Int J Pharm Bio Sci 2012 Oct; 3(4): (P) 802 - 809

Research Article Pharmacy Practice

International Journal of Pharma and Bio Sciences

ISSN 0975-6299

NEONATAL SEPSIS: ANTIBIOTIC SENSITIVITY & RESISTANCE PATTERN OF COMMONLY ISOLATED PATHOGENS IN A NEONATAL INTENSIVE CARE UNIT OF A TERITIARY CARE HOSPITAL, SOUTH INDIA

SAMIYA NAZEER KHAN[1] *, SIBY JOSEPH[1]

[1]Department of Pharmacy Practice, Amrita School of Pharmacy, Amrita institute of medical sciences, cochin, kerala, India.

ABSTRACT

Neonatal bacterial sepsis is one of the major causes of morbidity and mortality in neonates. Bacterial pathogens and drug resistance are different in hospitals of each country. In this study we identified bacterial pathogens and its sensitivity and resistance pattern for various antibiotics in the neonatal intensive care unit (NICU) in Amrita Institute of Medical Sciences (AIMS), kochi during September 2011 to April 2012. A total of 150 newborns admitted in the NICU with symptoms/signs of bacteremia/septicemia or developed sepsis during their stay in NICU were included in the study. 57 (38%) out of 150 patients admitted during the study period had proven sepsis confirmed by positive blood culture. Gram negative organisms accounted for 87.72 % of all positive cultures. Among the culture positive specimens, *Klebsiella pneumoniae* (45.61 %) and *Coagulase Oxidase Negative Staphylococcus* (CoNS) (12.28%) were the commonly isolated gram negative and gram positive organism respectively.

KEY WORDS: ***Neonates, Bacterial sepsis, sensitivity, resistance***

SAMIYA NAZEER KHAN
Department of Pharmacy Practice, Amrita School of Pharmacy, Amrita institute of medical sciences, cochin, kerala, India.

Corresponding author

INTRODUCTION

Neonatal bacterial sepsis (NBS) remains as an important cause of mortality and morbidity among neonates. 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).[1] Sepsis occurring in the first 72 hours of life is defined as early-onset sepsis (EOS) and that occurring beyond 72 hours as late-onset sepsis (LOS). Usually EOS is due to vertical transmission of pathogens and LOS is due to horizontal transmission of the pathogens from care givers. The pattern of bacterial pathogen responsible for neonatal sepsis has changed with time and varies from place to place.

There is a difference in the causative organisms for neonatal sepsis between the developed and developing countries[2]. In the developing world, *E. coli, Klebsiella species*, and *S.aureus* are the most common pathogens of EOS, whereas *S.aureus*, *Streptococcus pneumonia*, and *Streptococcus pyogenes* are the most commonly reported organisms in LOS. According to the National Neonatal Perinatal Database of India, *Klebsiella pneumonia*, *Staphylococcus aureus*, and *E.coli* are the three most common organisms causing neonatal sepsis both in hospital and community.[3]

MATERIALS AND METHODS

This prospective, observational study was carried out at the department of Neonatology of Amrita Institute of Medical Sciences (AIMS), Kochi during September 2011 to April 2012. A total of 150 newborns admitted in the NICU with symptoms/signs of bacteremia/septicemia or developed sepsis during their stay in NICU were included in the study. AIMS is a 1200 bedded tertiary care, teaching and super-speciality referral hospital located in a huge campus at Ponekkara in Cochin. It is one of the top most hospitals in Kerala where even the poor have access to advanced medical care in an atmosphere of love and compassion. The hospital has a well functioning Neonatal Intensive Care Unit (NICU) which combines advanced technology and trained healthcare professionals to provide specialized care for the critically ill or premature neonates. The blood culture reports of all the babies suspected to have or develop sepsis at any time during hospitalization were observed to establish the diagnosis and also to find out the pathogen. The percentage of pathogens isolated from the blood cultures of in-born and out-born patients were also observed. The sensitivity and resistance pattern of various antibiotics against the isolated pathogens were noted and then the percentage of sensitivity and resistance was calculated.

