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Prevalence and factors associated with maternal and neonatal sepsis in sub-Saharan Africa: a systematic review and meta-analysis

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Objectives: This study aimed to determine the prevalence and factors associated with maternal and neonatal sepsis in sub-Saharan Africa.

Methods: This systematic review and meta-analysis used the PRISMA guideline on sepsis data in sub-Saharan Africa. The bibliographic search was carried out on the following databases: Medline/PubMed, Cochrane Library, African Index Medicus, and Google Scholar. Additionally, the reference lists of the included studies were screened for potentially relevant studies. The last search was conducted on 15 October 2022. The Joanna Briggs Institute quality assessment checklist was applied for critical appraisal. Estimates of the prevalence of maternal and neonatal sepsis were pooled using a random-effects meta-analysis model. Heterogeneity between studies was estimated using the Q statistic and the I2 statistic. The funnel plot and Egger's regression test were used to assess the publication bias.

Results: A total of 39 studies were included in our review: 32 studies on neonatal sepsis and 7 studies on maternal sepsis. The overall pooled prevalence of maternal and neonatal sepsis in Sub-Saharan Africa was 19.21% (95% Cl, 11.46–26.97) and 36.02% (Cl: 26.68–45.36), respectively. The meta-analyses revealed that Apgar score <7 (OR: 2.4, 95% Cl: 1.6–3.5), meconium in the amniotic fluid (OR: 2.9, 95% Cl: 1.8–4.5), prolonged rupture of membranes >12 h (OR: 2.8, 95% Cl: 1.9–4.1), male sex (OR: 1.2, 95% Cl: 1.1–1.4), intrapartum fever (OR: 2.4, 95% Cl: 1.5–3.7), and history of urinary tract infection in the mother (OR: 2.7, 95% Cl: 1.4–5.2) are factors associated with neonatal sepsis. Rural residence (OR: 2.3, 95% Cl: 1.01–10.9), parity (OR: 0.5, 95% Cl: 0.3–0.7), prolonged labor (OR: 3.4, 95% Cl: 1.6–6.9), and multiple digital vaginal examinations (OR: 4.4, 95% Cl: 1.3–14.3) were significantly associated with maternal sepsis.

Conclusion: The prevalence of maternal and neonatal sepsis was high in sub-Saharan Africa. Multiple factors associated with neonatal and maternal sepsis were identified. These factors could help in the prevention and development of strategies to combat maternal and neonatal sepsis. Given the high risk of bias and high heterogeneity, further high-quality research is needed in the sub-Saharan African context, including a meta-analysis of individual data.

Systematic review registration: PROSPERO (ID: CRD42022382050).

KEYWORDS

maternal sepsis, neonatal sepsis, prevalence, associated factors, sub-Saharan Africa

Introduction

Maternal and neonatal sepsis is a generalized inflammatory response with systemic manifestations caused by one or more infectious agents (1), which occurs during pregnancy, childbirth, after abortion, or during the postpartum period (42 days) in women or in the first 28 days of life in newborns (2-4). Sepsis is a major cause of maternal and neonatal morbidity and mortality (2, 3, 5-9). It is the third leading cause of death in women and accounts for a quarter of neonatal deaths (1, 10–14). It is an obstacle to achieving the third Sustainable Development Goal (SDG), which aims to reduce maternal and neonatal mortality and morbidity (15). Low- and middle-income countries (LICs) are particularly affected by maternal and neonatal sepsis (11, 16, 17). In sub-Saharan Africa (SSA), it is estimated to be responsible for 130,000 maternal deaths and 300,000 neonatal deaths per year, although this may be an underestimation (2, 18). These deaths reflect a number of challenges, including policy, poverty, health inequalities, and the health system (19). However, few data are available on the prevalence and factors associated with sepsis across the continuum from pregnancy to postpartum or post-abortion, making it difficult to make a real estimation of maternal and neonatal sepsis in these countries (2, 10, 11). In the literature, the factors associated with maternal and neonatal sepsis are diverse, including prolonged labor, failure to perform antenatal consultation (ANC), prolonged rupture of membranes, history of infection in the mother, repeated vaginal examinations, intrapartum fever, gestational age, parity, type of delivery, prematurity, chorioamnionitis, meconiumstained amniotic fluid, Apgar score <7, low birth weight <2.5 kg, resuscitation of the newborn, age of the newborn <7 days, and male sex (5-7, 20-23).

Prevention, early recognition of signs, and rapid and appropriate management of cases are the main factors associated with a reduction in the morbidity and mortality associated with maternal and neonatal sepsis (5, 11, 24–26). A recent meta-analysis carried out in SSA in 2022 identified several risk factors for neonatal sepsis (27) but did not explore the magnitude of neonatal and/or maternal sepsis nor the factors associated with maternal sepsis. Other studies have shown that the prevalence of maternal sepsis was 39% in Ethiopia (28), 12.20% in Keyna (29), and 20% in Tanzania (30); for neonatal sepsis, it was 77.9 in Ethiopia (31), 20.5% in South Africa (32), 49.8 in Tanzania (33), 37.6 in Nigeria (34), and 17.5 in Ghana (35). Although these single studies reported data on the prevalence and factors associated with maternal and neonatal sepsis, there are no regionally representative pooled data on the magnitude and factors associated with maternal and neonatal sepsis in SSA. However, a better understanding of the burden and a synthesis of the evidence on the factors associated with maternal and neonatal sepsis are needed to optimize prevention strategies and management guidelines against this scourge. The aim of this systematic review with metaanalysis was to estimate the prevalence and factors associated with maternal and neonatal sepsis in sub-Saharan Africa. To the best of our knowledge, this is the first systematic review and meta-analysis to examine both the prevalence of and factors associated with maternal and neonatal sepsis in SSA. It aimed to answer the following questions:

What is the prevalence of maternal and neonatal sepsis in sub-Saharan Africa?

What are the associated factors with maternal and neonatal sepsis in sub-Saharan Africa?

