

INPLASY PROTOCOL

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None declared.

Drug Resistant Bacterial Neonatal Early Onset Sepsis in Africa: A 20 year-prevalence review and metanalysis

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Review question / Objective: What is the prevalence of drug-resistant pathogens associated with neonatal Early Onset Sepsis (NEOS) in the African continent and their likelihood of resistance to commonly used antibiotics in the NEOS, and what is the trend through time?

Condition being studied: There is no consensus on the definition of neonatal sepsis. Two main categories of neonatal sepsis are widely accepted: early-onset sepsis (EOS) defined as occurring in the first 72 hours of life, hence representing perinatal vertical infection; and late-onset sepsis (LOS), which occurs between 72 hours to 28 days and can be hospital or community-acquired.

Information sources: Pubmed, EMBASE, Web of Science. All authors from papers with missing information were contacted before article exclusion.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 22 January 2022 and was last updated on 22 January 2022 (registration number INPLASY202210112).

INTRODUCTION

Review question / Objective: What is the prevalence of drug-resistant pathogens associated with neonatal Early Onset Sepsis (NEOS) in the African continent and their likelihood of resistance to commonly used antibiotics in the NEOS, and what is the trend through time?

Rationale: Neonatal mortality is a global health issue. It accounted alone for 45% of all under -5 mortality. By the end of Millennium Development Goals (MDGs) era, neonatal mortality reduced, but its share of the pediatric mortality increased by 13% worldwide from 1990 to 2015, and it is projected to reach up to 52% in 2030. Of

all neonatal deaths, almost 99% occurs in developing countries, 39% in Sub-Saharan Africa countries. Neonatal sepsis accounts alone for 15% of all neonatal deaths meaning 7% of all under 5 deaths worldwide. Ten years ago, Seale and colleagues made a call for trials and public health measures in a review of Neonatal Early Onset Sepsis (EOS) and maternal sepsis in sub-Saharan Africa. Recently, Lavoie et al. reminded the importance of Neonatal Sepsis (NS) in developing countries, highlighting the growing antimicrobial resistance, the diagnostic challenges, and the actual lack of epidemiological data. Reporting NEOS distinctly from neonatal Late Onset Sepsis (LOS) is fundamental since etiologies are different. Neonatal EOS occurs in the first days of life and emerges from maternal genitourinary and fecal colonization; it is linked to obstetric complications, notably prolonged rupture of membranes, maternal fever, maternal urinary tract infection, chorioamnionitis, prematurity, and low birth weight. Neonatal LOS is either hospital-acquired and reflects nosocomial-circulating bacteria, or community-acquired when occurring sometime after discharge. Hence, the prevention and treatment of EOS and LOS target different germs with specific resistances. While in high-income countries, Group B Streptococcus (GBS) and E.coli are the main causative agents of NEOS, in low- and middle-income countries, it has been reported otherwise. In sub-Saharan Africa, overall NS (EOS and LOS together) appears to present with a low prevalence of GBS and a high incidence of S. aureus, Klebsiella sp, and E.coli9. However, the bacterial etiology of EOS alone is infrequently reported and not well established. Antibiotic resistance has been declared a Global Health Priority by WHO and a rising threat to modern medicine, and to the modern era. In African settings, the true extent of the problem is unsure because surveillance is often limited, nevertheless, multi-drug-resistant neonatal sepsis and maternal colonization have been described all over Africa, and this is directly linked to the high neonatal mortality and low-decreasing Neonatal

Mortality Rates in this region. In order to reduce Neonatal Mortality due to infection and change the course of antibiotic resistance, Neonatal EOS should be characterized separately from LOS to allow the right antibiotic choice should be made in each condition, we, therefore, performed this prevalence review with metanalysis concerning drug-resistant Neonatal EOS in Africa.

Condition being studied: There is no consensus on the definition of neonatal sepsis. Two main categories of neonatal sepsis are widely accepted: early-onset sepsis (EOS) defined as occurring in the first 72 hours of life, hence representing perinatal vertical infection; and late-onset sepsis (LOS), which occurs between 72 hours to 28 days and can be hospital or community-acquired.

METHODS

Search strategy: We searched Pubmed, EMBASE and Web of Science for papers without language restrictions from Jan 1, 2000 to Jun 9,2021 We developed a search syntax based on following keywords: neonatal and maternal sepsis or infection, maternal and neonatal colonization, and bacterial drug resistance in Africa. All types of studies were considered. Two different reviewers performed the search independently, and article screening and data retrieval.

Participant or population: Neonates - infants with less than 28 days of life.

Intervention: Does not apply since its a prevalence review.

Comparator: Does not apply since its a prevalence review.

Study designs to be included: All.

Eligibility criteria: Studies describing: Neonatal colonization in the first 7 days of life, Neonatal sepsis (Early Onset) and meningitis, Maternal colonization, Maternal infection; Type of intervention: Newborns: skin swabs, gastric juices, blood culture;

Types of outcome measures: Bacterial identification and resistance profile (antibiogram); Specific testing for drug resistance.

Information sources: Pubmed, EMBASE, Web of Science. All authors from papers with missing information were contacted before article exclusion.

Main outcome(s): Prevalence of Drug-Resistant Early Onset Sepsis.

Additional outcome(s): Definition of EOS; Prevalence of EOS; Blood Culture Positivity for EOS; Etiological prevalence of EOS; Prevalence evolution through time of EOS.

Quality assessment / Risk of bias analysis: Two different authors used STROBE - Neonatal Infection for Quality assessment.

Strategy of data synthesis: The data abstraction was performed in accordance with PRISMA guidelines. The STROBE -NI was used to evaluate the quality of included studies and evaluate if possible to perform a metanalysis, that will be performed with a fixed-effects model.

Subgroup analysis: No.

Sensitivity analysis: No.

Language: No restriction.

Country(ies) involved: Switzerland.

Keywords: neonatal sepsis, EOS, Drug-resistant EOS.

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