Indian Academy of Pediatrics (IAP)

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Newer **R**esearch and recommendations **I**n **C**hild **H**ealth

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UNDER THE AUSPICES OF THE IAP ACTION PLAN 2023

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Dear fellow IAPans,

nRICH

Newer **R**esearch and recommendations **I**n **C**hild **H**ealth-aims to bring you the abstracts of some of the breakthrough developments in pediatrics, carefully selected from reputed journals published worldwide.

Expert commentaries will evaluate the importance and relevance of the article and discuss its application in Indian settings. nRICH will cover all the different subspecialities of pediatrics from neonatology, gastroenterology, hematology, adolescent medicine, allergy and immunology, to urology, neurology,vaccinology etc. Each issue will begin with a concise abstract and will represent the main points and ideas found in the originals. It will then be followed by the thoughtful and erudite commentary of Indian experts from various subspecialties who will give an insight on way to read and analyze these articles.

I'm sure students, practitioners and all those interested in knowing about the latest research and recommendations in child health will be immensely benefitted by this endeavor which will be published online on every Monday.

Happy reading!

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Procalcitonin for Detecting Culture-Positive Sepsis in Neonates: A Prospective, Multicenter Study

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BASED ON ARTICLE

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ABSTRACT

Introduction: It is unclear if serum procalcitonin (PCT) estimated at the time of suspicion of sepsis can help detect culture-positive sepsis in neonates. We evaluated the diagnostic performance of PCT in culture-positive sepsis in neonates.

Methods: This was a prospective study (February 2016 to September 2020) conducted in four level-3 units in India. We enrolled neonates suspected of sepsis in the first 28 days of life. Neonates with birth weight <750 g, asphyxia, shock, and major malformations were excluded. Blood for PCT assay was drawn along with the blood culture at the time of suspicion of sepsis and before antibiotic initiation. The investigators labeled the neonates as having culture-positive sepsis or "no sepsis" based on the culture reports and clinical course. PCT assay was performed by electrochemiluminescence immunoassay, and the clinicians were masked to the PCT levels while assigning the label of sepsis. Primary outcomes were the sensitivity, specificity, and likelihood ratios to identify culture-positive sepsis.

Results: The mean birth weight (SD) and median gestation (IQR) were 2,113 (727) g and 36 (32-38) weeks, respectively. Of the 1,204 neonates with eligible cultures, 155 (12.9%) had culture-positive sepsis. Most (79.4%) were culture-positive within 72 h of birth. The sensitivity, specificity, and positive and negative likelihood ratios at 2 ng/mL PCT threshold were 52.3% (95% confidence interval: 44.1-60.3), 64.5% (60.7-68.1), 1.47 (1.23-1.76), and 0.74 (0.62-0.88), respectively. Adding PCT when assessing neonates with clinical sepsis, a 12.9% pretest probability of sepsis generated posttest probabilities of 18% and 10% for positive and negative test results, respectively.

Conclusion: Serum PCT did not reliably identify culture-positive sepsis in neonates.

COMMENTARY

Early identification of neonatal sepsis is crucial as it significantly contributes to morbidity and mortality. Typically, diagnosis relies on observing clinical characteristics and assessing potential risk factors, leading to empirical treatment. To confirm the clinical suspicion, laboratory tests are

conducted. The ideal method for diagnosing sepsis is isolating the pathogen responsible from the bloodstream, although this is not always feasible. Additional tests, such as surrogate sepsis markers, serve as supplementary tools, and one such marker is Pro-calcitonin (PCT). The authors examined the effectiveness of PCT in detecting cases of sepsis where cultures yielded positive results.

In this observational study, conducted at four level III neonatal intensive care units (NICUs) in India, the authors recruited 1237 inborn infants (< 28 days) suspected to have clinical sepsis. Before starting antibiotic treatment, the infants underwent a sepsis screen, blood culture, and Pro-calcitonin (PCT) testing. The authors collected essential neonatal information and analyzed the data and categorized the infants into two groups: those with culture-positive sepsis and those without sepsis, based on blood culture results and the clinical progression, which were then correlated with PCT values. Of the total cohort, 155 infants (12.9%) were diagnosed with culture-positive sepsis. The sensitivity and specificity of PCT to identify culture positive sepsis at 2 ng/mL cutoff were 52.3% (95% CI: 44.1–60.3) and 64.5% (60.7–68.1), respectively. The positive and negative likelihood ratios were 1.47 and 0.74, respectively. Thus PCT was poor in predicting culture positive sepsis.

Pro-calcitonin (PCT) is an acute phase reactant that serves as a precursor to calcitonin. In the presence of an infection, PCT levels rise rapidly within 2-4 hours, reach their peak at 6-8 hours, and remain elevated for 24 hours. Compared to C-reactive protein (CRP), PCT demonstrates greater sensitivity as a marker for infection severity. Additionally, PCT is typically undetectable in healthy individuals, making it a promising indicator for sepsis. However, this particular study revealed a weak correlation between PCT levels and culture-positive sepsis. One possible explanation for this discrepancy could be the early assessment of PCT before the infection triggers a noticeable increase, or the single measurement of PCT instead of multiple serial evaluations. Furthermore, PCT values tend to fluctuate after birth, highlighting the need for distinct cut-off values based on gestational age and postnatal duration. It's important to note that a high PCT level does not always indicate the presence of sepsis, as it can also be elevated in non-infectious conditions such as asphyxia, post-resuscitation, meconium aspiration, pneumothorax, ventilation, intraventricular hemorrhage, trauma, and shock. The study indicated a false positive rate of 309 cases out of 1000, which suggests unnecessary exposure to antibiotics, while the false negative rate of 62 cases out of 1000 suggests withholding or delaying antibiotics when they may be necessary. Additionally, the requirement for a cold chain during sample transportation poses a logistical disadvantage.

The study possesses several strengths, such as its inclusion of multiple centers, the largest cohort of infants with culture-positive sepsis, a meticulous and clearly defined methodology, quality assurance monitoring, and the blinding of clinicians and lab technicians to PCT values. However, there are certain limitations to consider. These include sample loss due to power failure, the assessment of PCT only once, nearly 80% had only EOS (<72hr of birth) and the exclusion of out-born infants.

The search for single lab test to reliably predict neonatal sepsis at the time of initial presentation remains elusive.

IMPLICATIONS FOR PRACTICE

1. PCT should not be considered as 'standard of care' while evaluating infants with suspected sepsis especially those with early onset sepsis (<72hrs of birth)
2. More research is needed to determine whether PCT is beneficial for predicting culture positive sepsis in the NICU care settings.