Materials and methods

This systematic review was reported in accordance with PRISMA (Preferred Reporting Item for Systematic Review and Meta-analysis) guidelines (36). The protocol for this review was developed and registered in the "International prospective register of systematic reviews PROSPERO" (ID: CRD42022382050).

Search strategies

To identify eligible studies, Medline/PubMed, Cochrane Library, African Index Medicus, and Google Scholar databases were searched. We also conducted manual searches of the bibliographic references of included studies and meta-analyses. The adapted PECO format was used for this systematic review. This PECO included population (P), exposure (E), comparison (C), and outcome (O), as shown in Table 1. It consisted of using all the identified keywords and indexing terms to search different databases. All the search terms used and the MeSH terms for the search were added, as well as the Boolean operators, to guarantee the exhaustiveness of the search process. Key terms defining the same concept were introduced using the "OR" operator, and the "AND" operator was used to introduce different concepts.

Components	Characteristics
Population	Pregnant women, women in labor, postpartum women, newborns,
Exposure	Associated factors: prolonged labor, failure to perform ANC, prolonged rupture of membranes, history of infection in the mother, repeated vaginal examinations, intrapartum fever, gestational age, parity, cesarean delivery, prematurity, meconium amniotic fluid, Apgar score < 7, birth weight < 2.5 kg, age of newborn <7 days, prematurity.
Comparison	Absence of exposure
Results	Maternal sepsis and associated factors

TABLE 1 PECOT framework for the review objective.

Selection of studies/eligibility criteria

The result of bibliographic searches carried out on the various search tools was exported to Zotero, where duplicates were identified and removed using the Duplicates command and manually also removed during the screening. The study selection process followed two evaluation stages (37). The first evaluation was based on an examination of the titles and abstracts of the articles. The titles and abstracts that were outside the scope of the study were excluded. The second assessment consisted of examining the full text of eligible studies. The entire process was carried out by two reviewers (FBT and NHD). They independently performed abstract screening and full-text study selection, where both authors had to approve the included studies were screened for potentially relevant studies (38).

Studies reporting on the prevalence and/or at least one factor associated with maternal and/or neonatal sepsis in SSA in pregnant women from 28 weeks of amenorrhea (SA), postpartum women up to 42 days after delivery, post-abortion women, and newborns within 28 days of birth were included. Cross-sectional, cohort, and casecontrol studies on the prevalence, frequency, and factors associated with maternal and neonatal sepsis in SSA published in French and English between January 2012 and October 2022 were included. Qualitative studies, systematic reviews, and case series were excluded from the analysis, but the reference lists of these were screened.

Assessment of study quality and risk of bias

The quality of the included studies was assessed by two authors (FBT and NHD) using the Joanna Briggs Institute (JBI) quality assessment checklist (39). For cross-sectional studies, the following criteria were used: (1) conformity between target population and source population; (2) appropriate sampling technique; (3) representativeness of the sample; (4) description of the subject and context of the study; (5) data analysis with sufficient sample coverage; (6) valid methods for identifying the condition; (7) standard and reliable way of measuring the condition for all participants; (8) appropriate statistical test; and (9) adequate response rate. When items received a score \geq 6 out of 9, they were considered to be of high quality. The following were used to assess cohort studies: (1) similarity of groups, (2) similarity of exposure measurement, (3) validity and reliability of measurement, (4) identification of confounders, (5) strategies for dealing with confounders, (6) adequacy of groups/ participants at study entry, (7) validity and reliability of measured outcomes, (8) sufficient duration of follow-up, (9) completeness of follow-up or description of reasons for loss to follow-up, (10) strategies for dealing with incomplete follow-up, and (11) adequacy of statistical analysis. The criteria used to evaluate case–control studies are (1) comparable groups, (2) appropriateness of cases and controls, (3) criteria for identifying cases and controls, (4) standard exposure measurement, (5) similarity of exposure measurement for cases and controls, (6) treatment of confounding factors, (7) strategies for treating confounding factors, (8) standard evaluation of results, (9) appropriateness of duration of exposure, and (10) appropriateness of statistical analysis (see Table 2).

Data extraction

Two authors (FBT and NHD) independently extracted data using a tested form on Microsoft Excel. If discrepancies between data extractors continued, a third reviewer (EMD) was involved. Data extracted included author name and year of publication, country, study period, study setting, study design, study population, sample size, type of sepsis (maternal or neonatal), prevalence of neonatal sepsis, prevalence of maternal sepsis, and risk bias.

For the associated factors, data were extracted on the age of the newborn, Apgar score, gestational age, birth weight, resuscitation of the newborn at birth, sex of the newborn, antenatal consultation (ANC), presence of prolonged rupture of membranes, repeated vaginal examinations, intrapartum fever, gestational age, parity, type of delivery, prematurity, meconium amniotic fluid, history of infection in the mother, maternal fever, type of delivery, and prolonged labor.

Statistical analysis

Data were entered into Microsoft Excel and then exported into Stata version 17 software. We pooled maternal and neonatal sepsis prevalence estimates using a random-effects meta-analysis model because it accounts for variability between studies. We examined the heterogeneity of effect size using the Q statistic and the I² statistic (40). An I² value \geq 50% was considered strong heterogeneity, and a random-effects model was used (41, 42). The random-effect RELM method was mainly used. The funnel plot and Eggers's regression test were used to check for publication bias (43). To complete the tests for publication bias, we added the Begg and Thompson tests on R software. Forest plots were used to display the results graphically. A subgroup analysis was performed according to study design (prospective or retrospective), sepsis diagnostic criteria (clinic or clinic and biology), risk of bias (low or moderate), and different regions of SSA (East, West, or South Africa).

