Original Article

Bacteriological profile and antibiogram of blood culture isolates from a neonatal intensive care unit in a tertiary care hospital in north India

Natasha Sawhney[1*], Sandeep Dogra[2], Bella Mahajan[3]

[1]Demonstrator, [2]Assistant Professor, [3]Professor and Head, Department of Microbiology, Government Medical College and Associated Hospital, Jammu, INDIA.
Email: dr.natashakapahi@gmail.com

Abstract

Background: Septicaemia in newborn remains a significant cause of mortality and morbidity in developing countries. Changing bacterial flora and emergence of resistant strains adds to the problem. Thus, neonatal septicaemia requires accurate diagnosis and proper management for better outcome. **Methods:** This prospective study was conducted among suspected neonatal sepsis cases admitted to the NICU at SMGS hospital from Feb 2016 to Feb 2017. After taking applied assent from the parents of the neonates, a total of 380 samples were collected and processed by automated identification and susceptibility testing system as per validated laboratory protocols of Microbiology laboratory. Data of positive blood culture isolates was analysed by appropriate tools. **Results:** Out of 380 blood samples tested, a total of 111 (29.21%) were positive. Sixty neonates (54%) had gram-negative isolates including rare ones like Sphingomonas sp., Stenotrophomonas sp., Pasteurella sp., Providencia sp., Burkholderia sp. and Moraxella sp., forty two (37.9%) had gram-positive septicaemia and nine (8.1%) had fungal infection. Antibiotic pattern suggested high degree of resistance to first line penicillin, and gentamicin, moderate to amikacin and cefoperazone-sulbactum. Among gram-positive isolates, high degree resistance was seen in penicillin with all isolates as MRSA. Moderate to high level resistance was seen in aminoglycosides and quinolones. **Conclusion:** The present study highlights the presence of rare organisms causing septicaemia and increasing trend of high to moderate level of antibiotic resistance calling for continuous monitoring by rapid detection and consecutive adjustment of empirical treatment regime. Further studies are required to study the trends and pattern of antibiotic resistance to develop hospital antibiotic policy.

Key Words: Septicaemia, Blood culture, antibiotic resistance.

[*]**Address for Correspondence:**
Dr. Natasha Sawhney, Demonstrator, Department of Microbiology, Government Medical College and Associated Hospital, Jammu, INDIA.
Email: dr.natashakapahi@gmail.com

Received Date: 12/04/2017 Revised Date: 08/05/2017 Accepted Date: 04/06/2017

Access this article online	
Quick Response Code:	Website: www.medpulse.in
	DOI: 10 June 2017

INTRODUCTION

Neonatal septicaemia refers to a clinical syndrome characterised by systemic signs and symptoms due to generalised bacterial infections with a positive blood culture in the first four weeks of life.[1] It remains one of the main causes of mortality and morbidity despite the progress in hygiene, introduction of new and potent antimicrobial agents for treatment and advanced measures for diagnosis.[2] In 2015, infectious diseases accounted for more than 50% of all deaths in neonates and children aged under 5 years, especially in southern Asia out of which 4,01,000 deaths per year were attributable to neonatal sepsis. Antimicrobial resistance is a major factor determining clinical unresponsiveness to treatment and rapid evolution to sepsis and septic shock. Approximately 2, 14,000 neonatal deaths due to sepsis worldwide each year could be attributable to resistant pathogens.[3] For that reason, new strategies and continuous surveillance are required to monitor the changing epidemiology of pathogens, antibiotic susceptibilities and antibiotic use needed to overcome the increasing incidence of resistance to conventional drugs. Although most isolates remain

How to site this article: Natasha Sawhney, Sandeep Dogra, Bella Mahajan. Bacteriological profile and antibiogram of blood culture isolates from a neonatal intensive care unit in a tertiary care hospital in north India. *MedPulse – International Medical Journal.* June 2017; 4(6): 783-787. http://www.medpulse.in (accessed 12 June 2017).

