

Prevalence of rhesus isoimmunization among rhesus negative pregnant women in African hospitals: A systematic review and meta-analysis.

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Abstract

Introduction

Objective: This systematic review and meta-analysis aimed to determine the pooled prevalence of Rhesus isoimmunization among rhesus-negative pregnant women in African hospitals using the PICO framework.

Methods

Following PRISMA guidelines, a comprehensive literature search was conducted in PubMed, SCOPUS, Web of Science, Lens.org, and Google Scholar for observational studies (2010–May 2025) on Rhesus isoimmunization in African hospital settings. The PICO framework guided the research question (Population: pregnant women; Intervention: none; Comparison: subgroups (Regional variations); Outcome: prevalence of isoimmunization). Data were extracted using a standardized form, and study quality was assessed with the Joanna Briggs Institute checklist. A random-effects model with logit transformation pooled prevalence estimates. Heterogeneity was evaluated using I^2 and Cochran's Q , and publication bias was assessed via Fail-Safe N , Kendall's Tau, Egger's regression, and funnel plots.

Results

Nine studies, involving 28,188 pregnant women from Nigeria, Ethiopia, Uganda, and the Democratic Republic of Congo, were included. The pooled prevalence of Rhesus isoimmunization was 2.93% (95% CI: 1.58%–5.36%), with high heterogeneity ($I^2 = 85.12\%$, $Q = 48.320$, $p < 0.001$). Regional prevalence ranged from 0.31% (DR Congo) to 7.04% (Ethiopia). No significant publication bias was detected (Fail-Safe $N = 2,581$, Kendall's Tau $p = 0.761$, Egger's $p = 0.672$).

Conclusions

Rhesus isoimmunization affects ~2.93% of rhesus-negative pregnant women in African hospitals, posing a significant risk of hemolytic disease of the fetus and newborn. Routine Rhesus screening, accessible anti-D prophylaxis, and policy reforms are critical to reduce maternal and neonatal morbidity.

Recommendation

Further research should investigate heterogeneity determinants and cost-effective interventions across diverse African settings.

Keywords: Rhesus isoimmunization, Prevalence, Pregnant women, African hospitals, Meta-analysis

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Introduction

Rhesus incompatibility is a significant concern in pregnancy and can lead to obstetric challenges for some women (Allagoa et al., 2021; Uchenna Eleje et al., 2017).

The Rhesus factor is an antigen found on the surface of red blood cells, and among the various subtypes, the D antigen is the most commonly associated with Rhesus isoimmunization (Allagoa et al., 2021). Isoimmunization can occur when a Rhesus-negative pregnant mother is

exposed to Rhesus-positive fetal red blood cells, often due to fetomaternal hemorrhage during pregnancy, or when a Rhesus-negative woman receives a transfusion of Rhesus-positive blood (Allagoa et al., 2021; Uchenna Eleje et al., 2017). This process involves the production of antibodies against specific exogenous D antigens introduced into the body (Kanko & Woldemariam, 2021).

Rhesus alloimmunization remains a major factor contributing to perinatal morbidity (Mbalibulha et al., 2022; Uchenna Eleje et al., 2017). When antibodies formed in the mother cross the placental barrier, they can destroy the red blood cells of a Rhesus-positive fetus, potentially causing severe complications (Nyakio et al., 2024). These complications can include hemolytic disease of the fetus and newborn (HDFN), which may manifest as neonatal jaundice, anemia, hydrops fetalis, stillbirth, brain damage, and even in utero death (Aliyo et al., 2023; Nyakio et al., 2024).

