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ORIGINAL ARTICLE

Neonatal sepsis and its associated factors in East Africa: a systematic review and meta-analysis

Biruk Beletew Abate[1] · Ayelign Mengesha Kasie[1] · Melese Abate Reta[2,3] · Mesfin Wudu Kassaw[1]

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Abstract

Objectives This systematic review and meta-analysis aimed to reveal the magnitude of neonatal sepsis and its associated factors in East Africa.

Methods Using PRISMA guideline, we reviewed and meta-analyzed studies from Google Scholar, Cochrane library, and PubMed; last search date: October 15, 2019. Heterogeneity across the studies was estimated. The subgroup analysis was done. Publication bias was also assessed.

Results A total of 26 studies with 11,239 participants are included. The pooled prevalence of neonatal sepsis in East Africa was 29.765% (95% CI 23.36–35.94). Home delivery (AOR = 2.67; 95% CI 1.15–4.00), maternal history of urinary tract infection (UTI) (AOR = 2.083; 95% CI 0.24–3.93), gestational age/(preterm) (AOR = 1.56; 95% CI 1.04–2.08), prolonged labor (AOR = 3.23; 95% CI 0.04–6.51) and PROM (AOR = 1.95; 95% CI 0.53–3.37) were identified associated factors of neonatal sepsis.

Conclusions The prevalence of neonatal sepsis in East Africa remains high. The relevant stockholders should give attention for neonates delivered from women with intranatal fever to prevent neonatal sepsis. Pregnant women should be screened for UTI. Appropriate interventions should be put in place to manage PROM to decrease the chance of ascending microorganisms.

Keywords Neonatal sepsis · Prevalence · Risk factors · Systematic review · Meta-analysis · East Africa

Abbreviations

EONS	Early-onset neonatal sepsis
LONS	Late-onset neonatal sepsis
PROM	Prolonged rupture of membrane
UTI	Urinary tract infection
OR	Odds ratio
UNICEF	The United Nations Children's Fund
WHO	World Health Organization
CI	Confidence interval
DHS	Demographic and health surveys
EDHS	Ethiopian demographic and health survey

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✉ Biruk Beletew Abate
birukkelemb@gmail.com

Ayelign Mengesha Kasie
Ayelignmengesha59@gmail.com

Melese Abate Reta
melese1985@gmail.com

Mesfin Wudu Kassaw
mesfine12a@gmail.com

[1] College of Health Sciences, Department of Nursing, Woldia University, P. O. Box 400, Woldia, Ethiopia

[2] Department of Medical Laboratory Science, College of Health Sciences, Woldia University, P. O. Box 400, Woldia, Ethiopia

[3] Department of Medical Microbiology, Faculty of Health Sciences, University of Pretoria, Pretoria, South Africa

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Introduction

Neonatal sepsis is one of the most important reasons of morbidity and mortality in newborns (Simonsen et al. 2014). It includes numerous infections such as pneumonia, septicemia, meningitis, arthritis, urinary tract infections, and osteomyelitis, but it does not embrace muco-cutaneous infections such as conjunctivitis and oral thrush (Woldu et al. 2014). It is categorized as early-onset and late-onset neonatal sepsis (Cizmeci et al. 2014). Early-onset neonatal sepsis (EONS) occurs within seven days of life after birth, while late-onset neonatal sepsis (LONS) occurs after the seventh day of neonate's life (Adhikari et al. 2010).

As documented in previous studies, neonatal sepsis is caused by both maternal and neonatal factors such as prolonged rupture of membrane (PROM), urinary tract infection, intra-partum fever, instrumental delivery, prematurity, chorioamnionitis, repeated vaginal examination, never attend antenatal care (ANC), home delivery, meconium-stained amniotic fluid, consumption of unclean foods, low birth weight, complicated delivery, low appearance pulse grimace activity respiration (APGAR) scores, and invasive procedures during hospital admission (Gebremedhin et al. 2016b; John 2015, 8:339; Leal et al. 2012; Moges et al. 2017; Santhanam et al. 2017; Tewabe et al. 2017; Wang et al. 2016).

Worldwide, neonatal sepsis contributes for about 36% of neonatal death followed by preterm (28%) and birth asphyxia (23%) (Saugstad 2011). It accounts about 26% of under-five mortality with highest rate in sub-Saharan Africa (Aijaz et al. 2013). Globally, sepsis in neonates is still among the foremost reasons of neonatal death and morbidity, especially in the first seven days of life in low and middle-income countries (LMIC) (Liu et al. 2016; Seale et al. 2014).