sensitive to the new antibiotics, emergence of resistant strains cannot be excluded in the future.[4] Bacterial infection is the biggest cause of neonatal admissions to hospitals, and probably the biggest cause of morbidity in the community. Key pathogens are *Escherichia coli*, Klebsiella sp. and Staphylococcus species. Gram-negative bacteria, especially members of enterobacteriacae are important causes of bacteraemia in Neonatal ICUs.[4] The pattern of organisms causing sepsis also varies from place to place and can change in the same place over a period of time. This is due to the changing pattern of antibiotic use and changes in life style. These organisms have developed multi-drug resistance over the last two decades due to indiscriminate use of antibiotics, over the counter sale of antibiotics, lack of legislation to control their use and ineffective infection control in maternity services.[2] The gold standard for diagnosis of septicaemia is the isolation of bacterial agent from blood culture but the results of blood culture take hours to days. Early treatment and appropriate use of antibiotics would minimize the risk of severe morbidity and mortality in sepsis, and reduce the emergence of multi-drug resistant organisms in intensive care units by rational antibiotic use. For the success of early empiric treatment, periodic review of cases to assess any changing trends in the infecting organisms and their antimicrobial susceptibility is important.[5,6] This study was conducted to determine the changing profile and antibiotic sensitivity pattern of bacterial isolates from blood cultures of neonates with septicaemia admitted in the neonatal unit of our hospital.

MATERIAL AND METHODS

This collaborative study was done prospectively in the Department of Microbiology in association with Department of Paediatrics at Neonatal Intensive Care Unit (NICU) of SMGS Hospital, Jammu. A total of 380 suspected neonatal septicaemia cases admitted in the NICU, during the period from Feb 2016 to Feb 2017 were recruited in the study. A structured performa was used to collect demographic details after taking applied assent from the parents of the neonates. The information included age, gender, birth weight, gestational age, mode of delivery of the neonate and age of onset of illness. Two ml of venous blood samples for culture were collected following standard aseptic precautions in specific automated aerobic paediatric blood culture bottle [Bact/Alert PF Plus Fastidious Antibiotic Neutralization bottle (bioMerieux # 410853)]. The samples thus collected were transferred immediately and were cultured by automated BacT/Alert and VITEK2 system as per validated laboratory protocol of Microbiology laboratory for rapid isolation and sensitivity test. Data of positive blood cultures was analysed by appropriate tools.

RESULTS

Out of 380 clinically suspected septicaemia cases of neonates, a total of 111 (29.21%) were positive. 60 neonates (54%) had Gram-negative isolates, 42 (37.9%) had Gram-positive septicaemia and 9 (8.1%) had fungal infection. (Table 1) Among the Gram-negative isolates, common species isolated were Klebsiella sp. (31.6%), Acinetobacter sp. (18.3%) and *Escherichia coli* (16.6%) followed by Enterobacter sp. (15%), Pseudomonas sp. (5%) and Burkholderia sp. (5%) along with the isolation of rare organisms like Sphingomonas sp., Stenotrophomonas sp., Pasteurella sp., Moraxella sp. and Providencia sp. (Table 1)

Table 1: Distribution of Gram-negative isolates causing Neonatal Septicaemia

Bacterial pathogen (n=60)	No. (%)
Klebsiella sp.	19 (31.6%)
Acinetobacter sp.	11 (18.3%)
Escherichia coli	10 (16.6%)
Enterobacter sp.	9 (15%)
Pseudomonas sp.	3 (5%)
Burkholderia sp.	3 (5%)
Others	5 (8.3%)

Table 2: Percentage of antibiotic resistance in Gram-negative isolates causing Neonatal Septicaemia

Antibiotic	Kleb. sp. (n=19)	Acinetoacter sp. (n=11)	E. coli (n=10)	Enterobacter (n=9)	Pseudomonas sp. (n=3)	Burkholderia sp. (n=3)	Others (n=5)	No (%) (n=60)
Ampicillin	19	11	10	9	3	3	5	60 (100 %)
Gentamicin	16	10	8	7	3	0	5	48 (80 %)
Amikacin	7	5	5	3	1	0	4	25 (41.6%)
Cefoperazone- sulbactum	5	6	6	2	0	3	2	24 (40%)
Imipenem	1	1	1	1	1	0	1	6 (10%)
Meropenem	1	1	1	0	1	0	1	5 (8.3%)
Tigecycline	1	0	0	1	0	0	1	3 (5%)
Colistin	0	0	0	1	0	0	1	2 (3.3%)