RESULTS

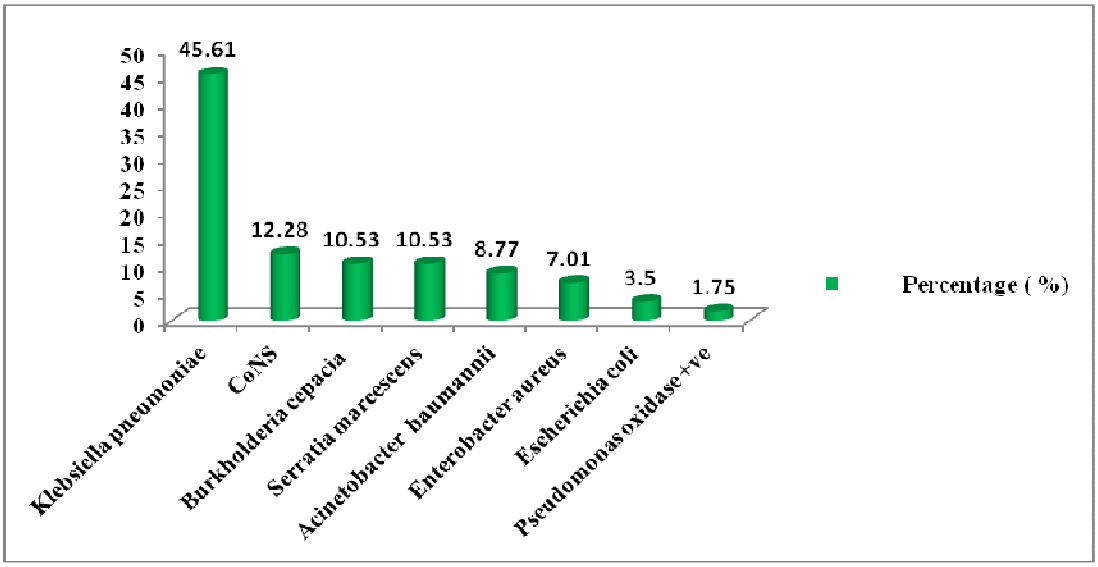
Out of 150 patients admitted, 86 patients were male and remaining 64 patients were female. The mean gestational age at birth was 35.55 ± 3.467 weeks (range = 24 – 40 weeks). Empirical antibiotic therapy was started in all neonates with risk factors or signs of suggestive sepsis before the results of blood culture susceptibility. 57 (38%) out of 150 patients admitted during the study period had proven sepsis confirmed by positive blood culture. Among the culture positive specimens, *Klebsiella pneumoniae* (45.61 %) was the most commonly isolated pathogen followed by *Coagulase Oxidase Negative Staphylococcus(CoNS)* (12.28%), *Burkholderia Cepacia* (10.53%), *Serratia Marcescens* (10.53%), *Acinetobacter Baumannii* (8.77%), *Enterobacter Aureus* (7.01%) and least for *Escherichia coli* (3.5%) and *Pseudomonas Oxidase positive* (1.75%). Gram negative organisms accounted for 87.72 % of all positive cultures. *Klebsiella pneumonia* and *CONS* were the commonly isolated gram negative and gram positive organism respectively. The percentage of

pathogens isolated from the blood cultures are illustrated in the Table 1 and Figure 1.

Table 1
Pathogens Isolated from the Blood Culture

Organisms Isolated	Number of Patients	Percentage (%)
Klebsiella pneumoniae	26	45.61
CoNS	7	12.28
Burkholderia cepacia	6	10.53
Serratia marcescens	6	10.53
Acinetobacter baumannii	5	8.77
Enterobacter aureus	4	7.01
Escherichia coli	2	3.50
Pseudomonas oxidase positive	1	1.75
Total	57	100

