

VAP in Neonatal Sepsis: An ET Tube Based Microbiological Study

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Abstract: Neonatal sepsis was found to be the singleton important cause of high mortality and morbidity of the Sick neonatal care Unit of our institution, where the majority of patients were still striving to find proper measures to access the medical facility in time, being entangled in the webs of poor socio-economic conditions, remoteness and lack of transport facilities, poor hygiene, malnutrition, inadequate antenatal care; and above all, ignorance. In this background, prematurity, low birth weight, birth asphyxia including Hypoxic Ischemic Encephalopathy, even sometimes congenital anomalies, were prominent predisposing factors for neonatal sepsis; often requiring intubation and mechanical ventilation which led to ventilator associated pneumonia (VAP). In this study extended over one year, we intended to search for the predictability of ET tube culture reports for VAP among neonatal sepsis cases, the bacteriological profile, and antibiotic susceptibility pattern of the isolates. We found that, intubation longer than 4 days was crucial for bacterial colonisation in the ET tube progressing to VAP. Bacteriological profile was monomicrobial and predominated by *Staphylococcus aureus*, followed by *Pseudomonas aeruginosa*, *Acinetobacter baumannii* complex, coliforms and CONS. Comorbid conditions mentioned above were important prognostic factors and prevalence of multi drug resistant strains made the situation grave.

Keywords: ET tube culture, Neonatal sepsis, VAP, Ventilator associated pneumonia

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I. Introduction

Neonatal sepsis is among the top three primary causes of morbidity worldwide with a high mortality rate, 99% of these deaths occurring in developing countries alone.^{1,2} Of the 6.9 million neonatal sepsis burden, 3.5 million cases occur in South Asia per year and India claims a large proportion of this disease thanks to its huge population.^{3,4} Although no population based figures are available, bulk of these sepsis related neonatal deaths are considered to be occurring in rural India, where more than 60% of Indian population lives. Inadequate information are available on these infections and deaths due to sub optimal public health surveillance systems and lack of transportation to appropriate health care facilities where culture, other diagnostic tools and antimicrobial testing may be available. In the context of worldwide increase in antimicrobial resistance, India's condition is considered more stark than any other place.⁴ Our institution, being a peripheral Medical College in West Bengal, India, reflects the same situation, where majority of the patients come from remote villages with limited access to transport facilities. Their poor socioeconomic conditions, malnutrition, lack of awareness regarding antenatal and child care, and many other cultural and social customs put hand in hand to serve them the ill-fate of a very high rate of neonatal morbidity and mortality. In the SNCU, patients of neonatal sepsis with or without co-morbid conditions are often compelled to put in intubation and mechanical ventilation, but unfortunately, development of ventilator associated pneumonia (VAP) is not uncommon.

As yet there is no gold standard for the microbiological diagnosis of VAP⁵ and the problems related to the excessive use of antibiotics and growing antimicrobial resistance have made the situation worse; improving the accuracy of microbiological diagnosis becomes an essential element for ensuring adequate antibiotic coverage for Multi-Drug Resistant Organism (MDRO), and to limit the use and duration of empirically prescribed broad spectrum antibiotic therapy.^{6,7} This study was a clinico-bacteriological analysis of the neonatal sepsis patients having intubated and subsequently developing VAP, their bacteriological profile and antimicrobial sensitivity against the commonly prescribed antibiotics.

II. Materials And Methods

In the SNCU, all the patients of neonatal sepsis who were put on endotracheal intubation for a period of 24 hours to 15 days were included in this one year study from November 2016 to October 2017. If immediate processing of ET tube was not possible, those were excluded. History was taken about the necessary parameters like gestational age, prematurity, birth weight, presence of comorbid conditions and congenital anomalies, duration of intubation, first line antibiotics given, follow up and progression to VAP and the final outcome. After extubation, ET tube tips were sent for staining and culture under standard conditions. The isolates were identified by standard biochemical tests and antibiotic sensitivity was done with Kirby Bauer Disc diffusion method with the first line antibiotics used in SNCU.

