

Research Article

## An evaluation of prescribing trends of antibiotics used in neonatal sepsis in a tertiary care hospital of Lahore, Pakistan

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To find out commonly used antibiotic combinations in the management of neonatal sepsis, prevalence of early onset sepsis (EOS) and late onset sepsis (LOS) in a public sector tertiary care hospital of Lahore. Neonatal sepsis is a clinical syndrome of bacteremia with systemic signs and symptoms of infection in the first 4 weeks of life. Neonatal sepsis is an important and common cause of morbidity and mortality in full term as well as preterm neonates. A retrospective observational study was conducted at the Neonatal Intensive Care Unit of a tertiary care hospital of Lahore from September 2013 to November 2013. 50 cases of neonatal sepsis suspected on clinical grounds were included in this study. LOS was more prevalent (60%) as compared to EOS (40%). Three combinations of antibiotics were frequently being used. Combination of Amikacin, Ampicillin & Cefotaxime was the most frequently used (48%) followed by combination of Amikacin, Ampicillin and Cefotaxime (30%), and combination of Vancomycin with Meropenam (22%). High potency antibiotics were being used frequently with less reliance on performance of culture tests for definitive therapy selection.

**Keywords:** Neonatal sepsis, Antibiotic, Prescribing practices, Amikacin, Cefotaxime.

### 1. INTRODUCTION

Neonatal sepsis is defined as a “clinical syndrome of bacteremia with systemic signs and symptoms of infection in the first 4 weeks of life”. When pathogenic bacteria gain access into the blood stream, they may cause overwhelming infection without much localization (septicemia) or may get predominantly localized to the lung (pneumonia) or the meninges (meningitis). Neonatal bacterial infections are classified into two different categories depending on the time of their presentation. Early onset sepsis (EOS) or congenital infections occur when an infant presents with signs and symptoms of the illness within the first 72 hours of life. Late onset sepsis (LOS) or acquired infections occur after 72 hours (Zaidi et al, 2009). Neonatal sepsis is an important and common cause of morbidity and mortality in full term as well as preterm

neonates and it is the result of interaction between the products of microorganism and host factors including cytokines and other mediators (Hotchkiss et al, 2003 ; Bashir et al, 2007). Neonatal sepsis currently causes about 1.6 million deaths annually in the developing countries (Anwer et al, 2000). The incidence of neonatal sepsis varies from 1-4/1000 live births in developed Countries, this is due to differences in the incidence, risk factors, pattern and antimicrobial sensitivities of pathogens (Gotoff et al, 2008).

World over, two-third of the global neonatal deaths are contributed by just ten countries, mostly in Asia (WHO, 2006). As in Bangladesh infant mortality rate and neonatal mortality rate are 56 and 42 per 1000 live birth respectively and the leading cause of these deaths are perinatal asphyxia, neonatal infection and premature birth (Bangladesh Demographic and Health survey 2004). Pakistan ranks at third

position with a share of 7%. A cohort study conducted in Pakistan showed that 45% of the neonatal deaths occurred within 48 hours of birth and 73% within 1st week. Preterm birth, birth asphyxia and infections were observed in 34%, 26% and 23% of the neonatal deaths respectively (Jehan et al., 2009).

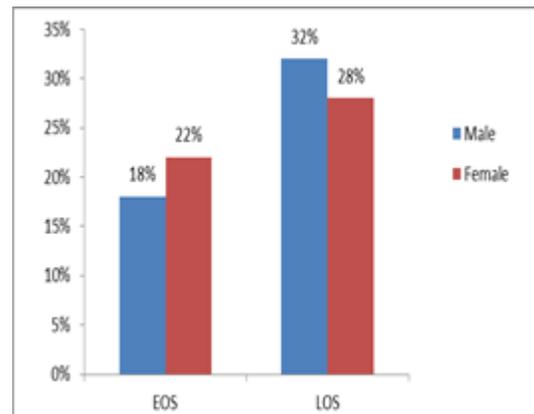
The optimal selection, dosage, appropriate administration of the antimicrobial treatment are the important factors for achieving the best clinical outcomes for the treatment or prevention of infection with minimal toxicity to the patient and minimal impact on subsequent resistance. The choice of antibiotics should be based on the causative organisms and the patterns of antibiotic susceptibility.

