

# Neonatal Sepsis in Tertiary Care Hospital: Bacteriological Profile and Antibiotic Susceptibility Patterns

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## ABSTRACT

**Aim:** To determine the most common pathogen responsible for neonatal sepsis and their antimicrobial sensitivity

**Method:** This retrospective cross-sectional study was carried out in the Department of Microbiology, Shaikh Zayed Hospital, Lahore from March 2017 to April 2018. A total of 618 samples were received with history of neonatal sepsis. All samples of blood culture were received from neonatal ward with history of sepsis. All patients were between the age of 1-28 days. Blood culture results and their antibiotic sensitivity were collected and analyzed.

**Results:** Blood cultures were positive in 85 (13.75%) cases. The isolated pathogens in early and late onset sepsis were 60% and 40% respectively. The blood cultures reported the most prevalent isolate in early and late onset neonatal sepsis was the coagulase negative Staphylococcus (CONS) 44.7%, followed by Klebsiella 16.47%, Staphylococcus aureus 8.23%, Citrobacter/Enterobacter 9.41%, and Acinetobacter 7.05%, Escherichia coli and Pseudomonas were 5.88%.

**Conclusion:** Coagulase negative Staphylococcus is a major cause of neonatal sepsis.

**Keywords:** Neonatal sepsis, Bacteriological profile, Antibiotic susceptibility

## INTRODUCTION

One of the leading global causes of neonatal mortality is considered to be Sepsis, especially in the developing countries<sup>1</sup>. With the emergence of antibiotic resistant strains and constrained resources of antibiotics antimicrobial resistance this has become a great challenge in the management of neonatal sepsis and is a cause of global concern<sup>2</sup>. Neonatal sepsis is recognized as a life threatening clinical emergency that requires an immediate and urgent diagnosis and thus becomes a typical reason for admittance in a neonatal care unit in developing countries<sup>3</sup>. It is caused by micro-organism usually received by the baby from the mother before or during birth and is repeatedly associated with obstetric complications as in premature onset of labor, chorioamnionitis, peripartum maternal fever and rupture of membrane.<sup>4</sup> The incidence and the type of bacterial isolates responsible for neonatal sepsis may vary from one country to another and may change in the same area at times<sup>5</sup>.

Neonatal sepsis is a systemic infection occurring in infants of  $\leq 28$  days of life and is an important cause of morbidity and mortality of newborn<sup>6</sup>. Neonatal sepsis is responsible for 30-50% of total deaths in developing countries<sup>7</sup>.

This disease (early onset sepsis) is most regularly explained as occurring during the first 3 days after the birth of the baby. The cause of this disease is a bacterial pathogen that is transmitted directly from the mother to the newborn child before or during the delivery.<sup>8</sup> Late onset sepsis is defined as a type of sepsis occurring after the first three days in the life of the newborn baby in neonatal intensive care unit in preterm infant and 7 days of life in term infant up to the age of 28 days.<sup>9,10</sup> This study was carried out to determine the bacteriological profile and

antibiotic susceptibility of neonatal sepsis in a tertiary care hospital of Lahore.

## MATERIALS AND METHODS

This retrospective cross-sectional study was carried out in the Department of Microbiology, Shaikh Zayed Hospital Lahore from March 2017 to April 2018. A total of 618 blood samples were received during this period, all were included. Blood culture bottles were incubated at 35-37°C for 7 days with daily manual examination for evidence of bacterial growth and subculture on solid media (blood agar MacConkey agar and chocolate agar) after 48 hours. The cultures showing negative results were held under observation for up to seven days before being awarded with a negative report.

Colony morphology, gram staining and other standard bio-chemical tests were used to identify the micro-organism growth in blood cultures showing positive results. In accordance with the directions of Clinical Laboratory Standards Institute guidelines, a modified version of Kirby-Bauer method was utilized to identify the antibiotic susceptibility of isolated micro-organisms.<sup>11</sup> Antibiotic discs were used according to gram positive and gram negative isolated micro-organism. The data entered and analyzed through SPSS-20.