The distribution of the Rh D antigen varies significantly across different populations (Kanko & Woldemariam, 2021; Otomewo et al., 2020). While the prevalence of Rh D-negative phenotype is generally lower among Africans compared to Caucasians (Otomewo et al., 2020; Uchenna Eleje et al., 2017), Rhesus isoimmunization continues to compromise women's obstetric care in sub-Saharan Africa (Allagoa et al., 2021; Uchenna Eleje et al., 2017). Studies in various African countries have reported varying prevalence rates of Rhesus negativity among pregnant women. For instance, studies in Nigeria found rates such as 2.27% in South-South Nigeria (Allagoa et al., 2021), 2.1% in Nnewi, South-east Nigeria (Uchenna Eleje et al., 2017), 5.5% in Ogbomoso, Southwestern Nigeria (Aliyo et al., 2023; Otomewo et al., 2020), and 8.4% among women of childbearing age in South-West Nigeria (Otomewo et al., 2020). In Ethiopia, reported prevalence rates include 6.4% in Bule Hora (Aliyo et al., 2023). Studies in Uganda reported prevalence rates of 2.3% in Kampala (Eipl et al., 2012), 3.6% in South Western Uganda (Natukunda et al., 2011), and 5.7% among pregnant women in South Western Uganda (Mbalibulha et al., 2022). Other reported prevalence rates in the region include 3.9% in Kenya, 4.06% in Guinea, and 2.4% in Cameroon (Nyakio et al., 2024). Despite these variations, a high risk of obstetric sensitization in Rhesus-negative women persists in developing countries, partly due to factors such as a high prevalence of unbooked antenatal cases and limited screening facilities (Allagoa et al., 2021).

Factors contributing to the risk of sensitization and adverse outcomes in Rh-negative women include previous pregnancies, previous abortions, stillbirths, and blood transfusions (Otomewo et al., 2020; Uchenna Eleje et al.,

2017). Challenges such as high cost of prophylactic anti-D immunoglobulin injections and insufficient access to adequate antenatal evaluation, monitoring, and effective anti-D immunoprophylaxis hinder prevention efforts in many African settings (Allagoa et al., 2021; Otomewo et al., 2020; Uchenna Eleje et al., 2017). Suboptimal antenatal management and a low uptake of Rhesus anti-D immunoglobulin have been noted as significant challenges (Uchenna Eleje et al., 2017).

Given the continued impact of Rhesus isoimmunization on maternal and neonatal health and the variability in prevalence and management challenges across different regions, a systematic review is warranted. This systematic review aims to synthesize the available evidence on the prevalence and determinants of Rhesus isoimmunization among pregnant women in African hospitals to provide a comprehensive understanding of the issue and inform strategies for prevention and management.

Methods

Protocol and registration

This systematic review adhered to PRISMA guidelines (Page et al., 2021) and was registered with PROSPERO (CRD420251067446). Ethical approval was not required as it involved published data.

Search strategy

We searched PubMed, SCOPUS, Web of Science, Lens.org, and Google Scholar for studies from January 2010 to May 2025, using MeSH and free-text terms for Rhesus isoimmunization (e.g., "Rh isoimmunization," "hemolytic disease of newborn"), African settings (e.g., "Nigeria," "sub-Saharan"), pregnancy (e.g., "pregnant women," "antenatal"), and hospital contexts (e.g., "hospitals," "tertiary care"). An example PubMed search string is provided in Supplementary File S1. No language restrictions were applied, but only English-language studies or translations were included.

Study selection

Eligible studies were observational (meta-analysis, cross-sectional, single-arm cohort studies), peer-reviewed, conducted in African hospitals, and reported primary data on Rhesus isoimmunization prevalence. Exclusions included randomized trials, case reports, non-African or community-based studies, and non-English texts without translations. Two reviewers independently screened

titles/abstracts using Rayyan, with full-text assessments resolving disputes via a third reviewer. The PRISMA flow diagram is shown in Figure 1.

PICO framework

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- The research question was structured using the PICO framework, tailored for an observational prevalence study:
 - **Population (P):** Pregnant women attending antenatal care or delivering in African hospitals.
 - **Intervention (I):** None (observational study focusing on prevalence).
 - **Comparison (C):** Subgroups (e.g., women with/without anti-D prophylaxis, urban/rural settings, or regions).
 - **Outcome (O):** Prevalence of Rhesus isoimmunization. The primary research question was “What is the pooled prevalence of Rhesus Isoimmunization among Rhesus negative pregnant women in hospital settings in Africa?”

Eligibility criteria

Included studies were observational, peer-reviewed, conducted in African hospital settings, and reported primary data on Rhesus isoimmunization prevalence. Exclusions included randomized controlled trials, case reports, reviews, non-African or community-based studies, and non-English texts without translations.