About four million worldwide deaths in neonates per year, from this 98%, are from developing countries particularly in sub-Saharan Africa (EMOH: 2015: 1-182a). The vulnerability of neonatal death is estimated to be six times more in the low and middle-income countries as compared to with developed countries (Edmond and Zaidi 2010).

Due to the presence of constitutional sign and symptoms, timely diagnosis of neonatal sepsis is so challenged. Besides, treating neonates with antibiotics merely by subtle manifestations is likely to over-treat non-infected neonates Besides, treating neonates merely by subtle manifestations is likely to over-treat non-infected neonates (Alkema et al. 2014). The superlative method will be recognizing high-risk neonates and steering them for intensive therapy (EMOH: 2015: 1-182b).

Incidence of neonatal sepsis is around 40-fold higher and mortality rates are two times higher in middle-income countries than in high-income countries (Fleischmann-Struzek et al. 2018). Neonatal sepsis postures a huge public health problem in sub-Saharan Africa with important economic costs (Ranjeva et al. 2018).

In Africa, neonatal sepsis accounts for 28% of neonatal mortality, and for 68 deaths per thousand live births (Tewabe et al. 2017). In sub-Saharan Africa, 17% among all neonatal death results from neonatal sepsis, while only 6% occurred in developed countries (Debelew et al. 2014). Neonatal sepsis is also one of the significant causes of neonatal mortality in East Africa; it is the cause for more than one-third of neonatal deaths in Ethiopia particularly (UNICEF: 2014:1-100b).

Guidelines for the treatment of neonatal sepsis have been formulated and its implementation along with timely initiation of better treatments would satisfactorily decrease neonatal morbidity and mortality of neonates by sepsis (Adhikari et al. 2010). Risk-based diagnosis through identification of the risk factors and timely initiation of treatments can significantly decrease neonatal mortality and morbidity (UNICEF: 2014:1-100a).

To achieve Sustainable Development Goal (SDG) reducing newborn as low as 12/1000 is one of the Global strategies of World Health Organization (WHO) in African countries by 2030. This could be achieved through better prevention and treatment of preterm births and severe infections as the key (Organization 2016). Notable improvement has been seen on maternal and child mortality; however, neonatal health is a part of the "unfinished agenda" (Gebremedhin et al. 2016b; WHO 2014).

In East Africa, previous studies were conducted to estimate the magnitude of neonatal sepsis. However, the magnitude of neonatal sepsis showed great inconsistencies across different geographical settings and different study periods which ranged from 4.7% (Gebrehiwot et al. 2012) to 77.9% (Seale et al. 2009). Besides, there are some contradicting or inconsistent findings on about risk factors and mortality associated factors of neonatal sepsis. Moreover, there is no regionally represented pooled data on the magnitude and associated factors of neonatal sepsis in East Africa. Thus, this systematic review and meta-analysis were aimed to estimate the pooled prevalence of neonatal sepsis and the associated factors' effect size in East African context.

Review question

The review questions of this systematic review and meta-analysis were:

- What is the pooled prevalence of neonatal sepsis in East Africa?
- What are the pooled estimates of associated factors of neonatal sepsis in East Africa?

Methods

Search strategy

This review identified studies that provide data on the prevalence and risk factors for neonatal sepsis with the context of East Africa. In the searching engine, PubMed, Google Scholar, Cochrane library, and institutional repositories were retrieved. The last search date was October 15, 2019. The search included keywords that are the combinations of population, condition/outcome, context, and exposures. A snowball searching for the references of relevant papers for linked articles was also performed. Papers with incomplete data were held through communicating with corresponding authors as described in other papers (Beletew et al. 2019b, 2020). The core search terms and phrases were "newborn," "neonate," "infant," and "sepsis," "septicemia," infection, East Africa. The search strategies were developed using different "AND" and "OR" Boolean operators. The following search strategy was applied: (prevalence OR magnitude) AND (causes OR determinants OR associated factors OR risk factors OR risk OR odd ratio OR predictors) AND (newborn [MeSH Terms] OR neonate OR infant OR child OR children) AND (sepsis [MeSH Terms] OR septicemia OR infection) AND (East Africa). Additionally, remaining papers were screened at the reference lists to identify additional relevant data.