## RESULTS

A total of 618 blood samples were collected during study period. Out of which growth was positive in 85 (13.75%). Early onset sepsis cases were 51 (8.25%) and late onset sepsis was 34 (5.50%). Dissemination of bacterial isolates with their relative prevalence is shown in Table 1. Gram positive isolated were 45 (53%) and gram negative isolated were 38 (44.75%). Candida was isolated in 2 (2.35%) cases. Among gram positive isolate coagulase negative Staphylococcus was 38 (44.70%) and Staph aureus was 7 (8.23%). Among gram negative isolate Klebsiella species was 14 (16.47%), enterobacter/Citrobacter 8 (9.41%), acinetobacter 6 (7.05%) and pseudomonas aeruginosa or Escherichia coli 5 (5.88%) and 5 (5.88%) respectively. No

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case of  $\alpha$ -haemolytic *Streptococcus* and group B streptococcus were seen. Resistance to commonly used antibiotic e.g. ampicillin and amoxicillin were up to 100%. Pattern of micro-organisms isolated in early onset and late onset sepsis is shown in Table 2.

Table 1: Dissemination of bacterial isolates corresponding to their relative prevalence (n=85)

Bacterial isolate	No.	%
CONS	38	44.7
<i>E. coli</i>	5	5.9
<i>Klebsiella</i> spp.	14	16.4
<i>Staphylococcus aureus</i>	7	8.2
<i>Pseudomonas</i>	5	5.9
<i>Enterobacter/Citrobacter</i>	8	9.4
<i>Acinetobacter</i>	6	7.0
<i>Candida</i>	2	2.4

Table 2: Pattern of micro-organisms isolated from blood cultures

Bacterial isolate	Early onset sepsis	Late onset sepsis
CONS	23 (60%)	15 (39.9%)
<i>E. coli</i>	4 (80%)	1 (20%)
<i>Klebsiella</i> spp.	12 (85%)	2 (14.3%)
<i>Staphylococcus aureus</i>	2 (28.5%)	5 (71.4%)
<i>Pseudomonas</i>	1 (20%)	4 (80%)
<i>Enterobacter/Citrobacter</i>	4 (50%)	4 (50%)
<i>Acinetobacter</i>	4 (66.6%)	2 (33.3%)
<i>Candida</i>	1 (50%)	1 (50%)

## DISCUSSION

Despite major scientific advances in neonatal care, neonatal sepsis is still considered to be a major cause of infant morbidity and mortality in intensive care units dealing with neonatal complications<sup>12,13</sup>. In our study positive blood cultures in neonates were 13.75% which is comparable to the studies from Nepal where in neonatal sepsis, blood culture positivity was 13.7% and 19.56%<sup>14,15</sup>. Similar results were found by another research conducted in the same country, prevalence of positive blood cultures was 20.5%.<sup>2</sup> Similar studies conducted by Garg et al<sup>16</sup> and Gohel et al<sup>17</sup> in India report the prevalence of positive cultures to 20.5% and 9.2% in the same order. Another study from Jordan showed blood culture positive upto 13.8%.<sup>3</sup> In Pakistan according to Chaudhry et al<sup>18</sup> and Latif et al<sup>19</sup> the reported prevalence rate of positive blood cultures was up to 20%.

Incidence of gram positive micro organisms represented the major class of isolates in this study (53.93%) and in gram positive isolates coagulase negative *Staphylococcus* being the most common 44.7%. In study done by Younis<sup>3</sup> coagulase negative *Staphylococcus* were reported to be 58.2% in neonatal sepsis.<sup>3</sup> In a study of Garg et al<sup>16</sup> reported incidence of coagulase negative *Staphylococcus* was 20.7%. One of the most prevalent and major cause of neonatal sepsis is Coagulase Negative *Staphylococcus* as reported by various research studies<sup>20,21</sup>. Similarly study on neonatal sepsis by Pokhrel et al<sup>2</sup> showed coagulase negative *Staphylococcus* up 20.3%.

Role of coagulase negative *Staphylococcus* in neonatal sepsis is still controversial.<sup>22</sup> Until 1970, coagulase negative *Staphylococcus* was mainly recognized as contaminant, however, since that time, several major studies have declared coagulase negative *staphylococcus*

to be a major reason for the increase in neonatal infections<sup>23-25</sup>.