## 2. METHODOLOGY

A retrospective based study was conducted at the neonatal intensive care unit of a public sector tertiary care hospital of Lahore to evaluate antibiotic prescribing in 50 cases of neonatal sepsis from September 2013 to November 2013. Each neonate was clinically evaluated through history (fever, reluctance to feed, seizure, vomiting), physical examination and investigations (blood culture and sensitivity). Different variables like prevalence of LOS and EOS, sex, presenting symptoms, culture performed, and combinations of antibiotics. Neonates were evaluated for frequency of different antibiotics combination used in neonatal sepsis. Frequencies of different variables were calculated by using descriptive statistics and percentages are represented in figures.

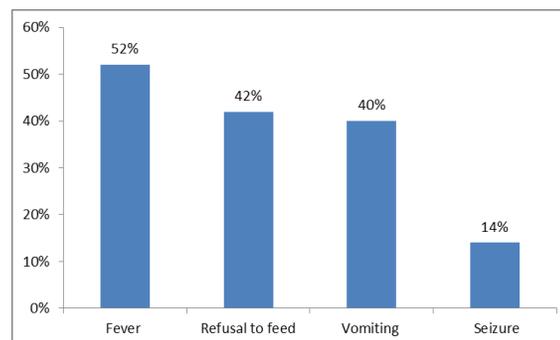
## 3. RESULTS

50 cases of neonatal sepsis suspected on clinical grounds were included and data were collected on predesigned questionnaire. Late onset sepsis was observed in 30 (60%) patient, whereas 20 (40%) were suffering with Early onset sepsis. Among 50 patients, 25 were male and 25 were female. Among male neonates 16 (32%) were suffering from LOS and 8 (16%) were suffering from EOS. And among females 14 (28%) were suffering from LOS and 11 (22%) were suffering from EOS (Figure 1).



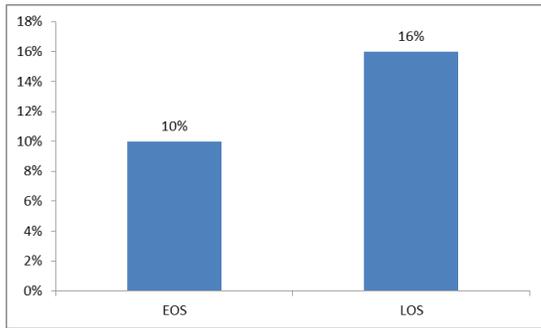
**Figure 1:** Gender wise percentage distribution of Early onset sepsis and Late onset Sepsis in Neonatal Intensive Care Unit of a Tertiary Care Hospital at Lahore (n=50)

Symptoms which were considered as clinical grounds for diagnosis of sepsis like fever, refusal to feed, vomiting and seizure were observed in neonates with occurrence percentages of 52%, 42%, 40% & 14% respectively (Figure 2).



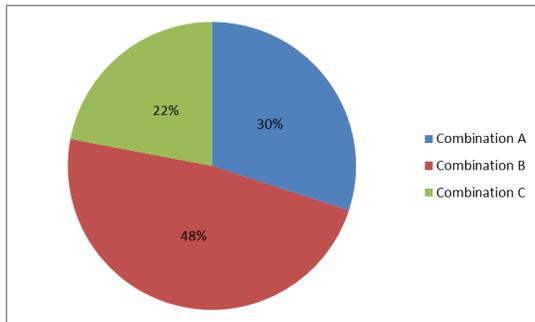
**Figure 2:** Percentage distribution of various clinical symptoms of the patients with suspected neonatal sepsis (n=50)

At an average of 5 drugs per prescription was observed out of which 3 were antibiotics. Out of 50 cases, culture was performed only in 13 cases while 37 patients were prescribed antibiotics without performing culture test throughout the course of treatment. Those patients in whom culture was performed 5 were of EOS and 8 of LOS. (Figure 3).



**Figure 3:** Percentage culture performance in LOS & EOS (n=50)

Three combinations of antibiotics were being frequently used. Combination of Amikacin, Ampicillin & Cefotaxime was used in 48% patients, followed by a combination of Amikacin, Ampicillin & Cefotaxime and combination of Vancomycin & Meropenam in 30% and 22% cases respectively (Figure 4).