Data extraction and quality assessment

Two reviewers independently extracted data using a standardized Excel form based on the PICO framework. Extracted variables included first author, year of publication, country of study, study design, sample size, prevalence rate, study participants, and outcome. Discrepancies were resolved through discussion with a third reviewer. The Joanna Briggs Institute (JBI) checklists were used to assess quality, with studies scoring $\geq 6/9$ deemed high quality.

Statistical analysis

Analyses were performed using Jamovi version 2.6.44 with the MAJOR module. Prevalence proportions were logit-transformed to stabilize variance and approximate normality, then back-transformed for interpretation. A random-effects model, using Restricted Maximum Likelihood (REML) for Tau^2 estimation, pooled prevalence estimates to account for expected clinical and methodological heterogeneity. Heterogeneity was assessed with I^2 , Tau^2 , H^2 , and Cochran's Q statistics. Publication bias was evaluated using Fail-Safe N, Kendall's Tau, Egger's regression, and funnel plots. Equivalence testing (two one-sided tests) assessed whether prevalence fell within pre-specified bounds (-0.500 to 0.500 on the logit scale).

Heterogeneity assessment

High heterogeneity was observed ($I^2 = 85.12\%$, $\text{Tau}^2 = 0.7903$, $H^2 = 6.719$, $Q = 48.320$, $p < 0.001$), indicating substantial between-study variation likely due to differences in location, population, or methodology (Table 3).

Publication bias assessment

No significant publication bias was detected (Fail-Safe N = 2,581, Kendall's Tau = 0.111, $p = 0.761$, Egger's Regression = 0.424, $p = 0.672$) (Table 3). The high Fail-Safe N suggests robust findings.

RESULTS

Study selection and characteristics

From 257 records (PubMed: 32, SCOPUS: 27, Web of Science: 18, Lens.org: 180), 59 duplicates were removed, 198 titles/abstracts screened, 16 full texts assessed, and 9 studies included ($n = 28,188$ women) from Nigeria, Ethiopia, Uganda, and DR Congo (Figure 1). Study designs included retrospective ($n = 4$), cross-sectional ($n = 4$), and retrospective cross-sectional ($n = 1$) (Table 1).