Study selection and screening

The retrieved studies were exported to Endnote version 8, reference manager software to remove duplicated studies. Two investigators (BBA and AMK) independently screened the selected studies using articles' titles and the abstracts before retrieval of full-text papers. We used pre-specified inclusion criteria to further screening of the full-text articles. During final selection of studies, the disagreements were resolved through discussion during a consensus meeting with third and fourth reviewers (MAR and MWK).

Inclusion and exclusion criteria

Newborn babies (any gestation) within 28 days of birth were included. All observational studies (cross-sectional, case–control, and cohort) were included. Those studies had reported the prevalence and/or at least one associated factor for neonatal sepsis and published in the English language from January 2000 to December 2019 were considered. For factors associated with neonatal sepsis, the presence of odds ratio (OR) or comparison group in the form of 2 by 2 table or raw data to calculate the odds ratio was considered as eligibility criteria.

Studies conducted on marginalized groups/populations like neonates from mothers with any medical diseases, chronic diseases, or street mothers were excluded. Citations without abstract and/or full-text, anonymous reports, editorials, and qualitative studies were excluded from the analysis. Intervention studies, mixed-methods studies, reviews, conference abstracts, and commentaries were also excluded. The prevalence of neonatal sepsis was considered as the proportion of neonates with sepsis among the general live birth of neonates within a specific population and multiplied by 100 to be prevalence rate.

Data extraction

The authors developed a data extraction form on the excel sheet and the following data were extracted for eligible studies: Prevalence of neonatal sepsis, year of publication, country, setting, study design, and the odd ratio of factors. The data extraction sheet was piloted using 4 papers randomly, and it was adjusted after piloted the template. Two of the authors extracted the data using the extraction form in collaboration. The third author checked the correctness of the data independently. Any disagreements between reviewers were resolved through discussions with third reviewer when required. The mistyping of data was resolved through crosschecking with the included papers.

Quality assessment

The authors appraised the quality of the studies by using the Joanna Briggs Institute (JBI) quality appraisal checklist (Markos et al. 2019). BBA and AMK independently review the quality of the papers and any disagreements were discussed with the third and fourth (MAR and MWK) reviewer. Studies were considered as low risk or good quality when it scored 4 and above for all designs (cross-sectional, case–control, and cohort) (Markos et al. 2019), whereas the studies scored 3 and below were considered as high risk or poor quality (Table S2).

Outcome measurement

Neonatal sepsis was considered and, neonates with the presence of at least one clinical sign plus at least two laboratory results which are suggestive for neonatal sepsis

(CRP, WBC, ANC, ESR, platelet count, and blood glucose) or neonates who are diagnosed as sepsis by attending physician and fulfill sepsis criteria in addition to culture-positive sepsis within 0–28 days of life.

Synthesis of results

The authors transformed the data to STATA 14 for analysis after it was extracted in an excel sheet considering prevalence, and categories of associated factors reported. We pooled the overall prevalence estimates of neonatal sepsis by a random effect meta-analysis model due to the presence of heterogeneity. We examined the heterogeneity of effect size using the Q statistic and the I^2 statistics. In this study, the I^2statistic value of zero indicates true homogeneity, whereas the value 25, 50, and 75% represented low, moderate, and high heterogeneity, respectively (Higgins and Thompson 2002; Ioannidis 2008). Subgroup analysis was done by the study country, study design, and year of publication to assess the difference of the pooled estimates across different study designs, country, and year of publication. Sensitivity analysis was employed to examine the effect of a single study on the overall estimation of the pooled prevalence. Publication bias was checked by the funnel plot and more objectively through Egger's regression test (Egger et al. 1997).

Reporting

The results of this review were reported based on the Preferred Reporting Items for Systematic Review and Meta-Analysis statement (PRISMA) guideline (Supplementary file1: -PRISMA checklist), and it is registered in the Prospero database: (PROSPERO 2019: CRD42019130792).

The preprint of this manuscript found online (Abate BB et al. 2019; Kassie M Beletew et al. 2019a).

Results

Study selection

A total of 4931 studies were identified; 4919 from electronic database (3282 from PubMed, 12 from Cochrane Library, 1610 from Google Scholar) and 27 from other sources. After duplication removed, 1235 remained (3696 studies were duplicated)). After full-text articles assessed for eligibility (301), 122 studies were excluded because the study subjects were other than neonates or greater than 28 days, another 56 and 71 studies were excluded due to exposure and outcome didn't meet the inclusion criteria for this study. Finally, 26 (n = 11,239) were selected for the prevalence and/ or associated factors analysis (Fig. 1).

