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Pediatrics

Changing Pattern of Antibiotic Flora And Susceptibility to Antibiotics in Level-III NICU of Eastern India

Biswal Seba R[1], Mishra Shubhankar[2*], Behera Chinmay K[1], Panigrahi Sambedana[3]
[1]Asso. Prof: Dept. Of Pediatrics, Kalinga Institute of Medical Science, Bhubaneswar, Odisha, India
[2]Senior Resident, Dept. Of Pediatrics, Kalinga Institute of Medical Science, Bhubaneswar, Odisha, India
[3]Junior Resident, Dept. Of O & G, S.C.B Medical College, Cuttack, Odisha, India

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***Corresponding author**
Mishra Shubhankar

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Abstract: Neonatal sepsis is responsible for approximately 25% of the neonatal deaths in the world[1]. High rate of antibiotic resistance and abuse of antibiotics in several hospitals without standard protocol against commonest bacterial pathogen has further worsened the situation. The aim was to study the bacterial pathogens causing neonatal sepsis and their changing sensitivity pattern in due course of time. It was a prospective analysis in a tertiary level NICU of eastern india for one year duration. The neonates, who presented with signs and symptoms of septicaemia, were studied and a detailed record of several epidemiological and clinical parameters was noted. The cases with suspected sepsis were screened and included in the study group after diagnosis by blood culture. Sensitivity of the isolated organism was tested and compared with previous studies done in same geographical area to know resistance pattern to commonly used antibiotics. SPSS version 20 was used for statistical calculations. Total 54 patients were included in the study. Among them 68% were male and 32% were female. 42(77.7%) were having late onset sepsis and others were early. Clinical or radiological pneumonia were observed in 10 (18%) patients. Septicaemia was the diagnosis in 36 (66.6%) cases. Lethargy and poor feeding were the most common symptoms. High sensitive C Reactive Protein was raised qualitatively in all the cases. 30 patients had Gram negative, twenty four had Gram positive septicemia. Resistance to penicillins have decreased and increased for vancomycin. 95% Gram negative isolates were resistant to gentamycin, ampicillin and amikacin. There is an increasing trend of antibiotic resistance to the commonly used and available drugs. Continuous surveillance for antibiotic susceptibility with judicious practice of antibiotics should be done to look for resistance pattern.

Keywords: late onset septicemia, neonatal sepsis, resistance mechanisms, surveillance.

INTRODUCTION

Neonatal sepsis is one of the major causes of morbidity and mortality among the newborns in the developing countries like India. It is responsible for approximately 25% of the neonatal deaths in the world [1]. High rate of antibiotic resistance and abuse of antibiotics in several hospitals without standard protocol against commonest bacterial pathogen has further worsened the situation. Neonatal sepsis can be defined as "a clinical syndrome characterized by systemic signs and symptoms and bacteraemia during the first month of life". Bacterial pathogens vary geographically. Children infected within 72 hours of life are termed as early onset sepsis (EOS) where as more than 72 hours termed as late onset sepsis (LOS) [2]. Objective of this study was to identify the organisms in culture positive sepsis patients and find their sensitivity patterns followed by making comparisons with previous studies. Ethical approval was obtained from the ethical committee of Kalinga institute of medical science.

SUBJECTS AND METHODS

Our study was a prospective observational study undertaken in NICU of large tertiary care hospital of eastern India. The time period was from august 2015 to august 2016. All the cases diagnosed as culture positive sepsis through Bactec method were enlisted and taken into consideration. Our hospital posses high level well equipped NICU with experienced neonatologists. The neonates who presented with signs and symptoms of septicaemia, along with culture positive organism in blood were included in the study. The details of the baby were noted along with the antibiotic sensitivity pattern. The pattern of antibiotic resistance was compared to previous studies undertaken in this area in different time period.