Author				Qı	uality as	sessme	nt ques	tions					
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Yes Total	Quality status
Cross-sectional st	udies												
Tsehaynesh G/ eyesus	N	Y	Y	UC	Y	Y	UC	Y	UC			5/9	Medium risk
Kumera Bekele	Y	Y	Y	UC	Y	Y	Y	Y	UC			7/9	Low risk
Abebe Sorsa	Y	UC	Y	Y	UC	Y	Y	UC	Y			6/9	Low risk
Abimbola Ellen Akindolire	Y	Y	Y	UC	Y	Y	Y	Y	Y			8/9	Low risk
Fortress Yayra Aku	UC	UC	Y	N	Y	Y	Y	Y	UC			5/9	Medium risk
Alemnew Wale	UC	Y	Y	UC	Y	UC	Y	Y	N			5/9	Medium risk
Bua John, 2015	N	Y	N	Y	Y	UC	Y	Y	Y			6/9	Low risk
Debora C. Kajegukaa, 2020	UC	Y	Y	N	UC	Y	Y	Y	UC			5/9	Medium risk
Aytenew Getabelew, 2018	Y	Y	Y	N	N	N	Y	Y	UC			5/9	Medium risk
Tchouambou SN Clotilde, 2022	UC	N	Y	UC	N	Y	Y	Y	Y			5/9	Medium risk
Abdulhakeem Abayomi Olorukooba, 2020	Y	Y	Y	Y	Y	N	UC	Y	Y			7/9	Low risk
Mekitrida L. Kiwone, 2020	UC	N	Y	Y	UC	Y	Y	Y	UC			5/9	Medium risk
Tilahun Tewabe, 2017	Y	Y	Y	UC	Y	Y	Y	UC	Y			7/9	Low risk
Endalk Birrie, 2020	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk
Abdurahman Kedir Roble, 2022	UC	Y	Y	Y	UC	Y	Y	Y	UC			7/9	Low risk
Zelalem Agnche, 2020	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk
Daniel Atlaw, 2019	Y	Y	Y	UC	Y	Y	Y	Y	Y			8/9	Low risk
Alemale Admas, 2020	Y	Y	Y	U	UV	Y	Y	Y	Y			8/9	Low risk
Yenew Engida Yismaw, 2019	Y	Y	Y	UC	Y	UC	Y	UC	Y			6/9	Low risk
Tinuade A Ogunlesi, 2010	Y	Y	Y	Y	UC	Y	Y	Y	Y			8/9	Low risk
Agricola Joachim, 2009	Y	Y	Y	UC	Y	Y	Y	Y	Y			8/9	Low risk
Neema Kayange, 2010	Y	Y	Y	UC	Y	UC	UC	Y	Y			6/9	Low risk
Ogundare Ezra Olatunde, 2015	Y	Y	Y	UC	Y	Y	Y	Y	Y			8/9	Low risk

TABLE 2 Quality assessment results of included studies in sub-Saharan Africa from January 2002–October 2022 using the Joanna Briggs Institute (JBI) quality appraisal checklist.

(Continued)

TABLE 2 (Continued)

Author	Quality assessment questions												
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Yes Total	Quality status
BA West, 2014	Y	Y	UC	Y	UC	N	Y	Y	Y			6/9	Low risk
Cohort studies													
Violet Okaba	Y	Y	Ν	Y	UC	Y	Y	Y	Y	Ν	Y	8/11	Low risk
Kayom													
Shatry N. A., 2022	Y	Y	Y	Y	UC	Y	Y	Ν	UC	Y	Y	8/11	Low risk
Case-control													
study													
Mulunesh Alemu	Y	Y	Y	UC	Y	Y	Y	Y	UC	Y		8/10	Low risk
Kalkidan Béjituel	Y	Y	Y	UC	Y	Y	Y	Y	Y	Y		9/10	Low risk
Getu Alemu Demisse	Y	Y	Y	UC	Y	Y	Y	Y	N	Y		8/10	Low risk
Dejene Edosa Dirirsa	Y	Y	Y	UC	Y	Y	UC	Y	Y	Y		8/10	Low risk
Gujo Teshome	Y	Y	Y	Y	Y	Y	N	Y	UN	Y		8/10	Low risk
Peter Adatara, 2019	Y	Y	Y	UC	Y	N	UC	Y	Y	Y		7/10	Medium risk
Peter Adatara, 2018	Y	Y	Y	N	UN	Y	Y	UC	UC	Y		6/10	Medium risk
Destaalem Gebremedhin	Y	Y	Y	Y	Y	UC	UC	Y	Y	Y		8/10	Low risk
Pendo P. Masanja	Y	Y	Y	Y	Y	N	N	Y	UC	Y		7/10	Low risk
Atkuregn Alemayehu, 2020	Y	N	Y	Y	Y	UC	UC	Y	Y	Y		7/10	Low risk
Tadesse Yirga AkaluID, 2020	Y	Y	Y	U	UC	UC	Y	Y	Y	Y		8/10	Low risk
Soressa Gemechu Kitessa, 2021	Y	Y	Y	Y	Y	UC	UC	Y	Y	Y		8/10	Low risk
Mate Siakwa, 2014	Y	Y	Y	UC	UC	N	UC	Y	Y	Y		6/10	Medium risk

Q, Question; Y, yes; N, no; UC, unclear.

Results

A total of 2,638 titles were screened (2,033 from PubMed, 58 from the African Index of Medicus, 41 from Cochrane, and 506 from Google Scholar). After removing duplicates, 2,145 studies remained. Evaluation of titles and abstracts led to the exclusion of 2,019 studies. Nine studies were excluded because the full text was not available. The full-text review involved 126 studies. The number of articles retained for inclusion was 39. The reasons for the exclusion of 87 studies were the lack of availability of the variable of interest and the difference in the target population (Figure 1).

Characteristics of the studies included in the meta-analysis

A total of 39 studies were included in our review: 32 studies of neonatal sepsis and 7 studies of maternal sepsis. There were 24 cross-sectional studies (22, 30–34, 44–60), 13 case–control studies (28, 35, 61–69), and 2 cohorts (29, 70).