Figure 1: Prisma flow

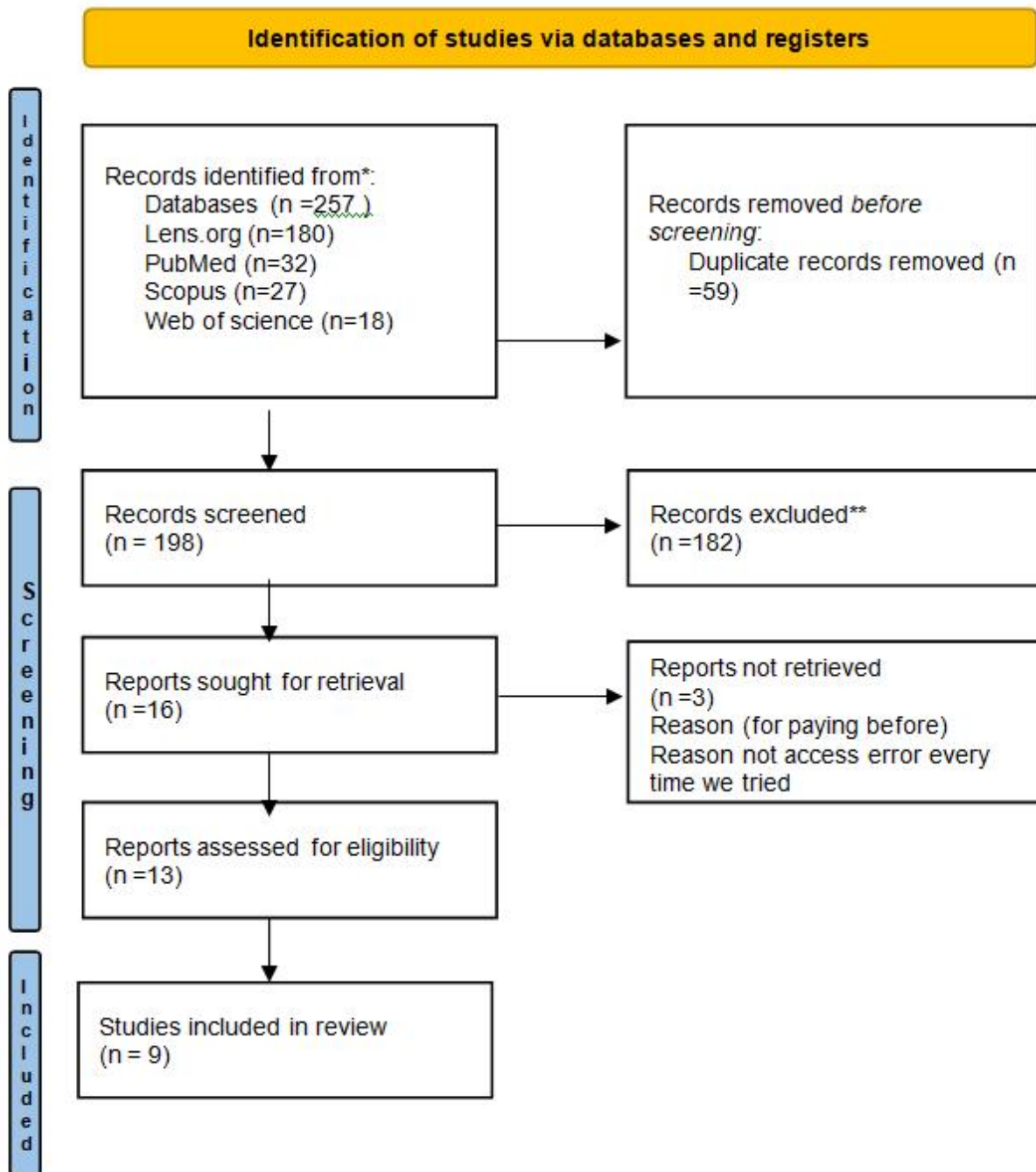


Table 1: Characteristics of included studies

Author (Year)	Country/Setting	Sample Size	Cases	Prevalence (%)	95% CI
Allagoa et al. (2021)	South-South Nigeria	4,571	104	2.28	1.85–2.70
Aliyo et al. (2023)	Bule Hora, Ethiopia	110	7	6.36	2.60–12.75
Chanko (2020)	Sodo, Ethiopia	270	19	7.04	4.27–10.88
Eipl et al. (2012)	Kampala, Uganda	1,001	23	2.30	1.46–3.45
Eleje et al. (2017)	Nnewi, Nigeria	5,561	117	2.10	1.73–2.53
Mbalibulha et al. (2022)	Southwestern Uganda	1,369	70	5.11	4.00–6.44
Natukunda et al. (2011)	Southwestern Uganda	2,001	72	3.60	2.83–4.50
Nyakio et al. (2024)	Bukavu, DR Congo	11,898	37	0.31	0.22–0.43
Tedbabe et al. (2025)	Addis Ababa, Ethiopia	2,407	144	5.98	5.06–7.02
Total/Pooled		28,188	593	2.93	1.58–5.36

Meta-analysis results

The random-effects meta-analysis yielded a pooled logit-transformed prevalence of -3.50 (SE = 0.325, 95% CI: -4.138 to -2.863), translating to a prevalence of 2.93% (95% CI: 1.58%–5.36%) (Table 2). This indicates that approximately 2.93 out of every 100 pregnant women in African hospitals have Rhesus isoimmunization.