RESULTS

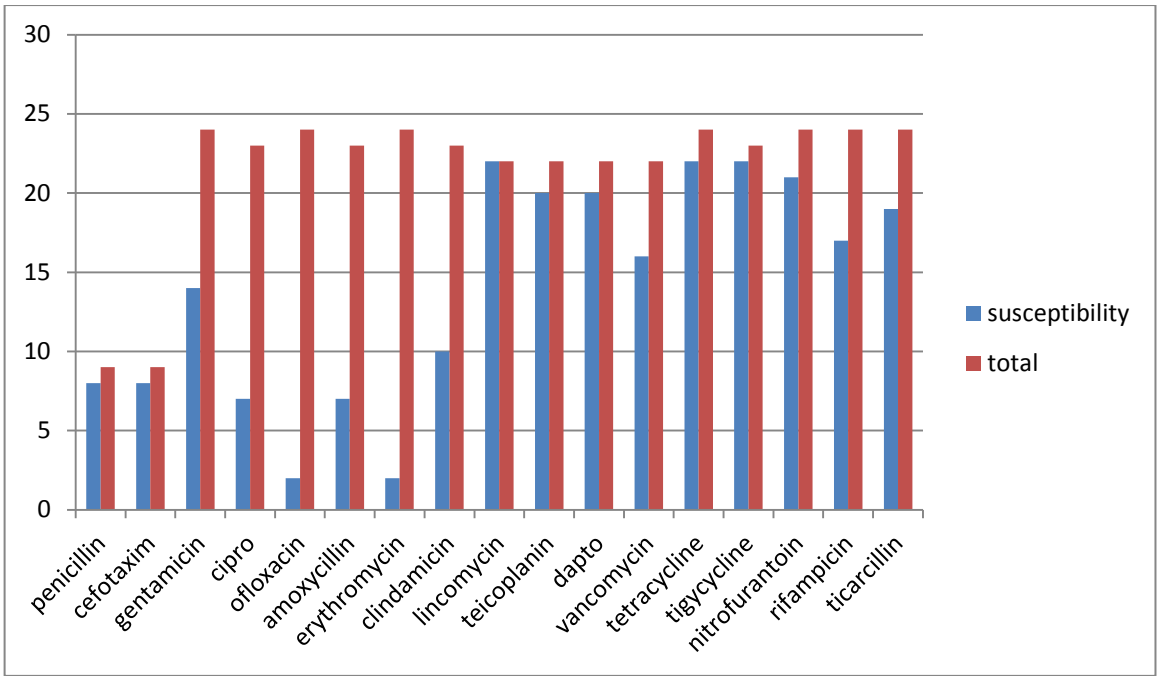
Culture positive sepsis patients were 54 in number. Among them 68% were male infants whereas 32% were female infants. 42(77.7%) were having late onset sepsis and others were early. The study group consisted of 76% out born patients and 24% inborn patients. Out of 12 inborn cases 8 mothers had 1 risk factor for sepsis, 2 mothers had 2 risk factors of sepsis and 2 mothers had 3 risk factors. 36 patients were preterm and 18 patients were term patients. 40 (74%) patients were small for gestational age.

Out of 54 patients clinical or radiological pneumonia was observed in 10 (18%) patients. Meningitis was diagnosed in 9 (16.6%) cases from CSF analysis. Septic arthritis and osteomyelitis was diagnosed in 2 (3.7%) cases. Septicaemia was the diagnosis in 36 (66.6%) cases. Lethargy and poor feeding were the most common symptoms. 89% of patients were having lethargy. High sensitive C Reactive Protein was raised qualitatively in all the cases. Other sepsis markers as well as radiological pictures and CSF analysis follow it.

Out of 54 culture positive organisms 24 were gram positive and 30 were gram negative. From gram positive coagulase negative staphyloccus are 11(45.8%). From gram negative cohort klebsiella was more common (40%) than others. The antibiotic sensitivity pattern is pictured (Table-1, 2 & Graph-1, 2). Several index studies, presenting different time and same geographic area were compared with our study in percentage resistance (Graph-3, 4).

Table-1: (Antibiotic sensitivity in gram positive no total sensitive/total tested)