Twenty-one studies were from Ethiopia (28, 31, 44–46, 49, 51–56, 60–64, 66, 68, 69, 71), five from Tanzania (22, 30, 33, 67, 72), five from Nigeria (34, 47, 59, 73, 74), four from Ghana (35, 48, 65, 75), two from Uganda (50, 70), one from Kenya (29), and one



from South Africa (32). The total study population was 12,777, including 10,494 newborns and 2,283 women. After quality assessment, 30 studies had a low risk of bias and 9 had a medium risk of bias (see Table 3).

Prevalence of maternal sepsis

The pooled prevalence of maternal sepsis in SSA was 19.21% (95% CI, 11.46–26.97). Significant heterogeneity was observed between studies (I² = 93.26%, p < 0.000). A random effects model was used to measure pooled prevalence. The highest prevalence was reported by Alemale et al. (54) (33.7%) and the lowest by Debora et al. (22) (11.5%); Figure 2 shows the details.

Subgroup analysis of the prevalence of maternal sepsis

A subgroup analysis of the prevalence of maternal sepsis was carried out according to the diagnostic criteria for sepsis (clinical or clinical and biological). It was 25.33 (9.28–41.38) for sepsis based on clinical signs and 15.43 (8.28–22.58) for sepsis based on clinical signs and biology (22, 29, 30). See Table 4 for details.

Prevalence of neonatal sepsis

The pooled prevalence of neonatal sepsis in SSA was 36.02% (95% CI, 26.68–49.36). A significant heterogeneity between the included

TABLE 3 Characteristics of included studies.

N	First author, publication year	Country	Study period	Setting	Study design	Study population	Sample size	Type of sepsis	Prevalence	Risk of bias
1	Tsehaynesh G/ eyesus, 2017	Ethiopia	September 2015 to May 2016	Hospital	Prospective Cross- sectional	Newborn	251	Neonatal	46.61%	Medium risk
2	Kumera Bekele, 2022	Ethiopia	January 2021 to March 2021	Hospitals	Transversale prospective	Newborn	378	Neonatal	52.27%.	Low risk
3	Mulunesh Alemu, 2019	Ethiopia	1 February to 30 March 2018	Hospitals	Case-control	Newborn	246	Neonatal	-	Low risk
4	Kalkidan Béjituel, 2022	Ethiopia	1 August to 30 September 2020	Hospitals	Case-control	Newborn	331	Neonatal	-	Low risk
5	Getu Alemu Demisse, 2019	Ethiopia	1 February to 30 April 2018	Hospitals	Case-control	Mother	280	Maternal	-	Low risk
6	Dejene Edosa Dirirsa, 2021	Ethiopia	May 2018 to August 2018	Hospitals	Case-control	Newborn	220	Neonatal		Low risk
7	Abebe Sorsa, 2019	Ethiopia	April 2016 to May 2017	Hospital	Prospective Cross- sectional	Newborn	303	Neonatal	34%	Low risk
8	Abimbola Ellen Akindolire, 2016	Nigeria	November 2013 and February 2014	Hospitals	Prospective Cross- sectional	Newborn	202	Neonatal	12.37	Low risk
9	Fortress Yayra Aku, 2020	Ghana	January and May 2016	Hospitals	Prospective Cross- sectional	Newborn	150	Neonatal	17.3%	Medium risk
10	Alemnew Wale, 2021	Ethiopia	May to November 2019	Hospital	Prospective Cross- sectional	Newborn	193	Neonatal	26.1%	Medium risk
11	Gujo Teshome, 2022	Ethiopia	1 October to 10 November 2021	Hospitals	Case-control	Newborn	293	Néonatal	-	Low risk
12	Peter Adatara, 2019	Ghana	January and December 2017	Hospital	Case-control	Newborn	900	Neonatal	-	Low risk
13	Peter Adatara, 2018	Ghana	4 weeks	Hospital	Case-control	Newborn	383	Neonatal	17.50%	Medium risk
14	Destaalem Gebremedhin, 2016	Ethiopia	December 2014 to June 2015	Hospitals	Case-control	Newborn	234	Neonatal	-	Low risk
15	Bua John, 2015	Uganda	January and August 2013	Health Center	Prospective Cross- sectional	Mother and newborn	174	Neonatal	21.80%	Low risk
16	Debora C. Kajegukaa, 2020	Tanzania	January 2015 to December 2015	Hospital	Retrospective Cross- sectional	Mother	183	Maternal	11.5%	Medium risk
17	Violet Okaba Kayom, 2018	Uganda	March to May 2012	Community	Prospective Cohort	Mother and newborn	335	Neonatal		Low risk
18	Pendo P. Masanja, 2019	Tanzania	May to July 2017	Hospitals	Case-control	Mother and newborn	322	Neonatal		Low risk

(Continued)

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TABLE 3 (Continued)