Figure 1
Pathogens Isolated from the Blood Culture

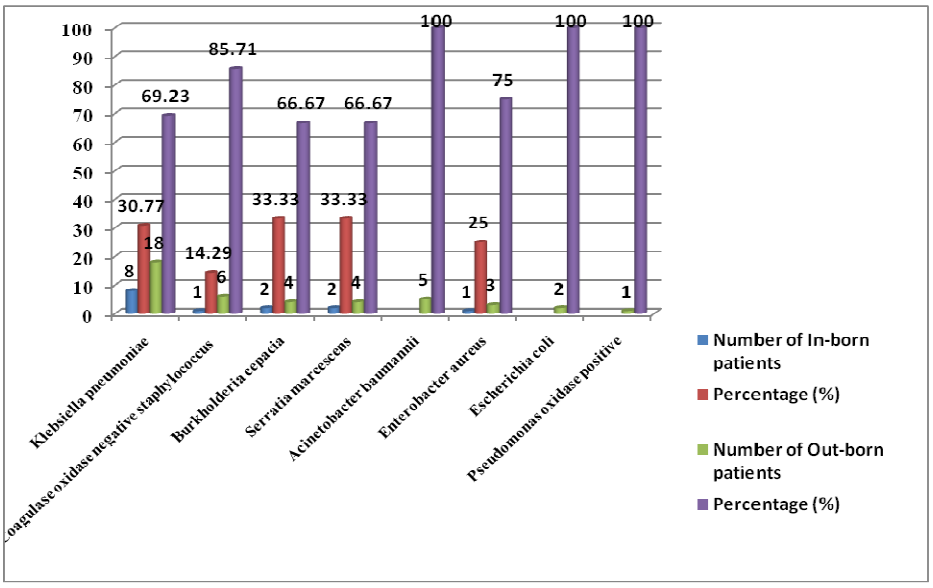


About 75.44% of the total pathogens are isolated from the out-born patients and remaining 24.56% are isolated from the in-born patients. The percentage of pathogens isolated from the blood cultures of in-born and out-born patients are depicted in Table 2 and Figure 2

Table 2
Pathogens Isolated from the Blood Cultures of In-Born and Out-Born Patients

Organisms Isolated	Total Number of Patients N=57	Number of In-born patients n = 14	Percentage (%)	Number of Out-born patients n =43	Percentage (%)
Klebsiella pneumoniae	26	8	30.77	18	69.23
Coagulase oxidase negative staphylococcus (CoNS)	7	1	14.29	6	85.71
Burkholderia cepacia	6	2	33.33	4	66.67
Serratia marcescens	6	2	33.33	4	66.67
Acinetobacter baumannii	5			5	100
Enterobacter aureus	4	1	25	3	75
Escherichia coli	2	-	-	2	100
Pseudomonas oxidase positive	1	-	-	1	100

Figure 2
Pathogens Isolated from the Blood Cultures of In-Born and Out-Born Patients



The results of antibiotic sensitivity and resistance pattern of various antibiotics for *Klebsiella pneumoniae*, commonly isolated gram negative organism is shown in Table 3

Table 3
Antibiotic sensitivity and resistance pattern of Klebsiella pneumoniae isolates

Antibiotic	*Klebsiella Pneumoniae*, n= 26		
	S/R	% Sensitivity	% Resistance
Amikacin	23/1	88.46	3.84
Amoxycillin-clavulanic acid	4/15	15.38	57.69
Ampicillin	1/20	3.84	76.92
Ampicillin- sulbactam	2/2	7.69	7.69
Cefazolin	7/14	26.92	53.84
Cefepime	0/1	-	3.84
Cefixime	0/1	-	3.84
Cefoperazone-sulbactam	20/3	76.92	11.54
Cefotaxime	8/11	30.77	42.30
Ceftazidime	6/16	23.07	61.54
Ceftriaxone	6/11	23.07	42.30
Cefuroxime	8/11	30.77	42.30
Ciprofloxacin	1/2	3.84	7.69
Colistin	3/1	11.54	3.84
Cotrimoxazole	11/14	42.30	53.85
Gentamicin	1/4	3.84	15.38
Imipenem-cilastatin	3/1	11.54	3.84
Levofloxacin	0/1	-	3.84
Meropenem	21/1	80.77	3.84
Ofloxacin	7/3	26.92	11.54
Pencillin G	1/0	3.84	-
Piperacillin-tazobactam	20/3	76.92	-
Tetracyclines	0/1	-	3.84
Ticarcillin-clavulanic acid	10/3	38.46	11.54
Tigecyclines	0/1	-	3.84
Tobramycin	14/2	53.85	7.69

The results of antibiotic sensitivity and resistance pattern of various antibiotics for *Coagulase oxidase negative staphylococcus(CONS),* commonly isolated gram positive organism was shown in Table 4

Table 4
Antibiotic sensitivity and resistance pattern of Coagulase oxidase negative staphylococcus(CONS) isolates

Antibiotic	*Coagulase oxidase negative staphylococcus*, n= 7		
	S/R	% Sensitivity	% Resistance
Amikacin	2/0	28.57	-
Cefotaxime	0/1	-	14.29
Cloxacillin/oxacillin	0/7	-	100
Cotrimoxazole	2/5	28.57	71.43
Levofloxacin	2/0	28.57	-
Linezolid	6/0	85.71	-
Ofloxacin	2/2	28.57	28.57
Pencillin G	0/7	-	100
Piperacillin-tazobactam	1/0	14.29	-
Vancomycin	7/0	100	-