Characteristics of included studies

Twenty six papers were included in this systematic review and meta-analysis (al 2018; al. 2008; Ayalew et al. 2015; Babiker et al. 2018; Berkley et al. 2005; Gebrehiwot et al. 2012; Gebremedhin et al. 2016b; Getabelew et al. 2018; Kheir and Khair 2014; Kiwanuka et al. 2013; Laving et al. 2003; Le Geyt and Hauck 2016; Mersha et al. 2019; Mobbs et al. 2019; Moges et al. 2017; Mugalu et al. 2006; Naulikha et al. 2018; Orwenyo 2011; Rijal and Shrestha 2018; S. 2010; Shitaye et al. 2010; T. 2018; Talbert et al. 2010; Woldu et al. 2014). Out of included studies, ten studies were from Ethiopia (al. 2008; Gebrehiwot et al. 2012; Gebremedhin et al. 2016b; Getabelew et al. 2018; Mersha et al. 2019; Moges et al. 2017; Shitaye et al. 2010; T. 2018; Woldu et al. 2014), seven studies from Kenya (Berkley et al. 2005; Laving et al. 2003; Le Geyt and Hauck 2016; Naulikha et al. 2018; Orwenyo 2011; S. 2010; Talbert et al. 2010), 3 studies in Sudan (Babiker et al. 2018; Kheir and Khair 2014; Rijal and Shrestha 2018), and 6 studies in Uganda (al 2018; Ayalew et al. 2015; Berkley et al. 2005; Kiwanuka et al. 2013; Mobbs et al. 2019; Mugalu et al. 2006). Nineteen of the studies were done by cross-sectional study design, three studies by case–control study design, whereas four of the studies were conducted through cohort study design, respectively. The studies included participants, ranging from 62 (Kheir and Khair 2014) to 4849 (Berkley et al. 2005) (Table 1).

Meta-analysis

Prevalence of neonatal sepsis

Of the total included studies, 21 studies (Ayalew et al. 2015; Berkley et al. 2005; Gebrehiwot et al. 2012; Getabelew et al. 2018; Kiwanuka et al. 2013; Le Geyt and Hauck 2016; Mersha et al. 2019; Mobbs et al. 2019; Moges et al. 2017; Mugalu et al. 2006; Naulikha et al. 2018; Shitaye et al. 2010; Talbert et al. 2010) reported the prevalence of neonatal sepsis. The prevalence ranges from 4.7% (Moges et al. 2017) to 77.9% (Getabelew et al. 2018). From those studies, the pooled prevalence of neonatal sepsis in East Africa was found to be 29.65% (95% CI 23.36–35.94) (Fig. 2). We found significant heterogeneity among the studies (I^2 = 98.8%; P < 0.001). We analyzed by random effects model analysis and we perform subgroup analysis (Fig. 2).