N	First author, publication year	Country	Study period	Setting	Study design	Study population	Sample size	Type of sepsis	Prevalence	Risk of bias
19	Atkuregn Alemayehu, 2020	Ethiopia	April to July 2019	Hospitals	Case-control	Newborn	385	Neonatal		Low risk
20	Tadesse Yirga AkaluID, 2020	Ethiopia	March 2018 to April 2018	Hospitals	Case-control	Newborn	231	Neonatal		Low risk
21	Aytenew Getabelew, 2018	Ethiopia	1 February 2016 to 1 February 2017	Hospitals	Retrospective Cross- sectional	Newborn	224	Neonatal	77.9%	Medium risk
22	Tchouambou SN Clotilde, 2022	South Africa	1 January and 30 June 2018	Hospitals	Prospective Cross- sectional	Newborn	210	Neonatal	20.5%	Medium risk
23	Abdulhakeem Abayomi Olorukooba, 2020	Nigeria	May 2017 to May 2018	Hospital	Retrospective Cross- sectional	Newborn	409	Neonatal	37.6%.	Low risk
24	Mekitrida L. Kiwone, 2020	Tanzania	August to October 2018	Hospital	Retrospective Cross- sectional	Newborn	263	Neonatal	49.8%	Medium risk
25	Tilahun Tewabe, 2017	Ethiopia	30 April to 30 May 2016	Hospital	Retrospective Cross- sectional	Newborn	225	Neonatal		Low risk
26	Endalk Birrie, 2020	Ethiopia	1 January to 30 July 2021	Hospital	Prospective Cross- sectional	Newborn	344	Neonatal	79.4%	Low risk
27	Abdurahman Kedir Roble, 2022	Ethiopia	1 January 2019 to 31 December 2019	Hospitals	Prospective Cross- sectional	Newborn	361	Neonatal	45.80%	Low risk
28	Zelalem Agnche, 2020	Ethiopia	March to April 2019	Hospitals	Prospective Cross- sectional	Mother and newborn	352	Neonatal	64.8%	Low risk
29	Soressa Gemechu Kitessa, 2021	Ethiopia	May to October 2020	Hospitals	Case-control	Mother	428	Maternal	-39%	Low risk
30	Shatry N. A., 2022	Kenya	March to November 2015	Hospital	Prospective Cohort	Mother	566	Maternal	12.20%	Low risk
31	Daniel Atlaw, 2019	Ethiopia	1 September to 30 December 2017	Hospital	Prospective Cross- sectional	Mother	219	Maternal	17.2%,	Low risk
32	Alemale Admas, 2020	Ethiopia	January to May 2017	Hospital	Prospective Cross- sectional	Mother	166	Maternal	33.70%	Low risk
33	Ayenew Engida Yismaw, 2019	Ethiopia	1st September to 30th November 2017	Hospital	Prospective Cross- sectional	Newborn	423	Neonatal	11.70%	Low risk
34	Tinuade A Ogunlesi, 2010	Nigeria	January 2006 to December 2008	Hospital	Retrospective Cross- sectional	Newborn	1,050	Neonatal	16.5	Low risk

TABLE 5 (Continued)	TABLE 3	(Continued)
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N	First author, publication year	Country	Study period	Setting	Study design	Study population	Sample size	Type of sepsis	Prevalence	Risk of bias
35	Agricola Joachim, 2009	Tanzania	October 2008 to March 2009	Hospital	Prospective Cross- sectional	Mother	300	Maternal	20%	Low risk
36	Neema Kayange, 2010	Tanzania	March to November 2009	Hospital	Prospective Cross- sectional	Newborn	770	Neonatal	39%	Low risk
37	Mate Siakwa, 2014	Ghana	January 2011 and December 2013	Hospital	Case-control	Newborn	196	Neonatal		Medium risk
38	Ogundare Ezra Olatunde, 2015	Nigeria	September 2008 to March 2009	Hospital	Prospective Cross- sectional	Newborn	360	Neonatal	16%	Low risk
39	BA West, 2012	Nigeria	July to December 2007	Hospital	Prospective Cross- sectional	Newborn	406	Neonatal	41.6%	Low risk



studies was observed (I2=99.1%, p < 0.000). Therefore, a random effects model was used to estimate the pooled prevalence. The prevalence ranged from 11.1 (56) up to 77.9% (31) (see Figure 3).

Subgroup analysis of the prevalence of neonatal sepsis

A subgroup analysis of prevalence was performed according to the design (prospective and retrospective), subdivision of SSA (East, West, or South Africa), definition of sepsis (clinical when diagnostic based on clinical signs or clinical and biological when diagnostic based on clinical signs and confirmed by biological tests), and risk of bias (low or moderate).

Depending on the design, the prevalence of neonatal sepsis was 32.88 (22.35–43.41) for prospective studies and 45.46 (25.97–64.94) for retrospective studies. According to the diagnostic criteria for sepsis, it was 44.11 (27.33–60.90) for sepsis based on clinical signs and 31.25 (22.24–40.26) for sepsis based on clinical signs and biology. According to the subdivision, the prevalence of neonatal sepsis was 42.96 (30.75–55.16) in East Africa, 23.59 (15.53–33.65) in West Africa, and 20.48 (15.0–25.93) in South Africa. The prevalence of neonatal sepsis was 34.45 (23.93–44.98) for studies with a low risk of bias and 39.69 (21.58–57.80) for studies with a medium risk of bias (see Table 5).

TABLE 4 Sub-group analysis of the prevalence of maternal sepsis in sub-Saharan Africa.

Variable	Characteristics	Pooled prevalence (95% CI)	I ² (value of <i>p</i>)
Diagnostic criteria	Clinical	25.33 (9.28-41.38)	92.54% (<0.000)
	Clinical and biological	15.43 (8.28–22.58)	89.72% (<0.000)

Publication bias

We assessed publication bias using the funnel plot and Egger's regression test (76). Compared with the maternal sepsis studies, a visual asymmetrical distribution was observed, and Egger's regression test (value of p = 0.01) indicated the presence of a publication bias (see Figure 4). We did not use the Begg and Thompson tests due to the number of studies less than 10.

For the study concerning neonatal sepsis, we assessed publication bias using the funnel plot, Egger's regression test, Begg's test, and Thompson test. The diagrams showed asymmetry, and the result of Egger's test showed the presence of bias (p = 0.04; see Figure 5). However, Begg's test (value of p = 0.06) and the Thompson test (value of p = 0.14) did not reject the city Ho. Therefore, the asymmetry on the funnel plot is reflected much more by a small study effect than by a publication bias.

Meta-analysis of factors associated with maternal sepsis

A total of eight risk factors were included in the meta-analysis: place of residence for 3 studies (22, 28, 63), parity for 3 studies (22, 30, 54), mode of delivery for 5 studies (22, 28, 54, 60, 63), prolonged labor for 5 studies (22, 28, 29, 54, 63), multiple vaginal examinations for 3 studies (28, 29, 63), performance of ANC for 4 studies (28, 54, 60, 63), history of urinary tract infection for 3 studies (22, 29, 30), and level of education for 4 studies (28, 29, 60, 63). Table 6 shows the details.

