

Bacteriological Profile of Endotracheal Tube Culture in Mechanically Ventilated Neonates Admitted in Neonatal Intensive Care Unit of a Tertiary Care center of Nepal

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Abstract

Introduction: Sepsis is a leading cause of mortality and morbidity among neonates admitted to NICU. Advances in sepsis management and ventilator strategies have improved chances of survival. However, neonates requiring ventilator support for prolonged periods have more chances of complications which lead to increased negative outcomes. Hence, this study aims to identify bacteriological profile and antibiotic sensitivity patterns in intubated neonates via endotracheal tube culture.

Methods: This study was conducted in the NICU of PoAHS, Pokhara, over two years (April 2022 to March 2024), and it included 169 intubated neonates who fulfilled the inclusion criteria.

Results: Among these intubated neonates, 15 (8.8%) endotracheal (ET) tube cultures were positive for organisms. *Pseudomonas aeruginosa* (46.6%) was the most commonly isolated organism which was followed by *Acinetobacter baumannii* (20%), *Escherichia coli* (13.3%), and *Enterobacter* species (6.6%). Most isolates were found to be resistant to ampicillin (73%) and gentamicin (60%) and were found to be sensitive to tigecycline (53.3%), ceftazidime (33.3%) and meropenem (20%).

Conclusion: We conclude that analysis of ET tube culture could lead to the identification of culprit organisms and their sensitivity pattern towards antibiotics commonly used in NICU.

Keywords: Antibiotic sensitivity, Endotracheal tube culture, Intubation, Neonatal Intensive Care Unit.

Introduction

Sepsis is the most important and leading cause of mortality and morbidity among patients admitted to the Neonatal Intensive Care Unit (NICU).^{1,2} Frequently changing patterns of microbial floras and their sensitivity patterns in NICU have made neonatal sepsis a major challenge.^{3,4} Neonates requiring ventilator support for prolonged periods have several-fold increments in their morbidity and mortality.^{5,6} While managing sepsis, the empiric antimicrobial agents are usually started before the availability of blood culture results and is upgraded frequently due to poor responses to initial antimicrobials.⁶ This leads to the spread of drug-resistant organisms in NICU which contributes to the poor prognosis.⁷ Hence proper protocol regarding empirical antimicrobial strategy is crucial and should be individualized according to the predominant organisms and their sensitivity

patterns of individual NICUs.

Routine endotracheal tube (ET) culture of intubated neonates is not a part of sepsis screening.⁸ However, if blood culture is sterile, ET culture results can play an important role in appropriate antibiotic coverage. Thus this study aims to identify bacterial pathogens isolated from ET culture in ventilated neonates and assess their antibiotic susceptibility patterns.

Methods

This is a cross sectional study conducted in NICU of Pokhara Academy of Health Sciences (PoAHS) after approval of the PoAHS Institutional Review Committee (Reference No 78/078). The study included all inborn and referred neonates (N= 169) who were mechanically ventilated via Endotracheal tube for at least 48 hours over a defined study period from April 2022 to

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March 2024 using consecutive sampling method.

Neonates who were extubated, died, or were discharged within 48 hours of intubation were excluded from the study. Aim of the study was explained to the parents or legal guardians and written informed consent was obtained . A thorough history taking and examination of the neonates was done by the pediatrician and pediatric residents. The clinical examination included general condition of the baby, age on admission, day of intubation, indication for intubation, gestational age, vitals (pulse, respiratory rate, temperature, capillary refill time, oxygen saturation), weight of the baby, day of life during sample collection. After detailed evaluation neonates suspected of sepsis were subjected to laboratory investigations. This included complete blood count (hemoglobin, total leukocyte counts, differential count), peripheral blood smear, platelet count, C-reactive protein (CRP), random blood sugar (RBS) and blood culture and sensitivity.

For each neonates fulfilling the extubation criteria, preextubation contamination prevention measures were followed and the neonate was extubated. The distal 5 cm of the ET tube was aseptically cut using sterile scissors by pediatric resident under strict sterile technique. The collected segment was then sent to microbiological laboratory for culture and antibiotic sensitivity. The ET tube specimen were cultured on blood agar base (5-10% human blood) and incubated for 48 hours at a temperature of 35 ± 2 degree centigrade. The antibiotics sensitivity of organisms isolated in ET tube culture was performed according to the Clinical and Laboratory Standards Institute (CLSI) guidelines (CLSI 2021).The zones of inhibition were measured and interpreted based on CLSI breakpoints The commonly used antibiotics like ampicillin, gentamicin, cefotaxime, amikacin, ceftazidime, vancomycin, piperacillin, meropenem, colistin, tigecycline, levofloxacin, cefipime were used to see sensitivity pattern. The obtained data were interpreted in SPSS version 22. Descriptive analysis like percentage and tabulation were used to interpret the data.