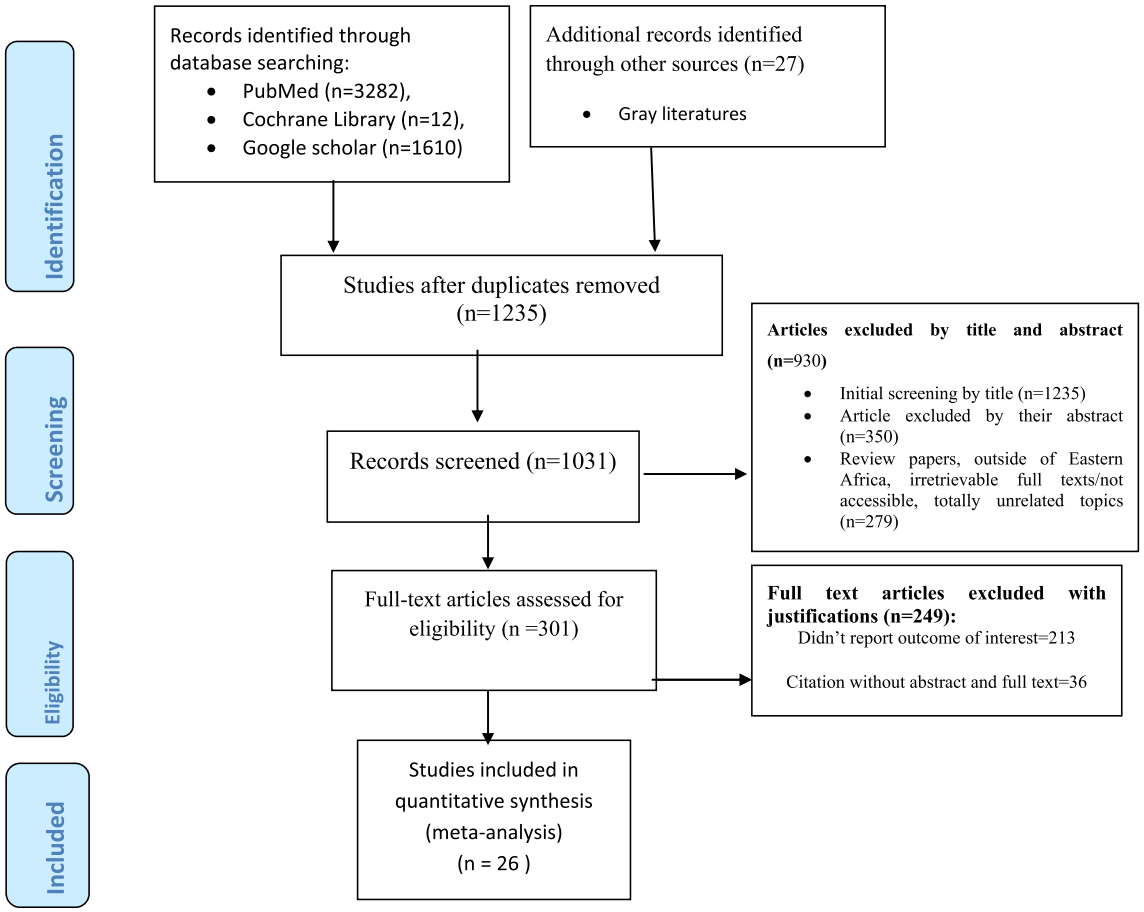

Fig. 1 PRISMA flow diagram showed the results of the search and reasons for exclusion

Subgroup analysis of the prevalence of neonatal sepsis in East Africa

The subgroup analysis was done based on the country, study design, and year of publication. Based on this, the prevalence of neonatal sepsis found to be 38.31% in Ethiopia, 24.4% in Uganda, 18.28% in Kenya, and 39.26 in Sudan. Based on study design, the prevalence of neonatal sepsis is 32.63% in cross-sectional studies and 17.08% in cohort studies. Based on the year of publication, it is 23.05% from 2000 to 2010, 33.01% from 2010 to 2015, and 31.39 from 2015 to 2019 (Table 2).

We have also checked publication bias; accordingly, a funnel plot showed asymmetrical distribution. Egger's regression test *P* value was 0.010. Both the funnel plot and Egger's regression test *P* value indicated the presence of publication bias. The estimated overall prevalence of neonatal sepsis is presented in a forest plot. The overall prevalence of LBW was 29.65% (95% CI 23.36–35.94; I^2 = 98.8%).

The results of this sensitivity analysis showed that our findings were not dependent on a single study. Our pooled estimated prevalence of neonatal sepsis varied between 27.15 (21.68–32.61) and 30.94 (24.96–36.92) after deletion of a single study. Abd Elrahman et al. (2019), Rijal and Shrestha (2018), Moges et al. (2017), Gebremedhin et al. (2016a, b), Getabelew et al. (2018) had shown an impact on the overall estimation.

Factors associated with neonatal sepsis in East Africa context

Out of the total included studies, the majority (Ayalew et al. 2015; Berkley et al. 2005; Gebrehiwot et al. 2012; Kiwanuka et al. 2013; Le Geyt and Hauck 2016; Mobbs et al. 2019; Moges et al. 2017; Naulikha et al. 2018; Shitaye et al. 2010; Talbert et al. 2010) of studies revealed the factors associated with (Table 3).

Nine studies (Berkley et al. 2005; Gebremedhin et al. 2016b; Getabelew et al. 2018; Mersha et al. 2019; Moges et al. 2017; Mugalu et al. 2006; Woldu et al. 2014) found a significant association between place of delivery (home delivery) and neonatal sepsis. The odds of neonatal sepsis

Table 1 Distribution of studies on the prevalence and determinants of neonatal sepsis in East Africa 2019/2020