Meta-analysis of factors associated with neonatal sepsis

A meta-analysis was carried out for 15 risk factors classified into maternal and neonatal factors. The maternal factors were history of urinary tract infection in the mother (13 studies) (31, 45, 53, 55, 56, 61, 62, 65, 66, 68-71), parity (10 studies) (31, 45, 48, 53, 56, 61, 62, 65, 67, 68), prolonged labor (5 studies) (31, 53, 62, 69, 73), intrapartum fever (13 studies) (31, 45, 48, 52, 55, 56, 61, 64, 66, 68, 70, 72, 73), multiple vaginal examinations (7 studies) (45, 53, 61, 64, 66-68), performance of ANC (13 studies) (45, 48, 50, 55, 61, 64, 65, 67-71), prolonged rupture of membranes (18 studies) (31, 33, 45, 46, 52, 53, 56, 61, 62, 65-73), and mode of delivery (14 studies) (31, 32, 35, 44, 46, 48, 52, 61, 62, 64, 66–68, 72). The neonatal factors reported were Apgar (18 studies) (31, 33-35, 44-46, 48, 52, 56, 61, 62, 64-66, 68, 69, 71), prematurity (17 studies) (31, 33-35, 44-46, 50, 52, 53, 61, 62, 64-67, 71), meconium amniotic fluid (12 studies) (31, 45, 46, 52, 61, 64-69, 72), birth weight (17 studies) (31-35, 44-48, 52, 53, 61, 62, 64-69, 72), neonatal resuscitation (09 studies) (33-35, 52, 53, 62, 65, 66, 71), neonatal age < 7 days (11 studies) (36, 38, 48, 53, 57, 65, 66, 69, 72, 75), and neonatal sex (14 studies) (32, 34, 35, 45, 46, 48, 53, 55, 61, 62, 65, 66, 72, 73) (see Table 7).

Associated factors with maternal and neonatal sepsis

Factors associated with maternal sepsis

Rural residence (OR: 2.32, IC 95%: 1.01–10.9, I2=90.3%), parity (OR: 0.5, IC95%: 0.3–0.7, I²=0%), prolonged labor (OR: 3.4, IC95%: 1.6–6.9, I2=81.5%), and multiple vaginal examinations (OR: 4.4, IC95%: 1.3–14.3, I2=90.4%) were independently associated with maternal sepsis.

Factors associated with neonatal sepsis

The meta-analysis identified 6 factors as being significantly associated with neonatal sepsis, including Apgar score <7 (OR: 2.4, CI95%: 1.6–3.5, I2=88.8%), the presence of meconium in the amniotic fluid (OR: 2.9, CI95%: 1.8–4.5, I2=78.6%), prolonged rupture of membranes >12 h (OR: 2.8, IC95%: 1.9–4.1, I2=82.9%), male sex (OR: 1.2, IC95%: 1.1–1.4, I2=0%), intrapartum fever (OR: 2.4, IC95%: 1.5–3.7, I2=84.2%), and history of urinary tract infection in the mother (OR: 2.76, IC95%: 1.4–5.2, I2=89.5%).

Discussion

Knowledge of the burden and risk factors of maternal and neonatal sepsis is crucial for developing preventive measures and reducing maternal and neonatal mortality. This systematic review with meta-analysis filled the gaps in the literature on the prevalence of maternal and neonatal sepsis and associated factors in SSA. Based on 39 studies included in the final analysis, we found a pooled prevalence of 19.21% for maternal sepsis and 36.02% for neonatal sepsis. However, considerable heterogeneity was observed.

Factors such as rural residence, parity, prolonged labor, and multiple vaginal examinations significantly increased the risk of maternal sepsis in our study. The factors associated with neonatal sepsis in this review are classified into maternal and neonatal factors. Maternal factors such as prolonged rupture of membranes > 12 h, intrapartum fever, and history of maternal urinary tract infection and neonatal factors such as Apgar score < 7, presence of meconium in amniotic fluid, and male sex were significantly associated with neonatal sepsis. Our estimate confirms that maternal and neonatal sepsis is a major public health problem in SSA. The pooled prevalence of maternal sepsis in our review is in line with other reviews conducted in 2009 (77) and 2021 (20). This high prevalence can be explained by various factors, such as the coverage of childbirth in health facilities, the asepsis and hygiene of surfaces and materials used, the personal hygiene of pregnant women, and certain harmful practices. Our study

Study					Effect size with 95% Cl	Weight (%)	
Tsehaynesh G/eyesus				⊢		46.61 [40.44, 52.78]	4.95
Abebe Sorsa						33.63 [30.54, 36.71]	5.04
Endalk Birrie					-	79.36 [75.08, 83.64]	5.01
Abdurahman Kedir Roble			-	_		45.79 [40.61, 50.96]	4.99
Ayenew Engida Yismaw	-	ŀ				11.11 [8.12, 14.11]	5.04
Aytenew Getabelew					-	77.87 [72.66, 83.08]	4.98
Neema Kayange			-			38.96 [35.52, 42.41]	5.03
Kumera Bekele			-	-		52.27 [47.21, 57.32]	4.99
Alemnew Wale						26.13 [23.16, 29.11]	5.04
Bua John		-				21.84 [15.70, 27.98]	4.95
Abdulhakeem Abayomi Olorukooba			-			37.63 [33.23, 42.04]	5.01
Zelalem Agnche						64.60 [59.51, 69.69]	4.99
Tchouambou SN Clotilde						20.48 [15.02, 25.93]	4.98
Mekitrida L. Kiwone			-	-		49.81 [43.77, 55.85]	4.96
Violet Okaba Kayom	-	·				11.04 [7.59, 14.49]	5.03
Tinuade A Ogunlesi						16.57 [14.32, 18.82]	5.05
Abimbola Ellen Akindolire		-				12.38 [7.83, 16.92]	5.00
Fortress Yayra Aku						17.33 [11.28, 23.39]	4.96
Ogundare Ezra Olatunde		-				16.11 [12.31, 19.91]	5.02
BA West						41.63 [36.83, 46.42]	5.00
Overall						36.02 [26.68, 45.36]	
Heterogeneity: τ ² = 448.44, l ² = 99.06%, H ² = 106.66			·				
Test of $\theta = \theta$: Q(19) = 1813.36, p = 0.00							
Test of $\theta = 0$: z = 7.56, p = 0.00							
	Ó	20	40	60	80		
Random-effects REML model							
ed prevalence of neonatal sepsis in SSA.							