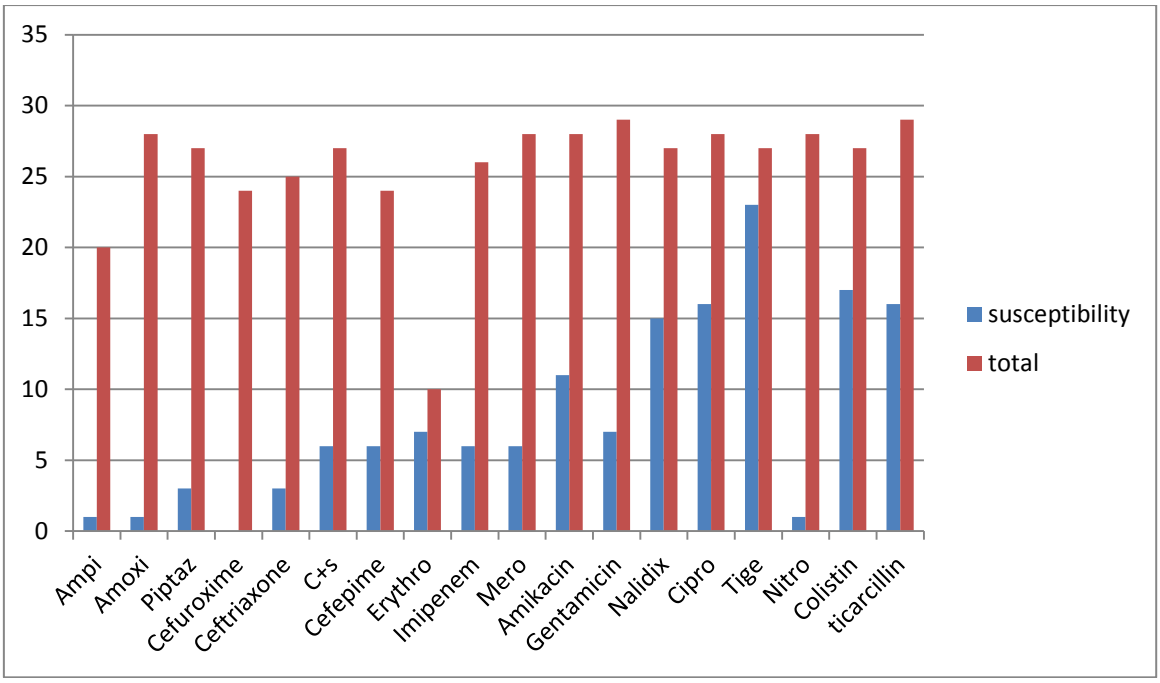
ANTIBIOTICS	CONS	STREPTOCOCCUS	S.AUREUS	GBS	TOTAL
Penicillin	2/2	4/5	1/1	1/1	8/9
cefotaxim	2/2	4/5	1/1	1/1	8/9
gentamicin	5/11	4/5	2/5	3/3	14/24
ciprofloxacin	1/10	2/5	1/5	3/3	7/23
ofloxacin	1/11	1/5	0/5	0/3	2/24
amoxycillin	1/10	2/5	1/5	3/3	7/23
erythromycin	1/11	1/5	0/5	0/3	2/24
clindamicin	4/10	2/5	1/5	3/3	10/23
lincomycin	9/9	5/5	5/5	3/3	22/22
teicoplanin	9/9	5/5	3/5	3/3	20/22
daptomycin	9/9	5/5	3/5	3/3	20/22
vancomycin	8/9	5/5	3/5	0/3	16/22
tetracycline	10/11	5/5	4/5	3/3	22/24
tigycycline	9/10	5/5	5/5	3/3	22/23
nitrofurantoin	11/11	5/5	5/5	0/3	21/24
rifampicin	8/11	4/5	2/5	3/3	17/24
Ticarcillin	9/11	5/5	2/5	3/3	19/24
total	11	5	5	3	24