S. no.	Study country	Study design	Sample size/participants	Prevalence (%)	Quality status
	Ethiopia	Cohort	306	–	Low risk
	Ethiopia	Case–control	231	–	Low risk
	Ethiopia	Cross-sectional	181	32.10	Low risk
	Ethiopia	Cross-sectional	251	0.466	Low risk
	Ethiopia	Case–control	232	–	Low risk
	Ethiopia	Cross-sectional	244	77.90	Low risk
	Ethiopia	Cross-sectional	302	44.70	Low risk
	Ethiopia	Cross-sectional	578	28.70	Low risk
	Ethiopia	Cohort	1189	4.70	Low risk
	Ethiopia	Cross-sectional	275	33.80	Low risk
	Uganda	Cross-sectional	258	24.00	Low risk
	Uganda	Cross-sectional	290	37.90	Low risk
	Uganda	Cohort	103	30.30	Low risk
	Uganda	Cross-sectional	80	32.50	Low risk
	Uganda	Cohort	325	11	Low risk
	Kenya	Case–control	100	–	Low risk
	Kenya	Cross-sectional	104	–	Low risk
	Kenya	Cross-sectional	256	13.29	Low risk
	Kenya	Cross-sectional	84	17.90	Low risk
	Kenya	Cross-sectional	4,849	23.00	Low risk
	Kenya	Cohort	1262	23.90	Low risk
	Kenya	Cross-sectional	1783	12.80	Low risk
	Uganda	Cross-sectional	174	21.80	Low risk
	Sudan	Cross-sectional	62	17.50	Low risk
	Sudan	Cross-sectional	119	37.80	Low risk
	Sudan	Cross-sectional	200	62	Low risk

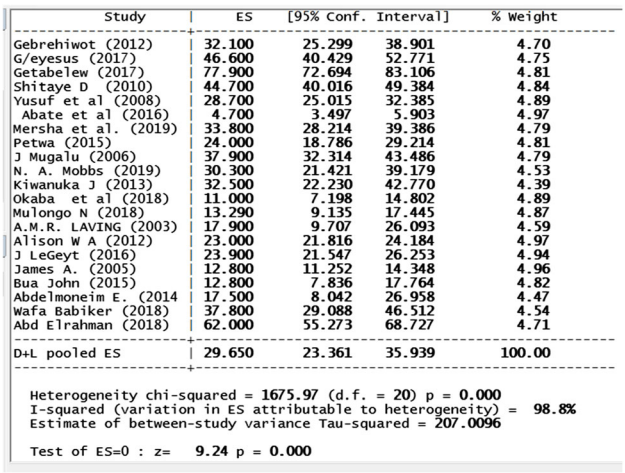

Fig. 2 Prevalence of neonatal sepsis in East Africa, 2019/2020

among neonates delivered at home ranges from 1.44 (Woldu et al. 2014) to 5.3 (Moges et al. 2017) (Table 3).

Regarding the heterogeneity test, the Galbraith plot, I-squared (I^2), and P value showed homogeneity, and combining the result of five studies, the forest plot showed the overall estimate of AOR of home delivery was 2.57 (95% CI 1.15–4.00; I^2 = 0.0%; P = 0.996) (Supplementary Fig. 1).

We have assessed publication bias of place of birth and a funnel plot showed an asymmetrical distribution. Egger's regression test p value was 0.003, which indicated the presence of publication bias. As a result, trim and fill analysis was done and 4 studies were added, and the total numbers of studies become 13 then the pooled estimate of AOR of home delivery becomes 2.36.

Maternal history of UTI

Nine studies (Berkley et al. 2005; Gebremedhin et al. 2016b; Getabelew et al. 2018; Mersha et al. 2019; Moges et al. 2017; Mugalu et al. 2006; Woldu et al. 2014) found a significant association between maternal history of UTI

Table 2 Subgroup analysis of the prevalence of neonatal sepsis in East Africa 2019/2020

Variables	Characteristics	Pooled prevalence (95% CI)	I^2 (p value)
By country	Ethiopia	38.31 (17.43–59.19)	99.5% (< 0.001)
	Uganda	24.4 (14.91–33.90)	93.9% (< 0.001)
	Kenya	18.28 (12.64–23.91)	96.9% (< 0.001)
	Sudan	39.26 (13.31–65.22)	96.6% (< 0.001)
By design	Cross-sectional	32.63 (25.53–39.73)	98.4% (< 0.001)
	Cohort	17.08 (5.22–28.95)	98.7% (< 0.001)
By year of publication	2000–2010	23.05 (12.38–33.73)	96.7% (< 0.001)
	2010–2015	33.01 (20.62–45.40)	96.5% (< 0.001)
	2015–2019	31.39 (19.68–43.10)	99.1% (< 0.001)

and neonatal sepsis. The odds of neonatal sepsis among neonates with maternal history of UTI ranges from 2.9 (Woldu et al. 2014) to 10.8 (Table 3 and Supplementary Fig. 2).