Figure 2: Forest plot

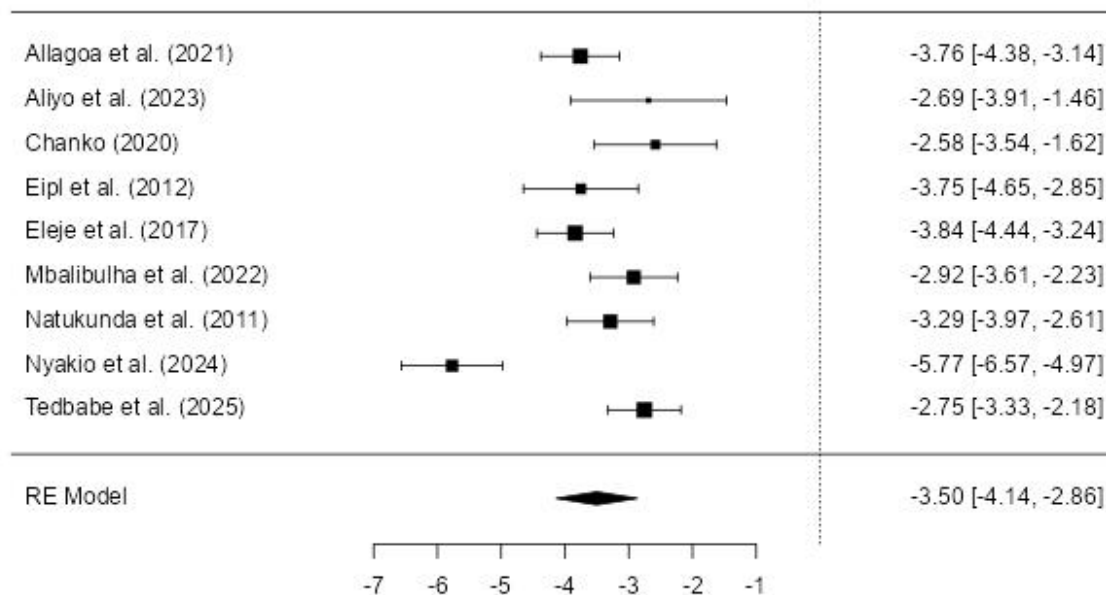
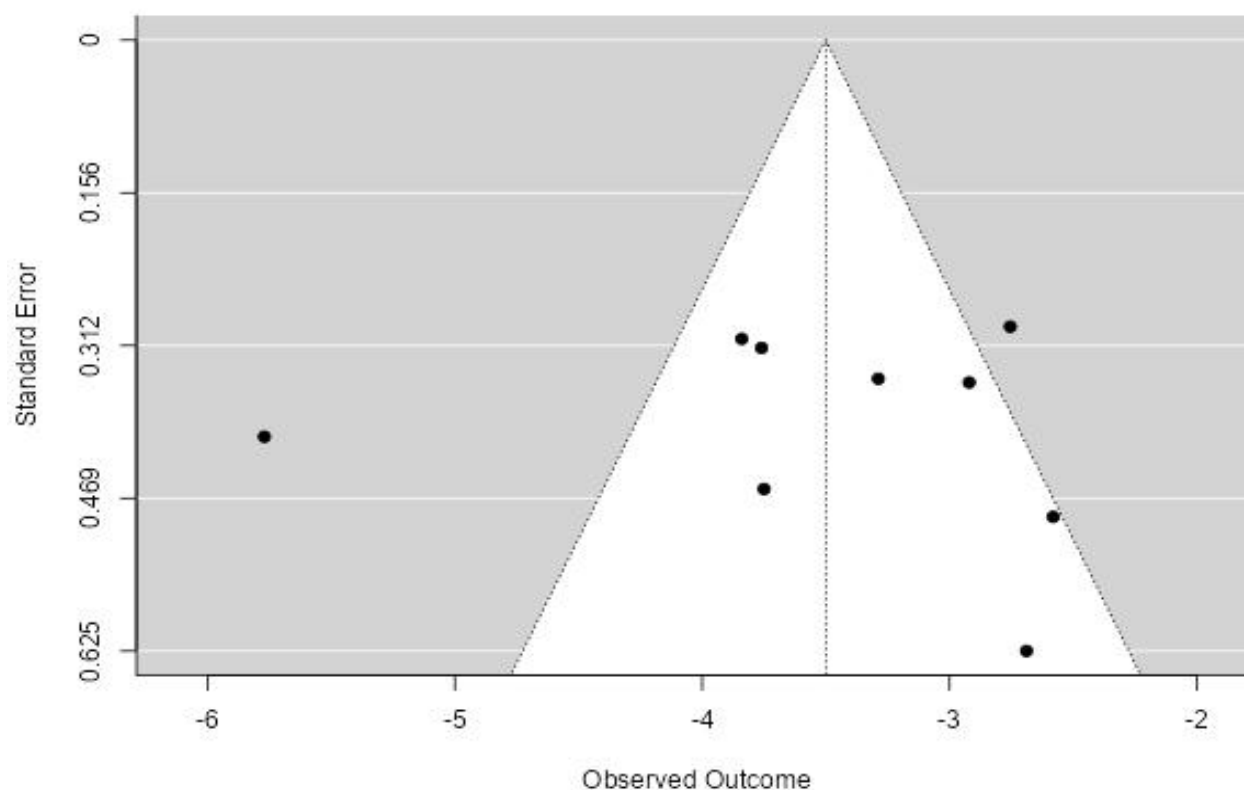