is the first to examine both the extent and the factors associated with maternal and neonatal sepsis, which sets it apart from other reviews. It identified other factors, such as rural residence and parity, which were not identified in the 2022 review or the WHO guidelines (78). Our results could serve as a broader database for the development of interventions for the prevention and management of maternal and neonatal sepsis.

All the maternal sepsis studies included were from East Africa. The subgroup analysis of the prevalence of maternal sepsis ranged from 15.43% based on clinical signs and biology to 25.33% based on clinical signs.

The subgroup analysis of the prevalence of neonatal sepsis varied from one subdivision to another. East Africa recorded the highest prevalence, 42.96%, which was higher than the pooled prevalence. This could be explained by the weakness of the health system, the quality of services offered, and socio-cultural factors. The underanalysis of sepsis in other parts of Africa, due to the small number of studies carried out there, masks a probable high prevalence in these countries, as areas of high prevalence in these countries have probably not been covered by the small number of studies published. The prevalence of neonatal sepsis was 44.11% for the diagnostic criterion based on clinical signs and 31.25% for clinical signs and biology. Despite the various subgroup analyses, they did not make it possible to explore the source of the heterogeneity. This could be explained by the heterogeneous definition of sepsis in the different studies. The clinical signs differed from one study to another, as did the laboratory tests, which is why a meta-analysis of the individual data was necessary to identify a single algorithm.

The factors associated with maternal sepsis in our review are partly in accordance with a review of the literature in other systematic reviews in 2009 and 2022 (27, 77), where the risk factors identified were intrapartum maternal fever, multiple vaginal examinations, foulsmelling vaginal discharge, prematurity, prolonged rupture of membranes, prolonged labor, and multiple vaginal touches.

Living in a rural area was significantly associated with maternal sepsis. Women living in rural areas were 2.3 times more likely to develop sepsis than those living in urban areas. The possible explanation could be poor hygiene levels, lack of water sources, poor cord care, overcrowding in homes, and low education level of mothers in rural areas (73, 75, 79). Another

Variables	Characteristics	Pooled prevalence (95% CI)	I ² (value of <i>p</i>)
Countries	East Africa	42.96 (30.75-55.16)	97.41% (<0.000)
	West Africa	23.59 (15.53–33.65)	98.98% (<0.000)
	South Africa	20.48 (15.0-25.93)	0%
Study design	Foresight	32.88 (22.35-43.41)	98.98% (<0.000)
	Retrospective	45.46 (25.97–64.94)	99.05% (<0.000)
Diagnostic criteria	Clinical	44.11 (27.33-60.90)	99.37% (<0.000)
	Clinical and biological	31.25 (22.24-40.26)	97.64% (<0.000)
Risk of bias	Low	34.45 (23.93-44.98)	99.06% (<0.000)
	Medium	39.69 (21.58–57.80)	98.95% (<0.000)

TABLE 5 Sub-group analysis of the prevalence of neonatal sepsis in sub-Saharan Africa.



possible explanation could be the fact that mothers living in urban areas are close to health facilities and have various means of transport to get to these facilities, and the availability of qualified staff and adequate technical platforms in urban areas. A vaginal examination ≥ 5 times was significantly associated with maternal sepsis. The probability of maternal sepsis was 4.4 times higher in women who had undergone a vaginal examination ≥ 5 times compared with those who had not. During vaginal examinations, there is a high likelihood of microorganisms ascending from the lower to the upper genital tract, which can lead to sepsis. Simple interventions accepted to reduce the incidence of maternal sepsis are using sterile and aseptic technical equipment by providers (hand washing, sterile drapes and instruments, and sterile gloves).

The factors associated with neonatal sepsis in our review are in line with other reviews in Pakistan (78), East Africa (21), SSA (27), and India (80), which reported maternal factors such as intrapartum maternal fever, prolonged rupture of water membranes, gestational age < 37 weeks, prolonged labor, multiple vaginal touches, history of maternal urinary tract infection and low

socioeconomic status, neonatal factors such as resuscitation at birth, low birth weight < 2.5 kg, Apgar score < 7, absence of crying immediately after birth, meconium-stained amniotic fluid, and male sex.

Intrapartum fever was significantly associated with maternal sepsis. The probability of maternal sepsis was 2.4 times higher in women with a fever during pregnancy than in those without a fever. Intrapartum fever is suggestive of a maternal infection that is transmitted to the baby *in utero* or during passage through the genital tract, leading to sepsis.

Membrane rupture > 12 h significantly increased the risk of neonatal sepsis, and a history of urinary tract infection in the mother was significantly associated with neonatal sepsis. The water membrane protects the upper genital tract; when it is ruptured, bacteria can proliferate through the dilated cervix into the upper internal genital tract, causing infection. These pathogens also colonize the birth canal, which could contaminate the newborn during passage through the canal. Intrapartum antibiotic prophylaxis has been recommended as an effective practice for at-risk mothers to reduce sepsis worldwide (81).



TABLE 6 Risk factors included in the meta-analysis for maternal sepsis.

