# NEONATAL SEPSIS IN A TERTIARY CARE HOSPITAL: BACTERIOLOGICAL PROFILE AND ITS ANTIMICROBIAL SENSITIVITY

**Madiha Ahmed, Muhammad Yasrab*, Arshad Khushdil, Khadija Qamar**, Zeeshan Ahmed**

Pak Emirates Military Hospital/National University of Medical Sciences (NUMS) Rawalpindi Pakistan, *Armed Forces Institute of Urology/ National University of Medical Sciences (NUMS) Rawalpindi Pakistan, **Army Medical College/National University of Medical Sciences (NUMS) Rawalpindi Pakistan

## ABSTRACT

*Objective:* To study the spectrum and antimicrobial sensitivity of bacterial pathogens causing neonatal sepsis, in neonatal intensive care unit (NICU) of Pak Emirates Military Hospital, Rawalpindi.

*Study Design:* Prospective cross sectional study.

*Place and Duration of Study:* This was a prospective cross sectional study, conducted at NICU of Military Hospital, Rawalpindi, from Jul 2017 to Dec 2017.

*Material and Methods:* All neonates admitted to our department who underwent evaluation for sepsis, from Jul 2017 to Dec 2017.

*Results:* Out of 2,480 admitted neonates, 733 were suspected with sepsis, making an incidence of suspected neonatal sepsis to be 29.5%. 421 (57.4%) babies were suspected with early onset sepsis (EOS) and 312 (42.6%) with late onset sepsis (LOS). Majority of the babies (70.3%) were preterm. In 281 (11.3%) neonates, blood culture came out to be positive. 73/281 neonates with culture proven sepsis died making a mortality rate of 25.9%. Gram negative bacilli were most predominant among isolated bacteria. Most of the organisms showed resistance to the first line antibiotics.

*Conclusion:* Sepsis has a high mortality rate in neonates admitted to our department. Gram negative organisms are the most common cause. Most of the isolated organisms are resistant to empirical antibiotics.

*Keywords:* Antimicrobial sensitivity, Bacteriological profile, Multi drug resistance, Neonatal sepsis.

## INTRODUCTION

Approximately 130 million babies are born each year[1]. According to UNICEF-2017 report 5 to 6 million children die before reaching the age of 5 years and 2.6 million babies die within first 04 weeks of life, accounting for 46% of deaths in under-5 age group[2]. Most of these deaths occur in developing world[3]. Neonatal mortality is approximately 34/1000 live births in developing countries while it is around 5/1000 in developed countries[4]. Among the 10 countries with highest neonatal mortality rate, most are in Asia. Unfortunately, Pakistan ranks third among these Asian countries. An estimated 298,000 neonates die each year in Pakistan, contributing to 7% of neonatal deaths globally[5]. Worldwide, most common causes of neonatal mortality are prematurity, sepsis and asphyxia. It has been estimated that almost 1 million neonates die each year because of sepsis[6]. Developing countries account for 98% of neonatal deaths, where sepsis is responsible for upto 30-50% of neonatal deaths. The prevalence of neonatal sepsis in India is estimated to be 36-55%[7]. In Pakistan; there is limited data about the incidence of neonatal sepsis, varying from 1.13 to 3.8 per 1000 live births[8]. Neonatal sepsis is a term used for systemic infections of newborns upto the age of 28 days. It can be early onset, occurring within 72 hours of birth or late, occurring from 4th day to 4th week after birth. The general fatality rate of early onset neonatal sepsis (EONNS) ranges from 15-40% and that of late onset neonatal sepsis (LONNS) is approximately 5%[9]. The signs and symptoms of neonatal sepsis can be highly variable ranging from mild symptoms to serious life threatening disease[10]. Successful management of neonatal sepsis depends on early detection and

**Correspondence: Dr Madiha Ahmed,** Obestetrics and Gynecology Department, Pak Emirates Military Hospital Rawalpindi Pakistan

*Email: madiha940@Yahoo.com*

appropriate choice of empirical antibiotics[11]. In order to treat neonatal sepsis effectively, itis very important to update the knowledge about common pathogens causing neonatal sepsis on regular basis and prescribe empirical antibiotics accordingly. The aim of our study was to evaluate the pattern of microorganisms causing neonatal sepsis in our NICU and also to see their antimicrobial sensitivity.