Antibiotic pattern suggested high degree of resistance to first line penicillins and gentamicin, moderate to amikacin and cefoperazone – sulbactum. (Table 2)

Table 3: Distribution of Gram-positive isolates causing Neonatal Septicaemia

Isolates (n=42)	No. (%)
CONS	25 (59.6 %)
Staphylococcus aureus	9 (21.4 %)
Enterococcus sp.	8 (19 %)

Table 4: Percentage of antibiotic resistance in Gram-positive isolates causing Neonatal Septicaemia

Antibiotic	CONS	*S. aureus*	*Enterococcus sp.*	No (%)
Penicillin	25	9	8	42 (100%)
Cefoxitin	25	9	8	42 (100%)
Aminoglycosides	21	6	5	32 (76%)
Quinolones	11	7	4	22 (52.3%)
Linezolid	0	0	0	0
Vancomycin	0	0	0	0

Among the Gram-positive isolates, CONS were found in highest numbers (59.6%), followed by *Staphylococcus aureus* (21.4%) and Enterococcus sp. (19%). Antibiotic pattern suggested 100% resistance to penicillins with all the isolates as Methicillin Resistant *Staphylococcus aureus* (MRSA). Moderate to high level resistance was seen in aminoglycosides (76%) and quinolones (53%). (Table 4).

DISCUSSION

Severe sepsis remains one of the leading causes of death in neonates. Physical signs and symptoms, have limited specificity. Definitive diagnosis is by bacteriologic culture of blood samples to identify organisms and establish antibiotic susceptibility. Neonatal sepsis is a life threatening emergency and any delay in the treatment may be fatal. Bacterial pathogens responsible for this serious condition vary with the geographical area and time. It is extremely important to diagnose the cases at the earliest so that appropriate antibiotic treatment can be given. Moreover, the bacterial pathogens responsible and their susceptibility pattern should be regularly monitored in a hospital setting.[7] With this aim, present study was designed with an objective to generate local evidence on spectrum of isolates causing septicaemia in paediatric critical care setting and their antibiotic resistance pattern. During one year study, out of 380 clinically suspected septicaemic cases of neonates, a total of 111 (29.21%) were positive. The frequency (29.21%) of bacterial isolation from the blood culture of neonates in this study was in accordance with many previous studies done in other countries.[1,8,9] The common isolates in blood culture in our study were *Coagulase Negative Staphylococcus (CONS)* 25 (59.6 %), Klebsiella sp. 19 (31.6%) and *Acinetobacter sp.* 11 (18.3%). The findings are consistent with those of the previous studies.[4,10-12] The weaker immune system in neonates and children explains this higher rate of isolation. This suggests that infections by these agents constitute a significant threat to child survival in this locale and other developing country settings. Many studies have been done depicting Gram-negative isolates as the main contributors to Neonatal septicaemia.[13] Among Gram-negative isolates, Klebsiella sp. was the predominant one, followed by Acinetobacter sp., *Escherichia coli* and other isolates. This is consistent with the study done by Mahmood *et al*[7] and Samya nazeer *et al*.[14] The newborns probably acquire the Gram-negative rods from the vaginal and faecal flora of the mother and the environment where the delivery occurs.[7] Our study also highlights the presence of rare organisms causing septicaemia like *Sphingomonas paucimobilis* which was isolated from a two day old baby with respiratory distress. It is a rare cause of healthcare associated infection. The route of infection can be endogenous or exogenous via implantation of indwelling devices or via contaminated fluids in hospital.[15] It has been associated with neonatal septicaemia in a study done by Priti Choudhary *et al*.[16] It is an emerging pathogen and it should not be discarded as a contaminant. Another rare organism isolated in our study is *Stenotrophomonas maltophilia* in a three day old low birth weight baby weighing 1 kg. Cases have been reported showing nosocomial Stenotrophomonas sp. infection in hospitalised newborns.[17] Other rare organisms causing neonatal septicaemia were Pasteurella spp, Providencia spp, Burkholderia sp. and Moraxella sp. Different studies have been done reporting these species as rare causative agents of the disease.[18,19] Another study states that *Burkholderia cepacia* should always be kept in mind as a cause of septicaemia in neonates so as to reduce mortality due to this organism.[20] In the management of sepsis in pediatric age group, empirical antibiotic therapy should be determined by the prevalent pattern of microbial agents and their antibiotic susceptibility pattern. Although isolation of a pathogen in culture is a prerequisite for proven bacterial sepsis, culture results takes at least few hours to be reported. The early and appropriate initiation of antimicrobial agents in high risk neonates before the result of blood culture susceptibility is defined as "empirical antibiotic therapy". The recommended initial empiric therapy for a neonate with suspected bacterial sepsis includes ampicillin and an aminoglyosisde.[6] In our study, antibiotic pattern suggested high degree of resistance to first line penicillin and gentamicin, moderate to amikacin and cefoperazone-sulbactum and least to carbapenems in case of Gram-negative isolates. Waseem