This study revealed that 13.75% of the neonates had positive blood culture, similar to the study by Younis<sup>3</sup> 13.8%. Our observed data is somehow higher than those reported in countries like Saudi Arabia 9%<sup>26</sup> and Kuwait 6.6%<sup>27</sup>.

In our study 2<sup>nd</sup> common gram positive isolate in sepsis was *Staph aureus* (8.23%) which is similar to the study conducted by Mahmood et al<sup>28</sup> and Ingale et al<sup>29</sup>. Similar was the case in the study conducted by Garg et al<sup>16</sup> shown higher incidence of coagulase negative *Staphylococcus* upto 20% and lower incidence of *Staph aureus* upto 8.3%. The study conducted by Sharma et al<sup>30</sup>, in India, displayed a predominance gram positive micro organisms out of which the most common was *Staph aureus*.

In gram negative isolated *Klebsiella* was the most common (16.47%) followed by *enterobacter/citrobacter* (9.41%), *acinetobacter* (7.05%), *Escherichia coli* and *pseudomonas* (5.88%) and 5.88% respectively in the present study.

In our study *Klebsiella* spp was the second common isolate upto 16.47% in neonatal sepsis. Similar finding was also seen in study of Shrestha et al<sup>31</sup> and in the study of Anjum et al.<sup>32</sup> *Klebsiella* spp. was 16.47%. This is comparable to the study of Panday et al<sup>33</sup> where he reported a higher incidence of *Klebsiella* spp. 19.56% while Garg et al also reported *Klebsiella* spp. as 7.3%<sup>16</sup>. While in the study done by Pokhrel et al<sup>2</sup>, *Klebsiella* species was 33.3% which is quite high.

Multi-drug resistance to antibiotic in our societies has increased over the last two decades, probably due to over the counter sales of broad spectrum antibiotic and ineffective infection control<sup>27,34</sup>.

In our study gram positive organism are completely resistant to amoxcillin 100%. This outcome is conferring with the research undertaken by Pandey et al and Garg et al which has shown that the gram positive organism are completely resistant (100%) to penicillin and their resistance to ampicillin lingered around 80.3%<sup>16,33</sup>.

Coagulase negative *Staphylococcus* has been reported to be most common cause of neonatal sepsis<sup>20,21</sup> and similar is the case in our study. Coagulase negative *Staphylococcus* shows low susceptibility to penicillin, cephalosporin and aminoglycoside and high susceptibility to vancomycin and linezolid in our study. This was shown that vancomycin and linezolid was the most effective antibiotic for gram positive micro-organism. For gram negative organism the most effective drug in our study were colistin, amikacin and meropenem 100%, 61% and 52% respectively.

Confirming to what was found by Pokhrel et al, Vancomycin and Linezolid showed high responsiveness (100%) towards the gram positive isolates.<sup>2</sup> Similar was also seen in Mulla et al<sup>35</sup>, Singh et al<sup>36</sup>, Sarangi et al<sup>37</sup> and Dalal et al<sup>38</sup>.

In our study a major percentage of coagulase negative *Staphylococcus* showed low susceptibility to penicillin, oxacillin, 3<sup>rd</sup> generation cephalosporin and aminoglycosides in India and Pakistan.<sup>14,28</sup>

Gram negative isolates showed high responsiveness to colistin, a result similar to the research findings of Pokhrel et al.<sup>2</sup> Moderate susceptibility to carbapenim is

observed in our study for gram negative isolates which is different from studies of Pokhrel et al<sup>2</sup>, Sheth et al<sup>21</sup> and Yusef et al<sup>39</sup> Third generation cephalosporin showed low susceptibility in our study similar to that finding of Pokhrel<sup>2</sup>.

## CONCLUSION

Coagulase negative *Staphylococcus* together with *Klebsiella* was the most common cause of neo natal sepsis in Sheikh Zayed Hospital, Lahore. These micro-organisms were highly resistance to commonly used antibiotic. The high resistance of these bacteria to antibiotics is corresponding to consequential neo natal morbidity and mortality.