## MATERIAL AND METHODS

This was a prospective cross sectional study, conducted at NICU of Pak Emirates Military Hospital, Rawalpindi, from July 2017 to December 2017. All neonates admitted to our unit during the study period, with clinical features suggestive of sepsis, were selected for the study through non-probability sampling technique. We also included babies who had risk factors for neonatal sepsis including prolonged rupture of membranes for more than 18 hours, maternal fever of >1000F, history of foul smelling vaginal discharge, raised maternal leucocyte count or raised maternal C-reactive protein(CRP). Babies who had received antibiotics before samples were collected, were excluded from study. For all included neonates, we noted their age, gender, gestational age, mode of delivery, birth weight and any risk factor for sepsis as already discussed. The sample size was calculated using WHO calculator, keeping confidence interval 95%, absolute precision 5% and anticipated population proportion 45%. Blood culture samples were collected from all neonates fulfilling the inclusion criteria, according to unit's protocol. 1-3ml of blood was collected from a peripheral vein, which was than inoculated into the culture medium and was sent to micro-biology department of Army Medical College for culture and sensitivity. Samples were also sent for complete blood count, CRP and other investigations depending on the clinical condition of the neonate. Permission was sought from hospital ethical committee. Results were analyzed using microsoft excel sheet and SPSS version 20. Percentages were calculated for categorical variables like gender, mode and place of delivery. Quantitative variables like weight and gestational age were expressed in terms of mean ± SD.

## RESULTS

During the study period, total 2,480 babies were admitted. Seven hundred and thirty three blood cultures were sent for analysis. The incidence of suspected sepsis was 29.5%. Out of 733, 421 (57.4%) babies were suspected with early onset sepsis (EOS) and 312 (42.6%) with late onset sepsis (LOS). Four hndred and twenty five (58%) babies were males and 308 (42%) were females. Majority (70.3%) of the babies were preterm. The mean gestational age was 33.2+ 3.6 weeks. Three hundred and ten (42.3%) babies had gestational

**Table-I: Epidemiological profile of neonates investigated for sepsis.**

| Characteristics | Number (Total 733) |
|---|---|
| **Gender** | |
| Male | 425 (58%) |
| Female | 308 (42%) |
| **Gestational age** | |
| <34 weeks | 310 (42.3%) |
| 34-37 weeks | 205 (28 %) |
| >37 weeks | 218 (29.7%) |
| **Place of delivery** | |
| Home | 39 (5.3%) |
| Other hospitals | 438 (59.8%) |
| Indoor | 256 (34.9%) |
| **Mode of delivery** | |
| Vaginal delivery | 315 (43%) |
| Cesarean deliver | 418 (57%) |

age <34 weeks. Two hundred and five (28%) babies were late preterm (34-37 weeks). Two hundred and eighteen (29.7%) were term neonates. Mean weight was 2.3 + 0.8kg. Four hundred and sicty two (63%) neonates had weight <2.5kg. Out of these, 152 (32.9%) babies had weight <1.5kg. Epidemiological profile of babies with suspected sepsis is shown in table-I. Blood cultures were positive in 281 (11.3%) samples. Among these 281 neonates, 182 (64.8%) had EOS and 99 (35.2%) had LOS 73 (26%) culture positive babies died while 208 (74%) were discharged to home. Forty nine (17.4%) babies died of early onset sepsis and 34 (12.1%) babies died from late onset sepsis. Mothers of 77 (27.2%)

babies had prolonged rupture of membranes before delivery. Four hundred and eighteen (57%) babies were delivered through cesarean section while 315(43%) were delivered vaginally. Most of the neonates (94.6%) were delivered in hospitals/clinics. Thirty nine (5.3%) neonates were delivered at home. Out of 281 culture positive babies, 107 (38%) had raised CRP while only 21 (7.4%) had raised TLC. 115 babies (40.9%)

to vancomycin and linezolid. Gram negative bacilli showed almost no sensitivity to penicillins and a very highresistance to cephalosporins. More than 50% of gram negative bacilli were resistant to aminoglycosides. They were sensitive to imipenem and meropenem. Incidence of multi drug resistance was 57.1% in gram positive isolates and 91.3% in gram negative isolates. Table-III shows sensitivities of the bacterial