Results

The majority of neonates requiring intubation were cases of perinatal asphyxia (19.2%), respiratory distress syndrome (18.6%), and early-onset neonatal sepsis (18%). Of all ventilated neonates, 67.4% were term neonates, and 32.54% were

preterm, as shown in Table 2. Among terms, 8.8% were ET culture positive, and 9.1% preterm were ET culture positive.

Table 1: Indications for intubation

| S.N | Causes | No | Percentage |
|-----|---------------------------------|-----|------------|
| 1 | Perinatal Asphyxia | 32 | 19.2% |
| 2 | Respiratory distress syndrome | 31 | 18.6% |
| 3 | Early Onset Neonatal Sepsis | 30 | 18% |
| 4 | Meconium Aspiration Syndrome | 28 | 16.8% |
| 5 | Congenital pneumonia | 19 | 11.4% |
| 6 | Complications of Prematurity | 7 | 4.2% |
| 7 | Neonatal Seizure | 6 | 3.6% |
| 8 | Apnea of prematurity | 6 | 3.6% |
| 9 | Late Onset Neonatal Sepsis | 6 | 3.6% |
| 10 | Congenital diaphragmatic hernia | 3 | 1.8% |
| 11 | Transient tachypnea of newborn | 1 | 0.6% |
| | Total | 169 | 100% |

Table 2: Distribution of neonates according to positive ET Culture Report

| ET Culture | Positive | Percentage |
|------------|----------|------------|
| Term | 10 | 66.6% |
| Preterm | 5 | 33.3% |
| Total | 15 | 8.8% |

Table 3: Bacterial profile of ET Culture-Positive Samples (N=15)

| Organisms isolated from ETT C/S | Number(15) | Percentage(100%) |
|---------------------------------|------------|------------------|
| Pseudomonas aeruginosa | 7 | 46.6% |
| Acinetobacter | 3 | 20% |
| E. coli | 2 | 13.3% |
| Enterobacter | 1 | 6.6% |
| Serratia | 1 | 6.6% |
| Staphylococcus aureus | 1 | 6.6% |

Pseudomonas aeruginosa was isolated in nearly half of culture positive ET tube, amounting to most common organism found in ET tube culture and sensitivity (C/S).

Table 4.1: Antibiotic Sensitivity Pattern of various organism isolated in ET tube C/S

| Organisms | Total | Ampicillin | | | Amikacin | | | Gentamicin | | | Cefotaxime | | | Cefepime | | | Meropenem | | | Vancomycin | | |
|----------------|-------|------------|---|----|----------|---|----|------------|---|----|------------|---|----|----------|---|----|-----------|---|----|------------|---|----|
| | | S | R | NA | S | R | NA | S | R | NA | S | R | NA | S | R | NA | S | R | NA | S | R | NA |
| Acinetobacter | 3 | | 2 | 1 | | 2 | 1 | | 2 | 1 | | 1 | 2 | | 1 | 2 | | | 3 | | | 3 |
| E coli | 2 | | 1 | 1 | 1 | | 1 | | | 2 | | | 2 | | | 2 | 2 | | | | | 2 |
| Enterobacter | 1 | | 1 | | | | 1 | | | 1 | | | 1 | | | 1 | | | 1 | | | 1 |
| Pseudomonas | 7 | | 5 | 2 | | 4 | 3 | 1 | 6 | | | 3 | 4 | | 2 | 5 | 1 | 2 | 4 | | 1 | 6 |
| Serratia | 1 | | 1 | | 1 | | | | | 1 | | | 1 | 1 | | | | | 1 | | | 1 |
| Staphylococcus | 1 | | 1 | | | 1 | | | 1 | | | 1 | | | | 1 | | | 1 | 1 | | |

In the present study, we obtained antibiotic resistance to Ampicillin and Gentamicin in nearly two-thirds (73%) of the isolates followed by Injection Gentamicin (60%) and Injection Amikacin (53%).

Table 4.2: Antibiotic Sensitivity Pattern of various organism isolated in ET tube C/S

| Organisms | Total | Ceftazidime | | | Ciprofloxacin | | | Piperacillin | | | Tigecycline | | | Colistin | | | Polymixin | | | Linezolid | | |
|---------------------|-------|-------------|---|----|---------------|---|----|--------------|---|----|-------------|---|----|----------|---|----|-----------|---|----|-----------|---|----|
| Sensitivity Pattern | | S | R | NA | S | R | NA | S | R | NA | S | R | NA | S | R | NA | S | R | NA | S | R | NA |
| Acinetobacter | 3 | | 3 | | | 2 | 1 | | 3 | | | | 3 | 3 | | | 1 | | 2 | | | 3 |
| E coli | 2 | | 3 | | 1 | | 1 | 1 | | 1 | 1 | | 1 | | | 2 | | | 2 | | | 2 |
| Enterobacter | 1 | 1 | | | | | 1 | | | 1 | 1 | | | | | 1 | | | 1 | | | 1 |
| Pseudomonas | 7 | 2 | 5 | | 1 | 1 | 5 | 1 | 3 | 3 | 6 | 1 | | 2 | | 5 | | 1 | 6 | | 1 | 6 |
| Serratia | 1 | 1 | | | 1 | | | | | 1 | | | 1 | | 1 | | | | 1 | | | 1 |
| Staphylococcus | 1 | 1 | | | | | 1 | | | 1 | | | 1 | | | 1 | | | 1 | 1 | | |

S: Sensitivity, R: Resistant, NA: not available

Antibiotic sensitivity pattern was most commonly obtained to Injection Tigecycline (53%) followed by Injection Ceftazidime and Injection Meropenem.