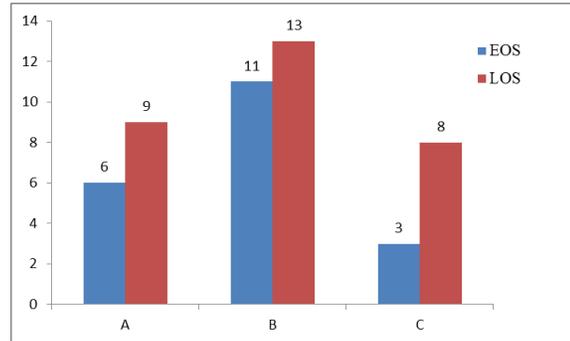


**Figure 4:** Percentage distribution of antibiotics combinations' used in neonatal sepsis (EOS & LOS);

Where, Combination A (Amikacin, Cefotaxime & Ampicillin), B (Amikacin, Ampicillin & Cefotaxime) and C (Vancomycin & Meropenam)

Amongst 20 cases of EOS combination of Amikacin, Ampicillin & Cefotaxime in 11, combination of Amikacin, Ampicillin & Cefotaxime was used in 6 patients and combination of Vancomycin & Meropenam were used in 3 patients. Amongst 30 cases of LOS combination of Amikacin, Ampicillin & Cefotaxime in 13 patients and combination of

Amikacin, Ampicillin, Cefotaxime was used in 9 and combination of Vancomycin & Meropenam in 8 patients (Figure 5).



**Figure 5:** Frequency distribution of antibiotic combinations used in different cases of neonatal sepsis; (n=50).

Combination A (Amikacin, Cefotaxime & Ampicillin), B (Amikacin, Ampicillin & Cefotaxime) and C (Vancomycin & Meropenam)

#### 4. DISCUSSION

Neonatal sepsis is one of the most common reasons for admission in neonatal units in developing countries (Anwer et al., 2000). The incidence of neonatal sepsis and its mortality are quite alarming all over the world (Rodrigo et al., 2002). The objective of this study was to check the prevalence of LOS & EOS and commonly used antibiotic combinations in the neonatal sepsis. Late onset sepsis was observed in 60% patient, whereas 40% patients were suffering from Early onset sepsis. While in other studies conducted in India by Jyothi et al in 2008-2010 and Pakistan by Ahmad et al in 2009 EOS was found to be more prevalent as compared to LOS (Ahmad et al., 2011; Jyothi et al., 2013).

According to International guidelines for management of severe sepsis and septic shock by Dellinger et al sepsis is diagnosed on the basis of some general symptoms such as fever, hypothermia, increased heart rate, altered mental status, tachypnea and inflammatory symptoms including leukocytosis, leukopenia & increased C-reactive protein (Dellinger et al., 2012). Symptoms which were observed as clinical grounds for diagnosis of sepsis in this study were fever, refusal to feed, vomiting and seizure with occurrence percentages of 52%, 42%, 40% & 14% respectively. In study conducted in Sheikh Zaid hospital by Ahmad et al in 2009 fever was the most frequent which was present in 46% patients followed by reluctance to feed 33% and seizures in 18% patient (Ahmad et al., 2011). High incidence of fever and refusal to feed was also observed in a study done in a tertiary care center in Bangladesh by S begum et al in 2012 (Begum et al., 2012).

The early identification of sepsis and implementation of definitive therapy have been documented by Levy et al to improve outcomes and decrease mortality due to sepsis (Begum et al., 2012). According to guidelines culture is recommended for starting definitive antimicrobial therapy without significant delay. To optimize the identification of causative organism guidelines recommend to take at least two set of blood culture (CEC, 2013). In this study culture was performed only in 26% cases which is inconsistent with other study

conducted in tertiary care hospitals (Ahmad et al., 2011; Jyothi et al., 2013).

According to WHO guidelines first line empiric antibiotic therapy for early and late onset sepsis include Gentamicin and Ampicillin. We observed in this study three combinations of antibiotics were being frequently used. Combination of Amikacin, Ampicillin & Ceftazidime (represented as Combination B in Figure 4) was used in 48% patients, followed by a combination of Amikacin, Ampicillin & Cefotaxime (represented as Combination A in figure 4) and combination of Vancomycin & Meropenam (represented as combination C in Figure 4) in 30% and 22% cases respectively. Results of this study regarding use of antimicrobial combinations were similar with guidelines of Department of Child and Adolescent Health and Development, World Health Organization. These guidelines suggest that amongst Penicillin's, Ampicillin is preferred for the treatment of neonatal sepsis as it is active against some gram negative pathogens, especially E. coli. A third generation cephalosporin in combination with an aminoglycoside is commonly used in treatment of newborn sepsis World Health Organization Geneva (2006).