**Table-II: Bacteriological profile in blood culture positive neonates.**

| Isolated organisms | Total Num (%) | EONNS Num (%) | LONNS Num (%) |
|---|---|---|---|
| Gram negative bacilli | | | |
| Escherichia coli | 118 (42) | 98 (53.8) | 20 (20.2) |
| Klebsiellapneumoniae | 33 (11.7) | 15 (8.2) | 18 (18.2) |
| Klebsiellaoxytoca | 10 (3.5) | 08 (4.4) | 02 (2.02) |
| Enterobacter cloacae | 14 (5) | 13 (7.14) | 01 (1.01) |
| Enterobacterfaecium | 12 (4.3) | 09 (4.9) | 03  (3.03) |
| Enterobacteraerogenes | 12 (4.2) | 08 (4.4) | 04 (4.04) |
| Serratialiquifacien | 04 (1.4) | 04 (2.2) | - |
| Serratiamarcescens | 00 (0) | - | - |
| Citrobacterfreundii | 03 (1.1) | 03 (1.1) | - |
| Enterobacter species | 02 (0.7) | 02 (1.1) | - |
| Pseudomonas aeroginosa | 09 (3.2) | 06 (3.3) | 03 (3.03) |
| Shigellaflexeneri | 01 (0.3) | - | 01 (1.01) |
| Stenotrophomonasmaltophilia | 01 (0.3) | - | 01 (1.01) |
| Others | | | 04(4.04) |
| Acinobacter & species | 06 (02.1) | 02 (1.1) | 27 (27.3) |
| Candida | 34 (12.1) | 07 (3.8) | |
| Kytococcus | | | |
| Micrococcus species | | | 12 (12.12) |
| Staphylococcus aureus | 19 (6.8) | 07 (3.8) | 01 (1.01) |
| Coagulase negative staphy | 01(0.3) | 00 (0) | 01 (1.01) |
| Escherichia coli | 01 (0.3) | - | 01 (1.01) |
| Total | 281 | 182 | 99 |

had thrombocytopenia. Gram negative bacilli were responsible for most of the neonatal sepsis. Highest number of cultures were positive for Escherichia coli-42%, followed by gram positive cocci 14.2%, Klebsialla pneumoniae 11.7%. Gram positive cocci were found mostly in babies with late onset sepsis. The frequencies of isolated bacteria in EOS and LOS are shown in the table-II. Gram positive organisms showed a markedly high resistance towards penicillins and cephalosporins. Only 27% of isolated gram positive cocci were sensitive to amoxicillin-clauvolanic acid. They showed highest sensitivity

isolates to various antimicrobial agents.

## DISCUSSION

Compared to adults, newborns are at a higher risk of developing sepsis and its complications because of a weak immune system[12]. Sepsis not only threatens the survival, but also affects neuro developmental outcome of the baby and significantly increases the cost of care[13]. For diagnosis of sepsis, blood culture is the gold standard. To avoid any delay in treatment, antibiotics are given empirically. The choice of empirical antibiotics is very important, which

should be based on pattern of culture and sensitivity results of individual NICU. In our study, the incidence of suspected neonatal sepsis was 29.5%. Other studies conducted in Pakistan also showed very high incidence. It was found to be 42% in Karachi[14] and 62.5% in Peshawar[15]. In Bangladesh, the incidence was 34.88% and in Nigeria 45.9%[3]. However in Iran and Saudi Arabia, the incidence was found to be 6.6% and 5% respectively[16,17], probably due to good hygienic conditions and good quality care in their NICUs. Out of 733 blood cultures, 281 (40.6%)

delivered by vaginal route (43%). A higher association of cesarean section with neonatal sepsis was also found in a similar study conducted in Hyderabad[20]. In our study, the predominant organisms causing neonatal sepsiswere gram negative bacilli, with E.coli being the most common organism. This finding was consistent with study carried out in Peshawar[12]. Bhutta and Yusuf found klebsiella to be the most common cause of neonatal sepsis in Karachi[21]. Anwer *et al* found Grampositive organisms to be the main cause of neonatal