Regarding test of heterogeneity, the Galbraith plot, I-squared (I^2), and P value showed moderate heterogeneity and the forest plot revealed the overall estimate of AOR through random effect models was 2.083 (95% CI 0.24–3.93; I^2 = 69.1%; P = 0.001) (Supplementary Fig. 2).

Test of publication bias has been done and both the funnel plot and Egger's regression test (P value was 0.928) showed the absence of publication bias.

Gestational age (preterm)

Ten studies (Gebremedhin et al. 2016b; Getabelew et al. 2018; Laving et al. 2003; Le Geyt and Hauck 2016; Moges et al. 2017; Naulikha et al. 2018; Woldu et al. 2014) found significant association between gestational age (preterm) and neonatal sepsis. The odds of neonatal sepsis among preterm neonates ranges from 1.49 (Moges et al. 2017) to 10.6 (Moges et al. 2017) (Table 3 and Supplementary Fig. 3).

Regarding test of heterogeneity, the Galbraith plot, I-squared (I^2), and P value showed moderate heterogeneity and the forest plot revealed the overall estimate of AOR of the place of birth was 1.56 (95% CI 1.04–2.08; I^2 = 27.8%; P = 0.000) (Supplementary Fig. 3). We have done publication bias and the funnel plot and Egger's regression test (p value = 0.000) indicated the presence of publication bias. As a result, trim and fill analysis was done and 2 studies were added, and the total numbers of studies become 12 and the pooled estimate of AOR of preterm becomes 4.69.

Prolonged labor

Six studies (Berkley et al. 2005; Getabelew et al. 2018; Moges et al. 2017; Woldu et al. 2014) found a significant association between prolonged labor and neonatal sepsis. The odds of neonatal sepsis among neonates delivered after prolonged labor ranges from 2.53 (Getabelew et al. 2018) to 12.4 (Table 3 and Supplementary Fig. 4).

Regarding test of heterogeneity, the Galbraith plot, I-squared (I^2), and P value showed moderate heterogeneity and the forest plot showed the overall estimate of AOR of the place of birth was 3.23 (95% CI − 0.04–6.51; I^2 = 62.7%; P = 0.020) (Supplementary Fig. 4). We have done publication bias a funnel plot and Egger's regression test (P value = 0.77) indicated the absence of publication bias.

Prolonged rupture of membrane (PROM)

Eleven studies (Berkley et al. 2005; Gebremedhin et al. 2016b; Getabelew et al. 2018; Laving et al. 2003; Mersha et al. 2019; Mobbs et al. 2019; Moges et al. 2017; Naulikha et al. 2018) found a significant association between PROM and neonatal sepsis. The odds of neonatal sepsis among neonates delivered after prolonged rupture of membrane ranges from 0.44 (Berkley et al. 2005) to 10.37 (Table 3 and Supplementary Fig. 5).

Regarding test of heterogeneity, the Galbraith plot, the I-squared (I^2), and P value showed moderate heterogeneity and the forest plot showed the overall estimate of AOR of a place of birth was 1.95 (95% CI 0.53–3.37; I^2 = 43.2%; P = 0.062) (Supplementary Fig. 5).

We have done publication bias accordingly the funnel plot and Egger's regression test (P value = 0.03) showed indicated the presence of publication bias. As a result, we have done trim and fill analysis was done and 4 studies were added and the total number of studies become 15. The pooled estimate of AOR of preterm becomes 5.86.

Table 3 Factors associated with neonatal sepsis in East Africa, 2019/2020

Factors	Odds ratio (AOR)
	1.44
	3.31
	5.31
	5.23
	4.79
	4.25
	2.56
	2.7
	2.5
Maternal history of urinary tract infection	2.9
	10.8
	7.06
	15.04
	6.45
	6.28
	3.37
	1.65
	1.12
Gestational age (preterm)	6.44
	3.49
	10.6
	38.6
	7.38
	2.92
	1.49
	4.66
	7.22
	6.45
Prolonged labor	6.95
	11.92
	1.29
	1.41
	2.53
	12.4
Premature rupture of membrane (PROM)	3.56
	0.44
	6.06
	1.92
	10.37
	3.39
	10.17
	1.25
	0.62
	7.37
	7.13

Discussion

In this systematic review and meta-analysis, we explored the prevalence and determinants of neonatal sepsis in East Africa. 26 studies were included in the final analysis. Based on the meta-analysis a significant proportion (more than 1 in 4) of neonates had neonatal sepsis in East Africa. This shows that neonatal sepsis is a significant public health problem in East Africa. We also identified factors that were significantly associated with neonatal sepsis in East Africa. The pooled prevalence of neonatal sepsis in East Africa was 29.65% (95% CI 23.36–35.94). The results of this meta-analysis were higher than in studies conducted in other low and middle-income countries (LMICs), 17.2% (Grace J Chan 2015). These differences might be due to the socioeconomic and cultural differences between the countries.