DISCUSSION

Klebsiella pneumoniae (45.61 %) was the most commonly isolated pathogen followed by *Coagulase Oxidase Negative Staphylococcus* (12.28 %), *Burkholderia Cepacia* (10.53%), *Serratia Marcescens* (10.53%), *Acinetobacter Baumannii* (8.77%), *Enterobacter Aureus* (7.01%) and least for *Escherichia coli* (3.5%) and *Pseudomonas Oxidase positive* (1.75%). *Klebsiella pneumoniae* was the commonest gram negative organism isolated. This finding is consistent with the studies carried out by Dr. Kairavi.et al[4] et al, Anwer SK et al[5] and Mahmood A et al[6] where *Klebsiella pneumoniae* was the most commonly isolated micro-organism. As per the study by Movahedian AH et al[7] *Pseudomonas aeruginosa* (36%) was the most commonly isolated followed by *Coagulase Oxidase Negative Staphylococcus(CoNS)* (20.7%) and *Klebsiella pneumoniae.* According to the study by Shaw CK et al[8]*staphylococcus aureus* (42.75%) was the most common pathogen isolated followed by *Klebsiella pneumoniae* (18.32%) and *E.coli*(12.21%). Monsef A et al[9] reported that *E.coli* (66.7%) was the most commonly isolated pathogen followed by *Klebsiella pneumoniae(*10.5%). But in our study, *E.coli* constitutes only 3.5% of the total pathogens isolated. In our study, *CoNS* was the most commonly isolated gram positive organism. This finding is consistent with the study conducted by Movahedian AH et al[7]where *CoNS* was the most commonly isolated gram positive organism. The observation is in contrast with the study by Anwer SK et al[5] in which *enterococcus* was the most common gram positive organism isolated. As per the study carried out by Dr. Kairavi et al[4] and Shaw CK et al[8] *Staphylococcus aureus* was the commonly isolated gram positive organism followed by *CoNS.* As per the study carried out by Rao YK et al [10], the commonest organism isolated was *candida* species(22.3%).

38% of the patients admitted during the study were found to be culture positive. This observation in our study correlates with other studies carried out by Aurangazeb B et al[11], Shaw CK et al [8] and Monsef A et al[9] where positive cultures obtained were found to be 59.8%, 44.92% and 25.2% respectively. In our study, Gram negative organisms accounted for 87.71% of all positive cultures. According to the study done by Movahedian AH et al[7], gram negative organisms accounted for 72.1% of all positive cultures.

The percentage of pathogens isolated from the blood cultures of in-born and out-born patients are depicted in Table 2 and Figure 2. 75.44% of the total pathogens are isolated from the out-born patients and remaining 24.56% are isolated from the in-born patients. *Klebsiella pneumoniae,* commonly isolated gram negative organism was isolated from 8 (30.77%) and 18 (69.23%) of the cultures obtained from the in-born and out-born patients respectively. Whereas *CoNS,* commonly isolated gram positive organism was isolated from 1 (14.29%) and 6(85.71%) of the cultures obtained from the in-born and out-born patients respectively. But in a study conducted by Shaw CK et al [8] reported that *Klebsiella pneumoniae* isolated from 18.32% and 21.05% of the cultures obtained from in-born and out-born patients respectively while *CoNS* was seen in 4.39% and 9.09% of the same groups respectively.

Table 3 shows the sensitivity and resistance pattern of various antibiotics for *Klebsiella pneumoniae*. Amikacin (88.46%) was found to be more sensitive followed by meropenem (80.77%), cefoperazone-sulbactam (76.92%)and piperacillin-tazobactam (76.92%). Whereas resistance was more in Ampicillin (76.92%) followed by ceftazidime (61.54%), amoxicillin-clavulanic acid (57.69%), cotimoxazole (53.85%), cefazolin (53.84%) and ceftriaxone(42.3%), cefotaxime (42.3%) and cefuroxime (42.3%). The findings in our study is consistent with the study conducted by Movahedian AH et al[7] which reported that *Klebsiella pneumoniae* showed a high degree resistance to commonly used antibiotics (ampicillin) as well as third generation cephalosporins . The observations in our study correlates with the

study done by Mahmood A et al [6] who reported that resistance to gentamicin was as high as 90.4% for *Klebsiella pneumoniae* and also majority of the isolates were susceptible to meropenem and amikacin.