Discussion

Sepsis remains the most common cause of morbidity and mortality among neonates admitted to NICU. With the emergence of newer life-saving technologies, the rate of admission and survival in NICUs has drastically increased.⁹ Intubation is an intrinsic part of resuscitation and is done in cases of severe birth asphyxia, respiratory distress syndrome, sepsis etc. Analysing ET tube culture is important as sensitivity to the antibiotics obtained differed from those given prophylactically at our center.

In our study, the majority of neonates requiring intubation were asphyxiated babies(19.2%) followed by preterms having respiratory distress syndrome (18.6%), early onset sepsis(18%), meconium aspiration syndrome (16.8%), congenital pneumonia(11.4%) and other complications of prematurity(4.2%). Similarly, in a study conducted by Menon and Pawar complications of prematurity (47%) were the most common indication of intubation followed by MAS(15.9%) which may be due to preterm admission outnumbering other causes of admission but the demography hasn't been well explained in the study.¹⁰ Birth asphyxia and HIE (31.6%) was the main indication of intubation in a study done by Mukherjee and Biswas. Our study showed 66.6% of term neonates had positive ET tube culture while only 33.3% preterm had positive organism isolated in ET tube.¹¹ 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 our study, the most common organism isolated in ET tube culture was *Pseudomonas aeruginosa* (46.6%) followed by *Acinetobacter* (20%), *E.coli* (13.3%), *Enterobacter* (6.6%), *Serratia* (6.6%), and *Staphylococcus aureus* (6.6%). Similarly gram negative organism were predominantly isolated in ET culture in a study done by Tandia et al.¹² "container-

title": "International Journal of Science and Research (IJSR In a study conducted by Johanson et al *Pseudomonas* followed by *Klebsiella* were isolated in majority.¹³ However in a study done by Mukherjee and Biswas *Staphylococcus aureus* was predominantly isolated in ET tube culture (40 %) followed by *Pseudomonas aeruginosa* (20%), *Acinetobacter baumannii* complex(14.3%) and *Klebsiella pneumonia* (8.6%).¹¹ 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 (VAPA study done by Singh et al showed that *Klebsiella* (62.5%) was most common organism isolated in ET culture followed by *Streptococcus viridians* (12.5%), and *Staphylococcus coagulase* (12.5%).¹⁴

Almost all cases admitted in our facility were started on prophylactic antibiotics (Inj Ampicillin and Inj Gentamicin) before intubation (100%). However, our present study showed that nearly two-third (73%) organisms isolated from ET tube culture were found to be resistant to Inj ampicillin followed by Inj Gentamicin (60%). Similarly, in a study conducted by Mukherjee and Biswas in 2018 revealed resistance to beta lactams and aminoglycosides in approximately 90% of ET tube isolates¹¹ 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). This could be due to use of these antibiotics as first line empirical therapy in the aforementioned NICU and development of resistance of organisms towards these antibiotics over time. In our study, half (53%) of the ET tube isolated were sensitive to Inj Tigecycline followed by Inj Ceftazidime (33%). In 2018, a study conducted by Menon and Pawar concluded more than

one-third (38.7%) isolates were sensitive to Inj Colistin followed by Inj Tigecycline (13.6%).¹⁰

Sur et al conducted a study in 2016 in which majority (80%) of the ET tube isolates were sensitive to Inj Tigecycline and Inj Meropenem, comparable to afore-said studies.¹⁵ Disparity could be due to non-uniform exposure of all organisms to sensitivity patterns as per the Clinical Laboratory Standards Institute (CLSI) protocol. The diversity in incidence of *Pseudomonas* may be due to variability in study population, the standard of hand hygiene practices, and the possibility of adherence to infection prevention and control protocols.

Conclusion

In our study *Pseudomonas aeruginosa* was found to be the most common isolate in ET tube culture and most isolates were sensitive to injection Tigecycline. Analysis of ET tube culture is crucial as sensitivity to antibiotics obtained differed from those used prophylactically at our centre, necessitating the need to review our antibiogram. These findings also support the inclusion of ET tube culture in routine sepsis workup for intubated neonates

Limitation

In this study, huge disparity between sterile and culture positive cases led to limited study population and thus restricted conclusion. Other limiting factors are single center study design and limited panel of antibiotic tested. Sensitivity pattern of antibiotics in relation to isolates were non uniform resulting into non availability of responsiveness of antibiotics to various organisms.

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