#### 5. CONCLUSION

Bacterial sepsis is considered to be an important cause of neonatal mortality (Movahedian et al., 2006). Neonatal sepsis currently causes about 1.6 million deaths annually in the developing countries. Bacterial sepsis is considered to be an important cause of neonatal mortality. Combination of Amikacin, Ampicillin & Ceftazidime was used frequently. Prescribing of antibiotics in a public sector tertiary care hospital of Lahore is according to (WHO 2002) guidelines and positive results are being obtained from this therapy, the malpractice observed in this study was, very less reliance on performance of culture tests for definitive therapy selection. There is need of hour to develop National Antibiotic Policy and Standard Treatment Guidelines to improve antibiotics' prescribing practices in the hospitals.

#### Conflict of Interests

Authors declared no competitive interests for the presented work.

## References

- Ahmad A, Hussain W, Lamichhane A, Aslam M, Riaz L (2011). Use of Antibiotics in neonatal sepsis. *Pakistan Pediatric Journal*, 35(1): 3-7.
- Anwer SK, Mustafa S, Pariyani S, Ashraf S, Taufiq KM (2000). Neonatal sepsis: an etiological study. *Journal of Pakistan Medical Association*, 50: 91-94.
- Bangladesh Demographic and Health survey 2004. National Institute of Population Research and Training (NIPORT) Dhaka, Bangladesh. [Online] Available: [aidsdatahub.org/en/reference-material](http://aidsdatahub.org/en/reference-material). <http://www.measuredhs.com>
- Bashir S, Tayyib M, Yousef NW (2007). Coagulation abnormalities in neonatal sepsis—a diagnostic approach. *Pakistan Journal of Pathology*, 18: 119-24.
- Begum S, Baki MA, Kundu GK, Islam I, Kumar M, Haque A (2012). Bacteriological Profile of Neonatal Sepsis in a Tertiary Hospital in Bangladesh. *Journal of Bangladesh College of Physicians and Surgeons*, 30: 66-70.
- Dellinger RP et al, (2012). Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock. *Critical Care Medicine*. 41 (2), 580-637.
- Gotoff SP (2008). Neonatal sepsis and meningitis. *Nelson Text book Pediatrics* (16th ed) W.B. Saunders Philadelphia.
- Hotchkiss RS, Kari IE (2003). The pathophysiology and treatment of sepsis. *New England Journal of Medicine*, 348: 138-50.
- Jehan I, Harris H, Salat S, Zeb A, Mobeen N, Pasha O (2009). Neonatal mortality, risk factors and causes: a prospective population-based cohort study in urban Pakistan. *Bull World Health Organ*, 87: 130–8.
- Jyothi P, Basavaraj MC, Basavaraj BV (2013). Bacteriological profile of neonatal septicemia and antibiotic susceptibility pattern of the isolates. *Journal of Natural Science, Biology and Medicine*, 4(2): 306-309.
- Materna, Newborn, Child and adolescent health, World Health Organization. Geneva 30<sup>th</sup> September to 1<sup>st</sup> October 2002, WHO/FCH/CAH/04.1 [Online] Available: [http://www.who.int/maternal\\_child\\_adolescent/en/](http://www.who.int/maternal_child_adolescent/en/)
- Movahedian AH, Moniri R, Mosaybi Z (2006). Bacterial culture of neonatal sepsis. *Iranian Journal of Public Health*, 35: 84–9.
- Rodrigo I. (2002). Changing pattern of neonatal sepsis. *J Pedi-atr Child Health*. 31, 3-8.
- Sepsis paediatric and neonatal blood culture sampling guidelines, clinical excellence commission, 2013. version 1. [Online] Available: [http://www.cec.health.nsw.gov.au/\\_\\_documents/programs/sepsis/july-2013/paediatrics-and-neonatal-blood-cultures-sampling-guide-ver1-2013.pdf](http://www.cec.health.nsw.gov.au/__documents/programs/sepsis/july-2013/paediatrics-and-neonatal-blood-cultures-sampling-guide-ver1-2013.pdf)
- Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock. Society of Critical Care Medicine. (2013) [Online] Available: <http://www.survivingsepsis.org/SiteCollectionDocuments/Implement-PocketGuide.pdf>
- World Health Organization Geneva (2006). Neonatal and perinatal mortality: country, regional and global estimates. [Online] Available: [http://whqlibdoc.who.int/publications/2006/9241563206\\_eng.pdf](http://whqlibdoc.who.int/publications/2006/9241563206_eng.pdf)
- Zaidi AKM, Thaver SM, Asad SA, Khan TA (2009). Pathogens associated with sepsis in newborns and young infants in developing countries. *Pediatric Infectious Disease Journal*, 28: S10-S18.

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