et al described high resistance of these bacteria's against ampicillin.[12] In another study done by Avinika Aggarwal *et al* the level of aminiglycoside resistance of the Gram-negative bacteria exceeded 50 % which correlates with our findings.[9] Also, aminoglycosides show variable pattern of resistance. Our study revealed 80% resistance to gentamicin and 58% resistance to amikacin which is nearby to the resistance percentage shown by Avinika *et al* and Shahzad *et al*.[4,9] Imipenem and meropenem, cefoperazone-sulbactum and colistin showed least antibiotic resistance in all the Gram negative bacterial isolates, including non-fermenters. Among Gram-positive isolates, Coagulase-Negative Staphylococcus (CONS) had highest incidence (59.6%) followed by *Staphylococcus aureus* (21.4%) and Enterococcus spp. (19%) Same pattern of distribution has been studied by Arpita *et al*[10] and Samiya Nazeer *et al*.[14] Trends show an increase in CONS sepsis. The infant's skin, respiratory tract, conjunctivae, gastrointestinal tract, and umbilicus may become colonized by CONS and such colonization lead to possibility of late-onset sepsis from invasive microorganisms. Vectors for such colonization may include vascular or urinary catheters, other indwelling lines, or contact with caregivers who have bacterial colonization.[21] Gram-positive pathogens show high degree resistance to penicillin and cefoxitin with all isolates as Methicillin resistant *Staphylococcus aureus* (MRSA) and moderate to high level resistance to aminiglycosides and quinolones. Many other studies have also described the emerging pattern of resistance against cephalosporins.[12] Moreover, Quinolones are not frequently used for neonatal sepsis but resistance is emerging against them because of the indiscriminate use of antibiotics. But still resistance to quinolones is low compare to commonly used antibiotics. Our study revealed 53% resistance to quinolones which is almost close to the findings by Shahzad *et al*.[4] *Staphylococcus* aureus and *Staphylococcus epidermidis* were 100 % sensitive to vancomycin and linezolid which is similar to sensitive percentage in other studies.[4,9,14] The occurrence of MRSA is more common because of indiscriminate use of higher antibiotics as an emergency empirical therapy. It is high time that MRSA should be treated with a combination of ciprofloxacin or vancomycin with amikacin. This study has shown that *CONS* and Gram-negative rods including *K. pneumoniae* are the leading causes of septicemia in pediatric age group, a pattern similar to that of other low income countries. Observed decline in susceptibility of these common pathogens to common antibiotics calls for increased efforts to ensure more rational use of these drugs. The main forces driving the increase in antimicrobial resistant bacteria are poor infection control practices and inappropriate use of antibiotics. Specific antibiotic utilization strategies like antibiotic restriction, combination therapy and antibiotic cycling may help to decrease or prevent the emergence of resistance.

CONCLUSION

Knowledge of epidemiological and antimicrobial susceptibility pattern of common pathogens in a given area helps to inform the choice of antibiotics. This study stresses on the need for continuous longitudinal surveillance at frequent intervals to describe the various pathogens attributable for early neonatal sepsis as well as their ever changing antibiotic sensitivity pattern so as to formulate an acceptable and rational antibiotic protocol. With increasing resistance of various pathogens to commonly used antibiotics, it becomes imperative to formulate appropriate unit specific antibiotic policies.