Result	Comparison	Number studies	Effect size	Pooled estimate	Q	Heterogeneity I², value of p
Residence	Rural, urban	3	Odds ratio	3.32 (1.1–10.96)	20.64	90%, 0.048
Parity	Primiparous, multiparous	3	Odds ratio	0.50 (0.32-0.78)	0.42	0.0%, 0.003
Delivery method	CS/ VD	5	Odds ratio	1.47 (0.54-4.01)	35.70	88.8%, 0.448
Prolonged labor	>12 h,<12 h	5	Odds ratio	3.37 (1.64-6.95)	21.60	81.5%, 0.001
Multiple vaginal examinations	>5, <5	3	Odds ratio	4.33 (1.31–14.36)	20.73	90.4%, 0.016
ANC	<4,≥4	4	Odds ratio	1.849 (0.77-4.42)	15.65	80.8%, 0.168
History of urinary tract infections	Yes or No	3	Odds ratio	1.672 (0.71–3.90)	5.02	60.2%, 0.234
Level of education	No education, education	4	Odds ratio	1.32 (0.93-1.86)	0.99	0.0%, 0.112

CS, Cesarean section; VD, Vaginal delivery.

Having an Apgar score <7 significantly increased the risk of neonatal sepsis. As a result, the probability of neonatal sepsis was 2.4 times higher in neonates with an Apgar score <7 compared with those with an Apgar score >7. This finding is consistent with studies from Iraq (82) and Indonesia (83). Neonates with low Apgar scores tend to have a poor adaptation to extrauterine life due to the stress experienced during labor and therefore are more prone to infection. In addition, resuscitation procedures following birth asphyxia tend to expose newborns to pathogenic microbes. In our study, however, we did not assess birth asphyxia as a risk factor for neonatal sepsis.

Male sex has been identified as a factor associated with neonatal sepsis, and this finding has been made in the journals in India and SSA. However, we suggest further research into this factor to give a more rational explanation.

Strengths and limitations

Our review used an appropriate search strategy, with the combination of global and regional databases reducing the risk of missing relevant regional studies. Duplicate screening and data extraction, as well as rigorous quality assessment of included data and subgroup analysis, was also performed. The relatively high number of included studies for neonatal sepsis is a strength. The number of articles included was small for maternal sepsis (7), which may limit the generalizability of the results. Most of the studies were cross-sectional, which could be a limitation. The majority of studies included in this systematic review were from East Africa, which may affect the generalizability of our results to sub-Saharan Africa. There were also publication biases between studies and a high degree of heterogeneity. We believe that this is

Results	Comparison	Number studies	Effect size	Pooled estimate	Q	Heterogeneity I², value of p
Apgar	<7 or>7	18	Odds ratio	2.38 (1.61-3.53)	151.21	88.8%, 0.000
Preterm	<37 or>37	17	Odds ratio	1.36 (0.81–2.26)	221.03	92.8%, 0.235
Birth weight	<2.5 kg>2.5 kg	17	Odds ratio	1.28 (0.85–1.93)	210.79	90.5%, 0.228
Mode of delivery	CS/VD	14	Odds ratio	1.05 (0.67–1.65)	93.07	86.0%, 0.807
Amios	Yes or No	12	Odds ratio	2.9 (1.83-4.58)	51.37	78.6%, 0.000
PROM	>12H, <12H	18	Odds ratio	2.8 (1.96-4.18)	99.27	82.9%, 0.000
Sex	Male/Female	14	Odds ratio	1.2 (1.1–1.42)	11.92	0.0%, 0.001
CPN	<4,≥4	13	Odds ratio	1.4 (0.82–2.18)	67.69	82.3%, 0.170
Vaginal examination	>5, <5	7	Odds ratio	1.2 (0.51-3.09)	126.14	95.2%, 0.616
Intrapartum fever	Yes or No	13	Odds ratio	2.4 (1.52-3.75)	76.14	84.2%, 0.000
Age of newborn	<7 days, >7 days	11	Odds ratio	0.9 (0.52–1.89)	108.72	90.8%, 0.995
Newborn resuscitation	Yes, No	9	Odds ratio	1,7 (0.94–3.30)	94.67	91.5%, 0.076
Parity	Primiparous, multiparous	10	Odds ratio	1.2 (0.83–1.69)	36.48	75.3%, 0.324
History of maternal UTI	Yes, No	13	Odds ratio	2.76 (1.38–5.21)	114.73	89.5%, 0.003
Prolonged labor	>12H, <12H	5	Odds ratio	1.8 (1.47–1.90)	40.15	90.0%, 0.128

TABLE 7 Risk factors included in the meta-analysis for neonatal sepsis.

an important subject that has not been sufficiently explored and that a meta-analysis of individual data will be necessary.

Conclusion

In our review, the prevalence of maternal and neonatal sepsis was high. Several factors were significantly associated with this prevalence, which could help prevent maternal and neonatal sepsis by developing appropriate standard infection prevention techniques, reducing certain harmful practices, and reducing susceptibility to infection by improving maternal health through nutritional supplementation and treating infections during pregnancy. However, there is a need for evidence on other important risk factors for maternal and neonatal sepsis, including in the community. Given the high risk of bias and high heterogeneity, further high-quality research is needed in the sub-Saharan African context.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Author contributions

FT: Conceptualization, Formal analysis, Investigation, Methodology, Software, Supervision, Writing – original draft, Writing – review & editing. CS: Conceptualization, Methodology, Writing – review & editing. ED: Conceptualization, Writing – review & editing, Investigation. BC: Investigation, Methodology, Writing – review & editing. SS: Software, Writing – review & editing, Formal analysis. ADI: Formal analysis, Validation, Writing – review & editing. ND: Conceptualization, Investigation, Writing – review & editing. BL: Methodology, Writing – review & editing. MA: Conceptualization, Writing – review & editing. KK: Formal analysis, Software, Supervision, Writing – review & editing. AT: Supervision, Writing – review & editing. AC: Writing – review & editing. ADe: Supervision, Validation, Writing – review & editing. HS: Supervision, Validation, Writing – review & editing. IT: Formal analysis, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. The authors declared no conflicts of interest.

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