Table 2: Meta-Analysis Results

Parameter	Estimate	Standard Error	Z-value	p-value	95% CI
Logit-transformed prevalence	-3.50	0.325	-10.8	<0.001	-4.138 to -2.863
Prevalence (%)	2.93	-	-	-	1.58 to 5.36

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Figure 3: Forest



Publication bias assessment

No significant publication bias was detected (Fail-Safe N = 2,581, Kendall's Tau = 0.111, $p = 0.761$, Egger's Regression = 0.424, $p = 0.672$) (Table 3). The high Fail-Safe N suggests robust findings.

Table 3: Heterogeneity and publication bias assessment

Statistic	Value	Interpretation
Heterogeneity		
I ²	85.12%	High heterogeneity
Tau ²	0.7903	Substantial between-study variance
Q-statistic	48.320 (p < 0.001)	Significant heterogeneity
Publication Bias		
Fail-Safe N	2,581	Robust against unpublished null studies
Kendall's Tau	0.111 (p = 0.761)	No significant rank correlation bias
Egger's Regression	0.424 (p = 0.672)	No significant small-study effects

Regional variation

Prevalence varied significantly: Ethiopia (5.98%–7.04%, average 6.47%), Nigeria (2.10%–2.28%, average 2.18%), Uganda (2.30%–5.11%, average 3.67%), and DR Congo (0.31%) (Table 4).

Table 4: Regional variation in rhesus isoimmunization prevalence

Region	Studies	Sample Size	Prevalence Range (%)	Average Prevalence (%)
Ethiopia	3	2,787	5.98–7.04	6.47
Nigeria	2	10,132	2.10–2.28	2.18
Uganda	3	4,371	2.30–5.11	3.67
DR Congo	1	11,898	0.31	0.31

Confidence in evidence

Using GRADE, the evidence was rated moderate due to high heterogeneity, despite a large sample size, robust methodology, and no publication bias.

Discussion

Main findings

This systematic review and meta-analysis, the first to estimate the continent-wide prevalence of Rhesus isoimmunization in African hospitals, found a pooled prevalence of 2.93% (95% CI: 1.58%–5.36%) among 28,188 pregnant women across nine studies from Nigeria, Ethiopia, Uganda, and the Democratic Republic of Congo (DR Congo). Key determinants, including previous pregnancies, abortions, stillbirths, blood transfusions, and lack of anti-D prophylaxis, are consistent across studies (Otomewo et al., 2020; Uchenna Eleje et al., 2017).

PICO-based implications

- **Population (P):** Pregnant women in African hospitals, particularly those in tertiary settings, face a notable risk of Rhesus isoimmunization, exacerbated by limited screening and prophylaxis access (Otomewo et al., 2020).
- **Intervention (I):** Observational design highlights the need for routine Rhesus screening and anti-D prophylaxis to prevent sensitization.
- **Comparison (C):** Regional variations (Ethiopia: 6.47%, DR Congo: 0.31%) suggest contextual influences, though limited data restricted subgroup analyses.
- **Outcome (O):** The 2.93% prevalence and determinants (previous pregnancies, abortions, stillbirths, transfusions, lack of prophylaxis) underscore a significant public health challenge.