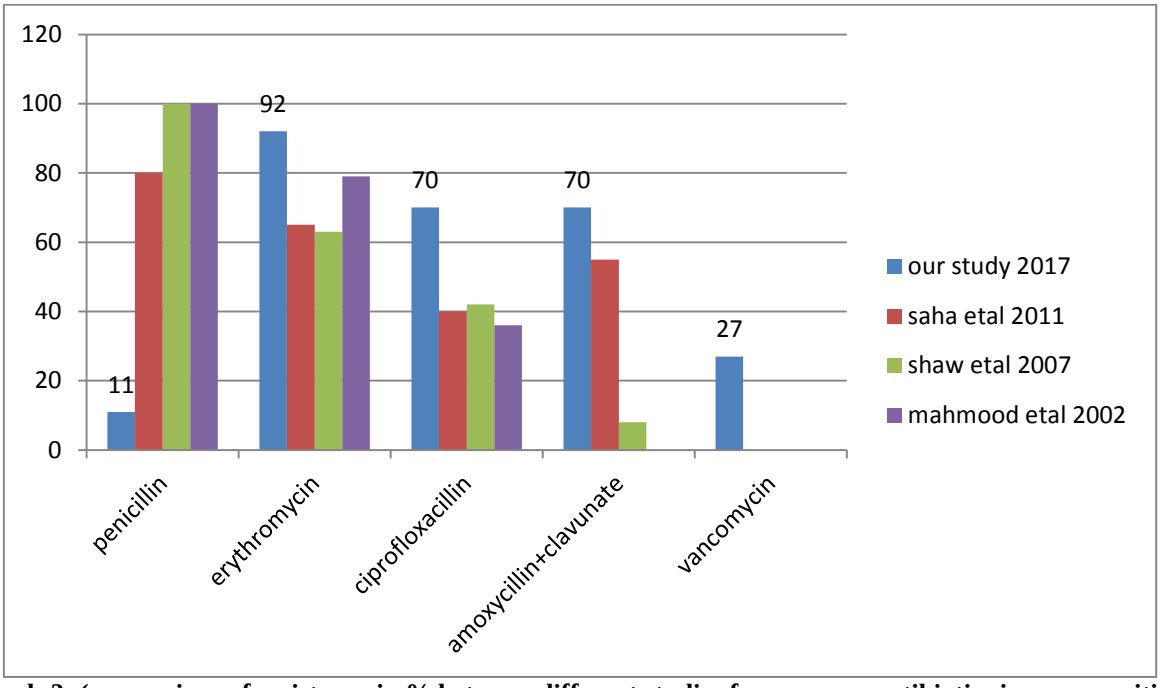
Graph-1: (Antibiotic sensitivity in gram positive)

Table-2: (Antibiotic sensitivity in gram negative no total sensitive/total tested)

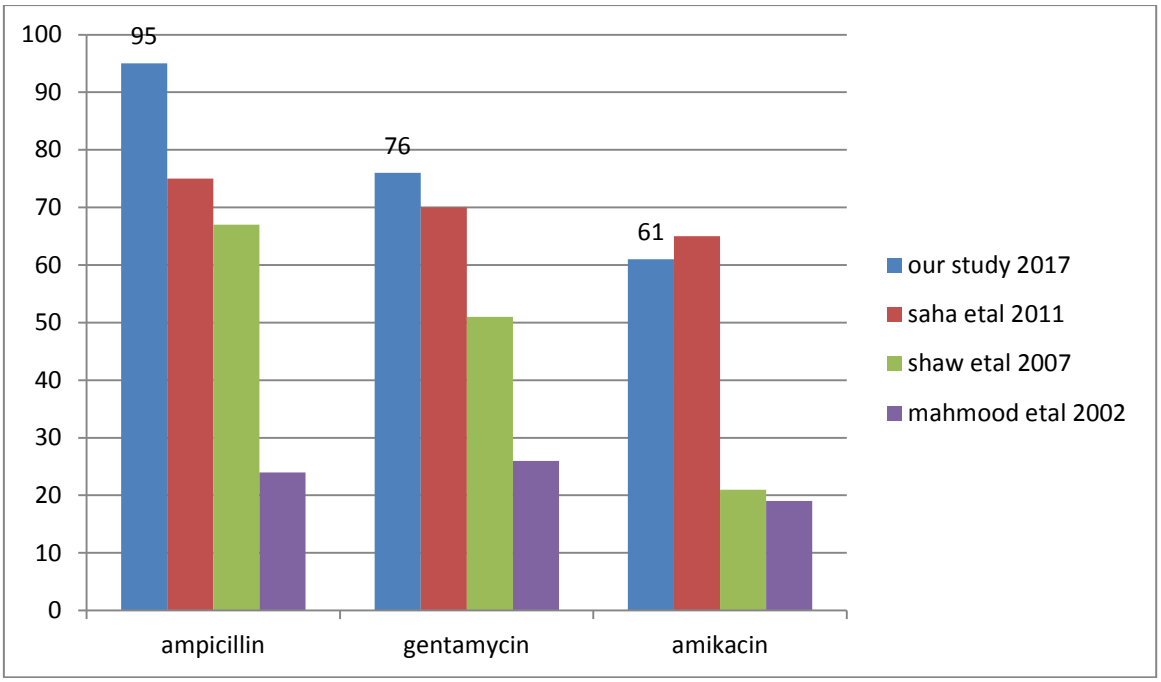
ANTIBIOTICS	klebsiella	enterobacter	bordatella	serratia	citobactor	pseudomonas	acinetobactor	total
Ampicillin	0/11	0/1	0/4	-----	--------	1/2	0/2	1/20
Amoxicillin	0/11	0/5	0/4	0/3	0/1	1/2	0/2	1/28
Piperacillin+tazobactam	0/12	0/6	0/3	0/1	1/1	1/2	1/2	3/27
Cefuroxime	0/11	0/4	0/4	0/3	0/1	0/1		0/24
Ceftriaxone	0/9	0/5	0/4	2/3	0/1	1/1	0/2	3/25
Ceftria+sulbactam	1/11	0/5	0/4	2/3	0/1	2/2	1/1	6/27
Cefepime	1/11	0/5	1/1	2/3	0/1	1/1	1/2	6/24
Erythro	4/4	0/1		2/3	1/2			7/10
Imipenem	4/12	0/5	0/4		0/1	1/2	1/2	6/26
Meropenem	3/12	0/5	0/4	2/3	0/1	1/1	0/2	6/28
Amikacin	5/12	2/5	0/4	2/3	0/1	1/1	1/2	11/28
Gentamicin	3/12	0/6	0/4	2/3	0/1	1/1	1/2	7/29
Nalidixic acid	4/11	5/5	0/4	3/3	1/1	1/1	1/2	15/27
Ciprofloxacin	5/11	6/6	0/4	3/3	0/1	1/1	1/2	16/28
Tigecycline	11/11	5/5	1/4	3/3	1/1	1/1	1/2	23/27
Nitrofurantoin	1/11	0/5	0/4	0/3	0/1	0/2	0/2	1/28
Colistin	11/11	2/5	0/4	0/3	1/1	1/1	2/2	17/27
Ticarcillin	5/12	2/6	3/4	2/3	1/1	1/1	2/2	16/29
TOTAL	12	6	4	3	1	2	2	30



