crucial to reducing HIV seroprevalence in these regions.

HIV-1 seroprevalence was significantly higher than HIV-2 seroprevalence, which has implications for HIV prevention and treatment. HIV-1 and HIV-2 are two distinct types of the virus that cause HIV infection, and they differ in their transmission, clinical

presentation, and response to treatment [286-288]. HIV-1 is more prevalent globally and is the predominant HIV type in sub-Saharan Africa, where the HIV burden is highest. In contrast, HIV-2 is primarily found in West Africa and is less prevalent globally [286, 287]. This has significant implications for prevention efforts, as HIV-1 is more easily transmitted than HIV-2 and associated with faster AIDS progression. Prevention efforts must therefore focus on reducing HIV-1 transmission through strategies such as condom use, pre-exposure prophylaxis (PrEP), and promoting HIV testing and treatment for people living with HIV. Antiretroviral therapy is the cornerstone of HIV treatment, and it suppresses both HIV-1 and HIV-2. However, HIV-2 is less responsive to some antiretroviral therapy regimens and may require different treatment strategies [286, 287, 289]. The high HIV-1 seroprevalence in the study population suggests that healthcare providers should know the HIV-1 predominance and tailor treatment accordingly.

There was no significant difference in seroprevalence based on gestational age, parity, or gravidity, indicating that HIV infection does not discriminate against these demographic characteristics. This finding is consistent with previous research that shows that HIV can affect anyone, regardless of their age, parity, or gravidity [290-292].

This systematic review and meta-analysis of HIV seroprevalence among pregnant women in Africa has some limitations. There was publication bias as studies with null HIV seroprevalence findings may be less likely to be published, leading to the exclusion of relevant studies. The lack of uniformity in testing methods and cutoffs used in included studies may have affected the results comparability. However, this systematic review and meta-analysis of HIV seroprevalence among pregnant women in Africa has several strengths. The comprehensive search strategy and pre-defined inclusion and exclusion criteria minimized the risk of missing relevant studies and ensured that only appropriate studies were considered. The large sample size and broad time frame of the review increased generalizability. Finally, meta-analysis allowed for the estimation of overall seroprevalence rates and identification of factors associated with HIV

seroprevalence among pregnant women in Africa, providing significant insights for clinicians, researchers, and policymakers.

CONCLUSION

This study reports that HIV seroprevalence in pregnant African women was estimated to be 9.3%, highlighting the substantial burden of HIV in Africa. Southern Africa had the highest HIV seroprevalence among pregnant women, followed by Eastern, Western, Middle, and Northern Africa, emphasizing the need for targeted efforts to prevent transmission and provide care and treatment in these regions. HIV-1 seroprevalence was considerably higher than HIV-2, underscoring the need for tailored prevention and treatment strategies.

ARTICLE HIGHLIGHTS

Research background

An extensive literature review was carried out in various databases up until February 2023, using key terms such as HIV, pregnancy, and Africa. Through this literature search, we noted a significant body of evidence detailing HIV infection prevalence among pregnant women in Africa.

Research motivation

Given the continued high incidence and impact of HIV among pregnant women in Africa, there is a critical need to enhance our understanding of the specific factors that contribute to this high prevalence and the variations in these proportions. There is also an urgent need to examine strategies that could effectively mitigate both horizontal (person-to-person) and vertical (mother-to-child) HIV transmission during pregnancy and breastfeeding.

Research objectives

This research aims to provide a comprehensive understanding of HIV prevalence among pregnant women in Africa by identifying and analyzing the regional and clinical characteristics that contribute to variations in study-specific estimates.

Research methods

This systematic review and meta-analysis, compliant with PRISMA guidelines and registered in PROSPERO, assessed the seroprevalence of HIV serological markers among pregnant women in Africa up to 2023. All types of study designs from any African region were eligible if the sample size was greater than 10 and published in English or French. A literature search was conducted in databases such as Pubmed, Web of Science, African Index Medicus, and African Journal online, with relevant search terms. The quality of the included studies was assessed using Hoy *et al* tool. The DerSimonian and Laird random-effects model was used to determine pooled HIV seroprevalence.

Research results

This systematic review analyzed data from 248 studies investigating HIV seroprevalence in pregnant women across various African countries from 1984 to 2020. The overall HIV seroprevalence was estimated at 9.3% (95%CI: 8.3-10.3). The highest seroprevalence was found in Southern Africa (29.4%, 95%CI: 26.5-32.4), while Northern Africa had the lowest (0.7%, 95%CI: 0.3-1.3). Among the different types of HIV, HIV-1 seroprevalence was significantly higher than HIV-2 ($P<0.001$).

Research conclusions

This comprehensive analysis identified a high HIV seroprevalence among pregnant women in Africa at an estimated 9.3%, highlighting the significant burden of HIV in the region.

Research perspectives

Considering the substantial HIV seroprevalence among pregnant women in Africa, this analysis underlines the need for sustained efforts to prevent ⁶ HIV transmission and provide effective care and treatment for HIV-positive pregnant women, especially in regions with high seroprevalence. Future research should aim to elucidate the factors contributing to high seroprevalence, especially in Southern Africa, and devise effective preventive and therapeutic strategies tailored to the region's needs.

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