Interpretation

The prevalence is lower than the ~15% Rh D-negative prevalence in Caucasian populations (Otomewo et al., 2020). but higher than expected for African settings, where Rh D-negative prevalence ranges from 2–8%(Kanko & Woldemariam, 2021; Otomewo et al., 2020). Significant regional variation from 0.31% in DR Congo to 7.04% in Ethiopia highlights the influence of local healthcare systems and diagnostic practices, with critical implications for reducing hemolytic disease of the fetus and newborn (HDFN). (Uchenna Eleje et al., 2017)

The 2.93% prevalence underscores Rhesus isoimmunization as a significant obstetric challenge in African hospitals, contributing to HDFN, which can cause neonatal jaundice, anemia, hydrops fetalis, and stillbirth(Allagoa et al., 2021; Uchenna Eleje et al., 2017). Unlike high-income settings, where universal Rhesus screening and anti-D immunoglobulin prophylaxis have minimized HDFN incidence (Allagoa et al., 2021), the higher prevalence in Africa likely reflects limited antenatal care (ANC) access, inconsistent screening, and prophylaxis shortages(Mbalibulha et al., 2022; Nyakio et al., 2024). Ethiopia's higher average prevalence (6.47%) may stem from rigorous ANC screening, as seen in studies from Bulehora and Sodo(Aliyo et al., 2023; Chanko, 2020), while DR Congo's low rate (0.31%) may be underestimated due to retrospective data and limited laboratory capacity (Nyakio et al., 2024).

High heterogeneity ($I^2 = 85.12\%$, $p < 0.001$) indicates substantial between-study variation, likely driven by differences in study design, diagnostic methods, and healthcare access. For instance, cross-sectional studies in Ethiopia used active antibody screening (Aliyo et al., 2023; Chanko, 2020), whereas retrospective studies in DR Congo relied on hospital records, potentially missing cases(Nyakio et al., 2024). Variations in ANC uptake are higher in urban Ethiopia than rural DR Congo may also contribute(Mbalibulha et al., 2022; Natukunda et al., 2011). Although subgroup analyses by region were conducted, limited data prevented meta-regression to explore sources of heterogeneity, such as parity or prophylaxis access. Standardized diagnostic protocols could reduce such variability in future studies. (Aliyo et al., 2023)

Strengths

This is the first continent-wide meta-analysis of Rhesus isoimmunization in African hospitals, with a large sample

size, PRISMA adherence, PROSPERO registration, and robust statistical methods (random-effects model, logit transformation). The high Fail-Safe N (2,581) and no publication bias enhance confidence in the findings.

Limitations

Hospital-based studies do not generalize to rural or primary care settings. Variability in study designs and diagnostic criteria may contribute to heterogeneity. Inconsistent determinant reporting prevented meta-regression. The focus on English-language studies and limited geographic scope (four countries) may miss broader African contexts.

Implications of the findings

The 2.93% prevalence supports routine Rhesus screening in ANC to identify Rh D-negative women for timely anti-D prophylaxis, particularly post-delivery or abortion. Healthcare providers should educate women on risks from prior pregnancies or transfusions. Policies should subsidize anti-D immunoglobulin, improve laboratory infrastructure, and mandate universal screening, especially in high-prevalence regions like Ethiopia. Increasing ANC uptake can address unbooked cases, a key risk factor (Allagoa et al., 2021).

Future research

Longitudinal studies should assess incidence and outcomes. Meta-regression of determinants (e.g., parity, transfusions) could quantify risks. Expanding research to rural settings and additional African regions, particularly Francophone countries, would enhance representativeness. Cost-effectiveness studies on screening and prophylaxis programs are needed to guide resource allocation.

Conclusions

This meta-analysis establishes a 2.93% prevalence of Rhesus isoimmunization in African hospitals, with significant regional variation and determinants like previous pregnancies and lack of prophylaxis. Routine screening, accessible prophylaxis, and policy reforms are critical to reduce HDFN and improve obstetric outcomes.

Supporting information

- PRISMA checklist, JBI quality scores, search strategies, excluded studies, and forest/funnel plots are provided as supplemental materials.
- Protocol amendments were documented with justifications.

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Author contributions

Brian Ochieng' Onyango: Conceptualization, Methodology, Data Curation, Formal Analysis, Writing – Original Draft.

[Co-Author 1]: Data Curation, Validation, Writing – Review & Editing.

[Co-Author 2]: Methodology, Supervision, Writing – Review & Editing.

[Co-Author 3]: Data Curation, Formal Analysis, Writing – Review & Editing.

Conflict of interest statement

Authors declare no conflicts of interest associated with this work

Data availability statement

Data are available upon reasonable request. The protocol is registered on PROSPERO (ID: CRD420251067446).