**Table-III: Comparative sensitivities of isolated bacteria to different anti microbial agents.**

| Organism | Staphylococus aureus | Eschirehiacoli | Klebsiellapne umoniae | Pseudomonas aeroginosa | Acinobacterba umannii |
|---|---|---|---|---|---|
| Ampicillin | 0% | 0% | 0% | 0% | 0% |
| Amoxicillin-clavulanic | 27% | 12% | 8% | 13% | 0% |
| Piperacillin | 83% | 88% | 76% | 91% | 30% |
| Cefoxitin | 24% | 22% | 24% | 27% | 0% |
| Cefotaxime | 47% | 30% | 35% | 29% | 65% |
| Ceftriaxone | 38% | 29% | 38% | 28% | 53% |
| Cefoparazone+salbactum | 44% | 36% | 41% | 43% | 55% |
| Imipenem | 85% | 84% | 86% | | 21% |
| Meropenem | 94% | 87% | 92% | 84% | 23% |
| Linezolid | 100% | | | | |
| Vancomycin | 100% | | | | |
| Tigecycline | | | | | 71% |
| Gentamicin | 37% | 37% | 31% | 46% | 15% |
| Amikacin | 51% | 31% | 25% | 52% | 22% |
| Erythromycin | 39% | | | | |
| Azythromycin | 47% | | | | |

were found to be positive. In India 43.1% of neonates had culture positive sepsis[15]. Neonatal mortalitydue to sepsis was 25.9% in our study. In Karachi, it was found to be 16%[8]. In Iran itwas 19.8%[16]. We found the incidence of EONNS to be 57.4% and LOS to be 42.6%. In Ayub Medical College and Hospital, LOS was found in 70.85% cases, significantly higher than EONNS (29.15%)[9]. In Egypt, incidence of LOS was 55.8%[3]. In Iran EONNS was found in 77.5% and LONNS in 22.5% of neonates[16]. Nigeria also showed incidence of EOS to be higher than LOS[18]. In US, incidence of EONNS was found to be 3.5/1000 live births (0.35%)[19]. We found a higher rate of neonatal sepsis among babies delivered by cesarean section (57%) as compared to those

sepsis, in Karachi, Pakistan[14]. In India, gram negative organisms were found to be responsible for 67.2% of neonatal sepsis[22]. We found Gram positive cocci to be the most common cause of LOS, indicating the source of infection to be hospital or community acquired in LOS. This finding was consistent with the study conducted in Nigeria[18]. However study in Egypt showed gram positive cocci to be the most common cause for both EOS and LOS[3]. We didn't find any culture to be positive for group B streptococcus. This finding was similar to most of the other studies conducted in Pakistan[12,9,8]. Among all bacterial isolates, we found a high degree of resistance to penicillins and cephalosporins. No commonly isolated pathogen was found sensitive

to ampicillin. This was much higher than the resistance seen in Peshawar[22]. Ecoli showed moderate resistance to aminoglycosides (>50%). This finding was consistent with other studies conducted in Pakistan and Nigeria[9,20]. Pseudomonas species were found sensitive to the antipseudomonal penicillins. Gram positive cocci showed a high sensitivity to linezolid and vancomycin. We found a very high incidence of multi drug resistant organisms,which was 57.1% in gram positive isolates and 91.3% among gram negative isolates. Antibiotic resistance has been increasing worldwide. It has increased the cost of treatment and also has increased failure of treatment. A study conducted in Taiwan showed that half of the neonates with persistent blood stream infection had initially been treated with inappropriate antibiotics[10]. This is specially seen in developing countries because of over the counter availability of antibiotics and no proper legislation of their use.

## CONCLUSION

We have a high incidence of neonatal sepsis. The most common pathogens for neonatal sepsis are gram negative bacilli. A very high percentage of these organisms are multi drug resistant, significantly increasing cost of treatment, morbidity and mortality of neonates.

## RECOMMENDATION

It is necessary to rationalize the use of antibiotics and to develop and implement the policies for their use, in order to slow down this rapid rise in multi-drug resistant organisms. This requires studies on spectrum of pathogens and their antimicrobial sensitivities to be carried out regularly and frequently in neonatal ICUs.

## CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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