As per the study by Dr. Kairavi et al[4], maximum sensitivity was seen by cefoperazone-sulbactam (97%) and piperacillin-tazobactam (98%) for gram negative organisms. The observation in our study is similar to the study conducted by Anwer SK et al[5] who reported that the organisms were least sensitive to Ampicillin (< 20%) and highly sensitive to Amikacin (90 to 100%). According to the study by Aurangzeb et al [11], gram negative organisms showed high degree of resistance to commonly used antibiotics, ampicillin (79.3%), amoxicillin (74.6%), ceftazidime (71.6%), cefotaxime (55.2%) and comparatively low resistance to gentamicin (43.2%), tobramycin (34.3%), imipenem (23.6%), amikacin (22.3%), ofloxacin and ciprofloxacin (11.9%) respectively.

Table 4 shows the sensitivity and resistance pattern of various antibiotics for *CONS*. Vancomycin(100%) was found to be more sensitive followed by Linezolid (85.71%). Whereas resistance was more in cloxacillin/oxacillin (100%) followed by pencillin G (100%) and cotrimoxazole (71.43%). This findings in the study correlates with the study conducted by Dr. Kairavi et al[4] which showed maximum sensitivity with Vancomycin (100%) for gram positive organisms. Another study by Shaw C K et al[8] reported that the gram positive organisms displayed a high degree of resistance to most pencillins and cephalosporins but glycopeptides and monobactams were effective in most cases.

CONCLUSION

Our experience showed that gram-negative bacteria were the most prevalent cause of infections in neonates in our hospital. *Klebsiella pneumoniae* was the most commonly isolated gram negative organism whereas *CONS* was the most commonly isolated gram positive organism. Drug resistance to conventional antibiotics is a common problem and it grows readily. Antimicrobials must be administered conservatively according to epidemiologic studies in the region, with confirmed indications, and based on the results of susceptibility tests. Although positive blood culture is the gold standard in the diagnosis of neonatal sepsis, but in the absence of proof of sepsis many neonatologists felt obliged to continue antibiotics for a full of 10 day course. If the infant is not infected he or she is being subjected to unnecessary treatment. There is also danger of removing useful or susceptible organisms and encouraging resistant ones. If this occurs we shall reach a stage to go on to use more expensive antibiotics and also welcoming their adverse effects. Strict infection control in neonatal units, hand washing combined with judicious policy for antibiotic therapy are the main solution to this problem. It will be important, however, to continue surveillance of neonatal sepsis in order to follow closely changes in trends and risk factors, to obtain information for empiric antibiotic therapy and to react rapidly in case of major changes in susceptibility patterns and occurrence of outbreaks.

ACKNOWLEDGEMENTS

The authors would like to acknowledge Ms. Sabitha. M, principal of Amrita school of pharmacy, Dr. Sasidharan. P, HOD of Neonatology and all the staff members of the NICU, AIMS for their contribution and generous cooperation.

REFERENCES

1. Ghai OP , Gupta P , Paul VK .Ghai Essential Pediatrics, 6th Edn, New Delhi CBS publishers: 136-137, (2004)
2. Zaidi AKM. , Thaver D, Ali SA, Khan TA.Pathogens associated with sepsis in newborns and young infants in developing countries. Pediatric Infectious Disease Journal, 28: S10–S18, (2009)
3. Report of the National Neonatal Perinatal Database (National Neonatology Forum), 2002-2003.
4. Dr. Kairavi. Neonatal Septicemia: Bacterial Isolates & Their Antibiotics Susceptibility Patterns. NJIRM, 1:12-15, (2010)
5. Anwer SK. Neonatal Sepsis: An Etiological Study. J Pak Med Assoc. , 50:91-4, (2000)
6. Mahmood A. Neonatal Sepsis: High Antibiotic Resistance of the Bacterial Pathogens in a Neonatal Intensive Care Unit in Karachi. Journal of Pakistan Medical Association, 52: 348-50, (2002)
7. Movahedian AH. Bacterial Culture of Neonatal Sepsis. Iranian J Publ Health, 35: 84-89, (2006)
8. Shaw CK . Neonatal sepsis bacterial isolates and antibiotic susceptibility patterns at a NICU in a tertiary care hospital in western Nepal: a retrospective analysis. KUMJ.,5:153-60, (2007)
9. Monsef A. Antibiotic sensitivity pattern of common bacterial pathogens in NICU and neonatal ward in Hamedan province of Iran. Health, 2: 625-629, (2010).
10. Rao YK. Neonatal septicemia in north india due to extended spectrum Beta lactamase (esbl) producing gram negative bacteria. International Journal of Pharma and Bio Sciences.3:B 282-290, (2012)
11. Aurangzeb B. Neonatal sepsis in hospital-born babies: bacterial isolates and antibiotic susceptibility patterns. Journal of the college of physicians and surgeons, 13: 629-32, (2003).