III. Result And Analysis

In this one year study, 38 patients of neonatal sepsis- who were intubated and eventually developed Ventilator associated pneumonia, were included in this study. Out of the 38 neonates, 18 were male and 20 female; their birth weights were in the range of 1.62 Kg to 2.6 kg, with a mean of 2.16 kg and median of 2.0 kg. Congenital anomalies were present in 4 babies (10.5% of cases) - all of them with very low birth weight, were intubated to put on mechanical ventilation within the first 24 hours of birth and rapidly progressed to neonatal sepsis and VAP. Birth asphyxia and Hypoxic ischemic encephalopathy (HIE) was pointed out to be another important cause resulting in mandatory intubation in 12 neonates (31.6% of cases). In 57.9% cases i.e. 22 neonates, it presented as primary neonatal sepsis which required intubation later as a life- saving respiratory support but eventually developed VAP. 10 patients (26.3%) were able to survive the battle thanks to rapid diagnosis and timely intervention with proper antibiotic therapy guided by the sensitivity reports. Their mean birth weight was 2.5 kg, with no history of birth asphyxia and they required minimum duration of intubation. We lost rest 28 patients making the mortality rate of 'neonatal sepsis with VAP' in this institution as high as 74%.The duration of intubation varied between 3 to 15 days, where duration of 4 day became an important clinical cut off for bacterial colonisation. Out of 38 cases, 35 were culture positive, with a mean intubation period of 9 days. The bacteriological profile was solely monomicrobial, predominated by *Staphylococcus aureus* (40%), followed by *Pseudomonas aeruginosa* (20%), *Acinetobacter baumannii* complex (14.3%), *Klebsiella pneumoniae* (8.6%), other coliforms (*Escherichia coli* 5.7%, *Citrobactor species* 5.7%) and *Staphylococcus epidermidis* (5.7%). No growth was obtained from the ET tube cultures in 3 cases; the duration of intubation was less than 4 days in all those culture negative cases.

Analysis of antibiotic resistance pattern of the gram positive isolates showed that increasing resistance is a matter of concern for both *S.aureus* and CONS strains. Resistance to beta lactams and cephalosporins was near and above 90%, aminoglycosides resistance was also increasing simultaneously, whereas, Vancomycin resistance was creeping in, leaving linezolid as the lone effective drug. The situation for all the Gram negative isolates was alarming. All the isolates of *Pseudomonas* and *Acinetobactor*, became fully resistant to ampicillin, amoxy-clav, ceftriaxone, cephotaxime, piperacillin-tazobactam and aminoglycosides like amikacin and netilmycin; leaving the only hope for the carbapenems like meropenem and imipenem- to which they showed relatively lesser level of resistance-43% and 40% respectively. Coliforms like *Klebsiella*, *Escherichia coli*, and *Citrobactor species* are not lagging far behind, yet they still held some responsiveness to Amoxyclav, piperacillin-tazobactam and aminoglycosides (86% resistance for all three), along with 25 % resistance to meropenem/Imipenem.

IV. Figures And Tables

Table 1: Bacteriological profile of positive ET tube cultures N=35

Bacterial isolates	Numbers (%)
<i>Staphylococcus aureus</i>	14 (40)
<i>Pseudomonas aeruginosa</i>	7 (20)
<i>Acinetobactor baumannii</i> complex	5 (14.3)
<i>Klebsiella pneumoniae</i>	3 (8.6)
<i>Escherichia coli</i>	2 (5.7)
<i>Citrobactor species</i>	2 (5.7)
<i>Staphylococcus epidermidis</i>	2 (5.7)
Total	35 (100)

