

## Neonatal Sepsis: Prevention is Better Than Cure!

Sukrita Dhaneria<sup>1</sup>, Kirti Hemwani<sup>1</sup>, Sonali Waske<sup>1\*</sup>, Yogyata Marothi<sup>1</sup>, Vinod Diwan<sup>2</sup>

### Introduction

The word sepsis, derived from the Greek word “sepo” meaning “I rot,” was first used medically in Homer’s poems. Also mentioned in the writings of Hippocrates around 400 BC, who thought of it as a dangerous biological decay in the body, sepsis has been the nightmare of a clinician ever since one can recall. Over the years, several definitions of sepsis have been deduced, and in 2016, an updated definition of sepsis was published, which stated that ‘sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection.’<sup>1</sup>

Sepsis in neonates has been a much-feared problem, especially in middle and low-income countries, which account for 99% of global neonatal mortality. Neonatal sepsis is the third major cause of neonatal deaths worldwide.<sup>2</sup> A major burden of neonatal mortality in India (24.9 per 1000 live births) is attributed to neonatal sepsis, which varies from 6.7 to 7.1 per 1000 live births in various studies.<sup>3-5</sup> In Madhya Pradesh, 9.1% of total neonatal deaths have been attributed to neonatal sepsis.

### Why is Neonatal Sepsis such a Mammoth Problem?

During the first 8 to 12 weeks of gestation, a fetus is immunologically incompetent. IgG antibodies are passively transferred from the mother to the fetus around 3<sup>rd</sup> month of gestation, and a major part of these antibodies are passed on during 3<sup>rd</sup> trimester.<sup>6</sup> This explains the fact that prematurely born babies have lower levels of this passively transferred IgG, making them more susceptible to infections.<sup>6</sup> On the other hand, neonates with severe intrauterine growth retardation

suffer from poor cell-mediated immunity, lower transfer of immunoglobulins, lower levels of complement components and poorer neutrophil function. Other predisposing factors to neonatal infections include contaminated in-utero environment due to premature rupture of membranes, unhygienic and multiple vaginal examinations, poor personal hygiene, and prolonged labor. Infected birth passages and infection at birth due to contaminated hands of personnel are also potent sources of microbes. A very high risk of neonatal sepsis is the exposure of neonates to a variety of fomites such as incubators, linen, suction catheters, thermometers, and resuscitation equipment. Overcrowding in the nursery is also associated with an increased risk of nosocomial infections. Top feeding is considered a major risk factor predisposing the baby to infection due to the lack of humoral, cellular, and other anti-infective factors available in breast milk. Misuse of antibiotics has been an independent risk factor in the intensive care units for the development of sepsis, especially with drug-resistant bacteria and a major risk factor for severe forms of fungal infections.

Unlike sepsis in adults, neonatal sepsis is mimicked by multiple conditions like dehydration, meconium aspiration syndrome, inborn errors of metabolism, etc. The baby “does not look well,” and “off the feeds” may sound vague to an inexperienced clinician but can still be useful in the diagnosis of a major health concern. Microbes responsible for early-onset and late-onset

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<sup>1</sup>Department of Microbiology, RD Gardi Medical College, Ujjain, madhya Pradesh, India.

<sup>2</sup>Senior Professor Epidemiology Department of Global Public Health Karolinska Institute Stockholm, Sweden.

**Correspondence to:** Sonali Waske, Department of Microbiology, RD Gardi Medical College, Ujjain, madhya Pradesh, India. E-mail: drsonalip@gmail.com

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neonatal sepsis vary, attributing to causative factors with gram-negative organisms like *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter*, *Pseudomonas aeruginosa* having a big impact.<sup>7</sup> Also, coagulase-negative *Staphylococcus* species, *Staphylococcus aureus* and *Enterococcus* species have been repeatedly isolated from blood cultures of neonates.<sup>7</sup> Blood culture remains the gold standard investigation in proving neonatal sepsis. However, it turns out to be negative in a major chunk of cases. In such cases, the sepsis screen that includes a battery of indicators such as total leukocyte count, absolute neutrophil count, immature or band cells to total neutrophil ratio, micro-ESR, and C-reactive protein comes to the rescue.<sup>6</sup> Acute phase reactants like procalcitonin are also a reliable marker of late-onset sepsis, which is independent of the gestational age at birth of the baby.

### ***A Stitch in Time Saves Nine!***

As the cliché goes, focusing on the prevention of infections in neonates can benefit the outcome in the newborn. The “baby steps” that can be taken in this regard include 100% compliance with hand hygiene at all times, proper personal hygiene, a clean environment for the newborn, early breastfeeding and avoidance of top feed, judicious use of antibiotics according to antimicrobial stewardship policy of the hospital, proper bundle care approach to managing healthcare-associated infections like central line-associated bloodstream infections when central lines are in place, ventilator-associated pneumonia, surgical site infections and catheter-associated urinary tract infections.<sup>8</sup> With proper infection control practices, it is possible to decrease the burden of neonatal sepsis in our country. Early identification of sepsis clinically (clinical sepsis) and with the help of an equipped laboratory (definitive sepsis) makes the target of preventing neonatal deaths possible while making judicious use of the resources. The use of Artificial Intelligence (AI) tools has a controversial role in this regard as AI alerts of sepsis may lead to a lot of false positives, leading to unwarranted use of antibiotics, which may further lead to multiple diseases that have now found their roots in gut microbiota dysbiosis.<sup>9,10</sup> However, when exercised with caution and with checks and balances in place, AI

can prove to be a useful tool in the prevention and early detection of neonatal sepsis.

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