REFERENCES

1. Kausik Kumar Sarangi et al. 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. International Journal of Advances in Medicine. 2015;2(4):387-392
2. Ari Yunanto et al. Bacteriological pattern and antibiotic sensitivity in neonatalogy ward Ulin General Hospital, Banjarmasin, Indonesia. Journal of Harmonized Research in Pharmacy. 2014;3(4);148-153
3. World Health Organisation Report – Improving the prevention, diagnosis and clinical management of sepsis. Available at: http://apps.who.int/gb/ebwha/pdf_files/EB140/B140_12-en.pdf (Accessed on 06-06-2017
4. Shahzad Najeeb et al. Causative bacteria and antibiotic resistance in Neonatal Sepsis. J Ayub Med Coll Abbottabad. 2012;24(3-4):131-134
5. Aftab R and Iqbal I. Changing pattern of bacterial isolates and their antibiotic sensitivity in neonatal septicaemia: A hospital based study. NMJ. 2009;1(1):3-8
6. Sivanandan S et al. Choice and duration of antimicrobial therapy for neonatal sepsis and meningitis. Int. Journal of Pediatrics. 2011:1-9
7. A. Mahmood et al. Neonatal Sepsis: High antibiotic resistance of the bacterial pathogens in a Neonatal Intensive Care Unit in Karachi. Journal of Pakistan Medical Association. 2002:1-2
8. Sharma M et al. Microbial profile of septicaemia in children. Indian J Pract Doct. 2008;5:16-18
9. Avinika Agarwal and Sevitha Bhat. Clinico-Microbiological study of Neonatal Sepsis. JIMD. 2015;2(1):22-29
10. Arpita Jigar Shah et al. Neonatal Sepsis: High antibiotic resistance of bacterial pathogens in a Neonatl Intensive Care Unit of a teriary care hospital. J Clin Neonatol. 2012;1(2):72-75
11. Bhutta ZA. Epidemiology of neonatal sepsis in Pakistan. An analysis of available evidence and implication for care. J Coll Physicians Surg Pak 1996;6(1):12

12. Waseem R, Khan M, Izhar TS. Neonatal sepsis. Professional Med J 2005;12:451–6
13. Karlowicz MG, Buescher ES, Surka AE. Fulminant late onset sepsis in a neonatal intensive care unit, 1988–1997 and impact of avoiding empirical vancomycin therapy. J Pediatr 2000;106:1387–90
14. Samya Nazeer Khan and Siby Joseph. Neonatal Sepsis. International Journal Of Pharma and Bio Sciences. 2012;3(4):802-809
15. Kawasaki S et al. The cell envelope structure of the lipopolysaccharide lacking Gram negative bacterium. Sphingomonas paucimobilis. J Bacteriol. 1994;176:284-290
16. Priti Chowdhary et al. Sphingomonas paucimobilis septicaemia in a neonate. A rare case report. Indian Journal of Pathology and Microbiology. 2016;59(1):119-121
17. Issaoui S et al. Neonatl infection with Stenotrophomonas maltophilia. Arch Pediatr. 2012;19(4):404-407
18. Parodi et al. Neonatl early onset sepsis due to Moraxella osloensis: Case report and revision of the literature. Ebsco. 2015;10(2);182-186
19. Christelle Guillet et al. Pasteurella multocida sepsis and meningitis in a 2 month old twin infants after household exposure to a slaughtered sheep. Clinical Infectious Diseases. 2007;45(6):80-81
20. Swati M et al. Burkholderia cepacia. An emerging case of septicaemia- An outbreak in a Neonatl Intensive Care Unit from a tertiary care hospital of central India. IOSR journal of dental and medical sciences. 2013;10:41-43
21. Ann L Anderson Berry, Linda L., Ted Rosenkantz. Pediatrics: Cardiac Diseases and critical care medicine, Neonatl Sepsis. Available at: http://emedicine.medscape.com/article/978352-overview. Accessed on 06-06-2017

Source of Support: None Declared
Conflict of Interest: None Declared