## REFERENCES

- United Nations Inter-agency Group for Child Mortality Estimation (UNIGME). Levels and trends in child mortality report 2017. New York: United Nations Children's Fund; 2017.
- Pokhrel B, Koirala T, Shah G, Joshi S, Baral P. Bacteriological profile and antibiotic susceptibility of neonatal sepsis in neonatal intensive care unit of a tertiary hospital in Nepal. *BMC Pediatrics* 2018; 18:208-15.
- Younis NS. Neonatal sepsis in Jordan: bacterial isolates and antibiotic susceptibility patterns. *Rawal Med J* 2011;36:169-72.
- Rodrigo I. Changing patterns of neonatal sepsis. *Sri Lanka J Child Health* 2002;31:3-8.
- Palazzi D, Klein J, Baker C. Bacterial sepsis and meningitis. In: Remington JS, Klein J, eds. *Infectious disease of the fetus and newborn infants*. 6<sup>th</sup> ed. Philadelphia: Elsevier, 2006:245
- Edwards MS, Baker CJ. Sepsis in the newborn. In: Gershon AA, Hotez PJ, Katz SL, eds. *Children's infectious diseases of children*. 11<sup>th</sup> ed. Philadelphia: Mosby 2004.
- Agrawal R, Sarkar N, Deorary A, Paul V. Sepsis in newborn. *Ind J Paediatr* 2003;68:1143-7, Jain NK, Jain VM, Maheshwari S. Clinical profile of neonatal sepsis. *Katmandu Univ Med J* 2003;1:117-20.
- Hornik CP, Fort P, Clark RH, Watt K, Benjamin DK, Jr, Smith PB, et al. Early and late onset sepsis in very-low-birth-weight infants from a large group of neonatal intensive care units. *Early Hum Dev* 2012 88:S69-S74.
- Guilbert J, Levy C, Cohen R, Bacterial Meningitis Group, Delacourt C, Renolleau S, Flamant C. Late and ultra late onset *Streptococcus B* meningitis: clinical and bacteriological data over 6 years in France. *Acta Paediatr* 2010; 99:47-51
- Cohen-Wolkowicz M, Moran C, Benjamin DK, Cotten CM, Clark RH. Early and late onset sepsis in late preterm infants. *Pediatr Infect Dis J* 2009; 28:1052-6.
- Performance standards for antimicrobial disk susceptibility tests. Approved Standard, 9th ed. CLSI document M2-A9. Clinical Lab Standards Institute. Wayne PA, USA, 2006.
- Brodie S, Sands K, Gray J, Parker R, Goldmann D, Davis R, et al. Occurrence of nosocomial bloodstream infections in six neonatal intensive care units. *Pediatr Infect Dis J* 2000;19:56.
- Cordero L, Sananes M, Ayers L. Blood stream infections in a neonatal intensive care unit: 12 years' experience with an antibiotic control program. *Infect Control Hosp Epidemiol* 1999;20:242-6.
- Shrestha S, Adhikari N, Shakya D, Manandhar L, Chand A. Bacteriological profile of neonatal blood cultures at Patan hospital. *J Nepal Paediatr Soc.* 2007 26(1):1-4.
- Shrestha S, Adhikari N, Rai BK, Shreepaili A. Antibiotic resistance pattern of bacterial isolates in neonatal care unit. *J Nepal Med Assoc.* 2010 49 (180): 277-81.
- Garg A, Anupurba S, Garg J, Goyal RK, Sen MR. Bacteriological profile and antimicrobial resistance of blood culture isolates from a university hospital. *J Ind Acad Clin Med* 2007; 8(2):139-43.
- Gohel K, Jojera A, Soni S, Gang S, Sabnis R, Desai M. Bacteriological profile and drug resistance patterns of blood culture isolates in a tertiary care nephrourology teaching institute. *Bio Med Res Int* 2014:5.
- Chaudhry I, Chaudhry NA, Munir M, Hussain R, Tayyab M. Etiological pattern of septicemia at three hospitals in Lahore. *J Coll Phys Surg Pak* 2000;10(10): 375-9.
- Latif S, Anwar MS, Ahmad I. Bacterial pathogens responsible for blood stream infection (BSI) and pattern of drug resistance in a tertiary care hospital of Lahore. *Biomed* 2009;25(2):101-5.