The result of this review revealed that maternal, obstetrics, and neonatal-related factors had a significant effect on the risk of neonatal sepsis. Home delivery, maternal history of UTI, being preterm, prolonged labor, and PROM were identified factors which significantly increase the risk of neonatal sepsis. A similar finding was also reported from the meta-analysis (Chan GJ1 2013; Shruti MurthyID 2019a, b).

This study revealed that preterm delivery as one of the significant associated factors of neonatal sepsis. This result is in line with the result from other studies in different countries (Aamir et al. 2015; Alemu et al. 2019; Jabiri et al. 2016; Siakwa et al. 2014). This might be because preterm neonates tend to have poor host defenses which easily expose them for neonatal sepsis. Besides, they are also more likely to receive parenteral nutrition through insertion of needle to vein, which might expose neonates to infections.

From obstetrics related variables, premature rupture of membrane ($\geq$ 18 h) (PROM) is found to be significant associated factors of neonatal sepsis. This finding is in agreement with the findings in Pakistan (Alam et al. 2014). However, the study in Ghana (Siakwa et al. 2014), did not identify PROM as a significant risk factor. The possible reason for the inconsistency might be due to appropriate interventions put in place to manage such cases in Ghana. The reason for significant association between PROM and neonatal sepsis might be because of "early rupture of membrane rises the chance of ascending microorganisms from the birth canal into the amniotic sac causing chorioamnionitis and fetal compromise" (Jiang et al. 2004).

Neonates delivered from mothers with history of URT were at high risk of acquiring neonatal sepsis. Similar finding was reported in Iran which indicates as there was a

significant relationship between maternal prenatal UTI and neonatal infection; 30.0% of the neonates with UTI versus 6.8% of those without UTI had mothers with a history of UTI (odds ratio, 5.9; 95% confidence interval, 1.9 to 18.3; $P = 0.001$) (Emamghorashi et al. 2012). This indicates a possible benefit of evaluation of neonates of mothers who had UTI during pregnancy.

This study revealed as prolonged labor increased the risk of neonatal sepsis. This finding is in line with other study findings (Gebremedhin et al. 2016a; SOMAN et al. 1985; Yancey et al. 1996). This significant association might be because of prolonged labor was associated with increased chorioamnionitis and third-degree or fourth-degree perineal lacerations which in turn predispose neonates for sepsis.

Conclusion and recommendations

The prevalence of neonatal sepsis in East Africa remains high. Home delivery, maternal history of UTI, being preterm, prolonged labor, and PROM were identified factors which significantly increase the risk of neonatal sepsis. The relevant institutions like ministries of health, policymakers, and other stockholders can be guided by this review report in formulation of evidence-based neonatal sepsis prevention interventions. Attention should be given for neonates delivered from women with intranatal fever to prevent neonatal sepsis. Pregnant women should be screened for UTI and those diagnosed with urinary tract infection should be treated with a full course of antibiotics for the prevention of neonatal sepsis. Appropriate interventions should be put in place to manage PROM to decrease the chance of ascending microorganisms from the birth canal into the amniotic sac causing chorioamnionitis and fetal compromise.

Strength and limitations

This study has several strengths: First, we used a prespecified protocol for search strategy and data abstraction and conducted quality assessment two independent investigators to lessen the possible assessor bias; Second, we employed subgroup and sensitivity analysis based on study country, study design, and publication year to identify the small study effect and the risk of heterogeneity in; third, the quality of the included studies was evaluated by two authors. Nevertheless, our systematic review and meta-analysis have some limitations: The result in this meta-analysis is derived from studies conducted in hospital settings. This limits the generalizability of the review findings. Some included studies reported outlier result which may affect the pooled prevalence of neonatal sepsis even though these studies fulfilled the inclusion criteria and passed the quality appraisal process. There were no RCTs included.

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Compliance with ethical standards

Conflict of interests The authors declare that they have no conflict of interests.

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