Supporting Information

- File S1: Search Strategies
- Table S2: Joanna Briggs Institute Quality Scores
- File S3: PRISMA 2020 Checklist.

Scopus

TITLE-ABS-KEY(("rhesus isoimmunization" OR "rh isoimmunization" OR "rhesus alloimmunization" OR "rh alloimmunization" OR "rh sensitization" OR "anti-d antibod*" OR "hemolytic disease of newborn" OR "hdn" OR "rh incompatibility" OR "rhesus incompatibility" OR "erythroblastosis fetalis")) AND

TITLE-ABS-KEY(("africa*" OR "nigeria" OR "egypt" OR "south africa" OR "ethiopia" OR "kenya" OR "ghana" OR "tanzania" OR "morocco" OR "algeria" OR "sudan" OR "uganda" OR "zambia" OR "zimbabwe" OR "cameroon" OR "mozambique" OR "angola" OR "mali" OR "senegal" OR "tunisia" OR "somalia" OR "libya" OR "sub-saharan")) AND

TITLE-ABS-KEY(("pregnan*" OR "maternal" OR "antenatal" OR "prenatal" OR "obstetric*")) AND

TITLE-ABS-KEY(("hospital*" OR "health center*" OR "health centre*" OR "medical center*" OR "clinic*" OR "tertiary care" OR "health facilit*" OR "healthcare setting*")) AND

TITLE-ABS-KEY(("prevalence" OR "incidence" OR "frequency" OR "occurrence" OR "determinant*" OR "predictor*" OR "risk factor*" OR "epidemiology" OR "characteristic*" OR "associated factor*"))

PubMed

((("Rh Isoimmunization"[Mesh] OR "Erythroblastosis, Fetal"[Mesh] OR "Rh-Hr Blood-Group System"[Mesh] OR "rhesus isoimmunization" OR "Rh isoimmunization" OR "Rh immunization" OR "Rhesus alloimmunization" OR "Rh alloimmunization" OR "Rh sensitization" OR "Anti-D antibodies" OR "hemolytic disease of newborn" OR "HDN" OR "Rh incompatibility")) AND ("Africa"[Mesh] OR "Africa South of the Sahara"[Mesh] OR "Africa, Northern"[Mesh] OR "African Continental Ancestry Group"[Mesh] OR "African*" [tiab] OR "Africa"[tiab] OR "Nigeria"[tiab] OR "Egypt"[tiab] OR "South Africa"[tiab] OR "Ethiopia"[tiab] OR "Kenya"[tiab] OR "Ghana"[tiab] OR "Tanzania"[tiab] OR "Morocco"[tiab] OR "Algeria"[tiab] OR "Sudan"[tiab] OR "Uganda"[tiab] OR "Zambia"[tiab] OR "Zimbabwe"[tiab] OR "Cameroon"[tiab] OR "Mozambique"[tiab] OR "Angola"[tiab] OR "Mali"[tiab] OR "Senegal"[tiab] OR "Tunisia"[tiab] OR "Somalia"[tiab] OR "Libya"[tiab]) AND ("Pregnant Women"[Mesh] OR "Pregnancy"[Mesh]

OR "Prenatal Care"[Mesh] OR "pregnant women"[tiab] OR "pregnancies"[tiab] OR "pregnancy"[tiab] OR "maternal"[tiab] OR "antenatal"[tiab] OR "prenatal"[tiab] AND ("Hospitals"[Mesh] OR "Tertiary Care Centers"[Mesh] OR "Primary Health Care"[Mesh] OR "hospital*"[tiab] OR "healthcare facilit*"[tiab] OR "health center*"[tiab] OR "health centre*"[tiab] OR "medical center*"[tiab] OR "clinic*"[tiab] OR "tertiary care"[tiab] OR "health facilit*"[tiab] AND ("Prevalence"[Mesh] OR "Incidence"[Mesh] OR "Risk Factors"[Mesh] OR "prevalence"[tiab] OR "incidence"[tiab] OR "frequency"[tiab] OR "occurrence"[tiab] OR "determinant*"[tiab] OR "predictor*"[tiab] OR "risk factor*"[tiab] OR "epidemiology"[tiab] OR "characteristic*"[tiab])

Lens.org

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