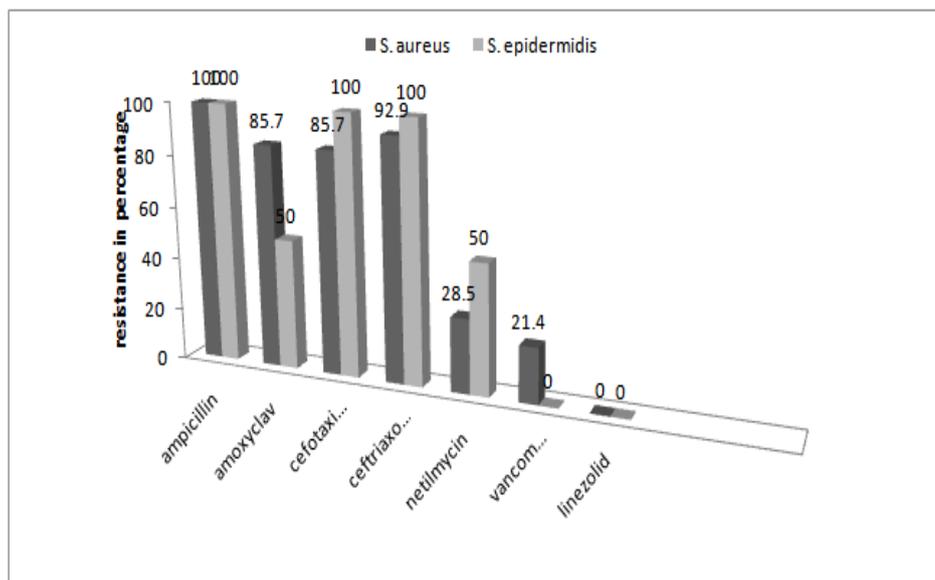


Figure 1: antibiotic resistance pattern (in percentage) of Gram positive cocci

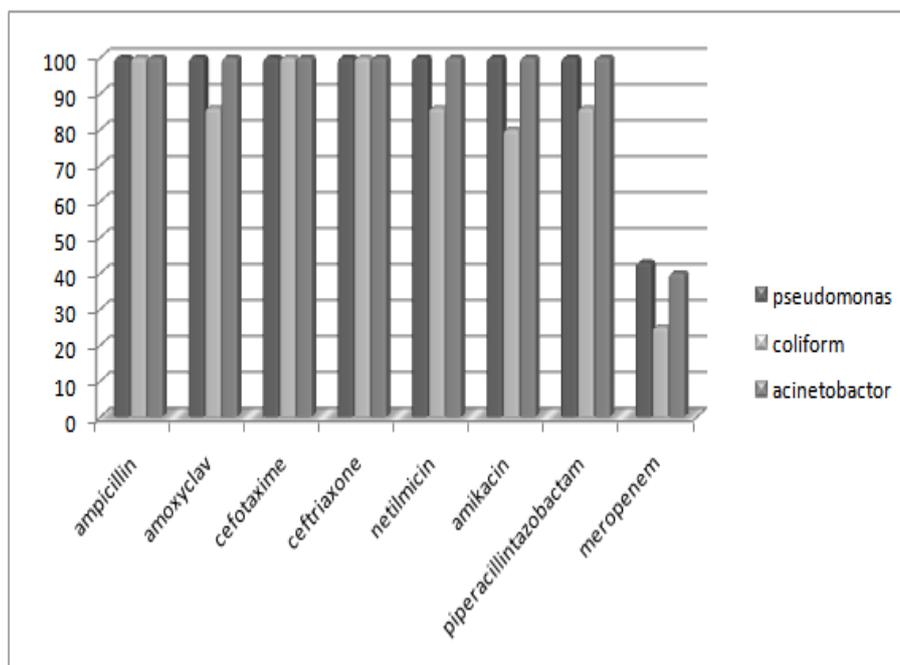


Figure 2: antibiotic resistance pattern (in percentage) of Gram negative bacilli

V. Discussion

Although neonatal sepsis is a matter of grave concern in our country, at present, limited data are available on various aspects of it at the community level.⁸ This study revealed that in presence of comorbidities like birth asphyxia, prematurity, HIE, congenital anomalies and other pathological conditions, neonatal sepsis and VAP collectively presented an overlapping clinical scenario with a significantly high neonatal mortality rate of 74%. This finding was supported by the works of Panigrahi, Chandel and Sharma in the settings of rural India.⁸ The clinical and laboratory parameters used to determine development of VAP were supported by various other studies.^{9, 10} The microbiological profile revealed monomicrobial infection pattern and predominance of *Staphylococcus aureus* (40%). *Pseudomonas aeruginosa* (20%), *Acinetobacter baumannii* complex (14.3%), *Klebsiella pneumoniae* (8.6%) and other coliforms (11.4%), and *Staphylococcus epidermidis* (5.7%) were the other isolates (TABLE- 1). The findings of Brown and Montgomery¹¹, David et al.¹² and Brown and Manning¹³ showed similar bacteriological pattern although Brown and Montgomery¹¹ and Brown and Manning¹³ showed on an average, more than two isolates per patient. Intubation more than 4 days showed a

significant difference in bacterial colonisation, development of VAP and subsequent mortality, which was supported by previous studies.^{12, 13} Inborn patients who received early intervention had a better outcome than outborn patients being late to have such opportunities. Finally the pivotal importance was on early implementation of rational antibiotic therapy, regarding which our study showed a higher incidence of resistance narrowing the choice to only one or two effective drugs- Vancomycin and linezolid for Gram positive cocci (Fig. 1) and meropenem for gram negative bacilli (Fig. 2). Even with those drugs, the resistance is creeping up.

VI. Conclusion

In the background of several socioeconomic restraints in a backward area of rural West Bengal, with limited resources to attend the clinical emergency named neonatal sepsis with VAP, progressive antibiotic resistance has been crippling us every day. Only earnest efforts to early diagnosis and implementation of rational antibiotic therapy guided by the drug sensitivity reports are our faithful army in this crucial crusade against multidrug resistant pathogens.

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