- Wu JH, Chen CY, Tsao PN, Hsieh WS, Chou HC. Neonatal sepsis: a 6-year analysis in a neonatal care unit in Taiwan. *Pediatr Neonatol* 2009;50(3):88-95.
- Sheth KV, Patel TK, Tripathi CB. Antibiotic sensitivity pattern in neonatal intensive care unit of a tertiary care hospital of India. *Asian J Pharm Clin Res* 2012 5(3):46-50.
- Boisson K. Characterization of coagulase negative *Staphylococci* isolated from blood infections: incidence, susceptibility to glycopeptides and molecular epidemiology. *Eur J Clin Microbiol Infect Dis* 2002;21:660-5.
- Choudhary P, Shrivastava DS, Agrawal L. Bacteriological study of neonatal infections. *Indian Pediatr* 1975;12:459-63.
- Guha D, Jaspal D, Krishna D. Outcome of neonatal septicemia, clinical and bacteriological profile. *Indian Pediatr* 1978;15:423-7.
- Thylefors J, Harbarth S, Pittet D. Increasing bacteremia due to coagulase negative *Staphylococci*: fiction or reality? *Infect Control Hosp Epidemiol* 1998;19:581-9.
- Haque K, Chaglia A, Shaheed M. Half a decade of neonatal sepsis, Riyadh, Saudi Arabia. *J Trop Pediatr* 1990;36:20-3.
- Kuruvilla A. Neonatal septicaemia in Kuwait. *J Kwt Med Assoc* 1980;14:225-31.
- Mahmood A, Karamat KA, Butt T. Neonatal sepsis: high antibiotic resistance of the bacterial pathogen in a neonatal intensive care unit in Karachi. *J Pak Med Assoc* 200252(8):348-50.
- Ingale HD, Kongre VA, Bharadwaj RS. A study of infections in neonatal intensive care unit at a tertiary care hospital. *Int J Contemp Pediatr* 20174(4):1349-56.
- Sharma P, Kaur P, Aggarwal A. *Staphylococcus aureus*: the predominant pathogen in the neonatal ICU of a tertiary care hospital in Amritsar, India. *J Clin Diagn Res* 2013;7(1): 66-9.
- Shrestha S, Shrestha NC, Dongol Singh S, Shrestha RPB. Bacterial isolates and its antibiotic susceptibility pattern in NICU. *Katmandu Univ Med J* 2013;41(1):66-70.
- Anjum MU, Shams N, Hussain SA, Shah SH. bacteriological profile and antibiotic susceptibility of blood isolates in blood stream infections. *Med Forum* 2015;26(2):32-5.
- Pandey S, Raza S, Bhatta CP. The aetiology of the bloodstream infections in the patients who presented to a tertiary care teaching hospital in Kathmandu, Nepal. *J Clin Diag Res* 2013;7(4): 638-41.
- Bhutta Z, Naqvi S, Muzaffar T, Farooqui B. Neonatal sepsis in Pakistan. *Acta Paediatr Scand* 1991; 80: 596601.
- Mulla SA, Revdiwala SB. Neonatal High antibiotic resistance of the bacterial pathogens in a neonatal intensive care unit of a tertiary Care hospital. *J Clin Neonatol.* 2012;1(2):72-75.
- Singh HK, Sharja P, Onkar K. Bacteriological profile of neonatal sepsis in neonatal intensive care unit (NICU) in a tertiary care hospital: prevalent bugs and their susceptibility patterns. *Eur J Pharmaceutical Med Res* 2016; 3(3):241-5.
- Sarangi KK, Pattnaik D, Mishra SN, Nayak MK, Jena J. Bacteriological profile and antibiogram of blood culture isolates done by automated culture and sensitivity method in a neonatal intensive care unit in a tertiary care hospital in Odisha, India: *Int J. Adv Med.* 2015;2(4):387-92.
- Dalal P, Gathwala G, Gupta M, Singh J. Bacteriological profile and antimicrobial sensitivity pattern in neonatal sepsis: a study from North India. *Int J Res Med Sci.* 2017;5(4):1541-5.
- Yusef D, Shalakhti T, Awad S, Algharaibeh H. Clinical characteristics and epidemiology of sepsis in the neonatal intensive care unit in the era of multi-drug resistant organisms: a retrospective review. *Pediatr Neonatol* 2017;59(1):35-41.