Graph-2: (Antibiotic sensitivity in gram negative)



Graph-3: (comparison of resistance in % between different studies for common antibiotics in gram positive)



Graph-4: (comparison of resistance in % between different studies for common antibiotics in gram negative)

DISCUSSION

Sepsis is one of the important causes of neonatal morbidity and mortality in hospitalized newborns [3]. The causative organisms in neonatal sepsis vary from place to place [4, 5]. In Western countries, Group B Streptococci (GBS) is mainly responsible for neonatal sepsis where as in developing countries like india gram negative bacterias like klebsiella and escherechia are commonest [6, 7]. In this study, 55.5% organisms causing neonatal sepsis were gram negative and 44.4% gram positive. This is in agreement with the studies done by Shrestha *et al.*, [8] the most common pathogens isolated from the patients of neonatal sepsis were *Klebsiella pneumonia (22.2%).* In present study CONS are more common than other gram positive bacterias (20.3%). These epidemiologic data are coincident to previous studies [9, 10].

As antibiotic use is prevalent now a days the incident of neonatal sepsis has decreased. A preponderance of male infants is apparent in almost all studies of sepsis in newborns [5]. In our study also, culture positivity was more in male infants. In present study, late onset septicemia was observed in more cases, while it was 51.4% in Shaw Ck *et al.*, [3] study. Low birth weight [11] and prematurity were the common risk factors associated with neonatal sepsis. Our study also go hand in hand with this.

Present study showed high increase in antibiotic resistance as compared to other 3 studies [3, 10, 13]. In gm+ cases penicillin G resistance has decreased markedly. But resistance to all other common antibiotics like erythromycin, ciprofloxacin, amoxicillin has increased markedly with respect to other comparison groups by shah *et al.*, shaw *et al.*, and mehmood *et al.*, In their study not a single case of vancomycin resistance is met. But in our study 27% gm+ bacterias are resistance to vancomycin. This discordance can be explained by the emergence of vancomycin resistant staphylococcus aureus (VRSA). Negligence antibiotic use and environmental acquired resistance may be common cause of this [14]. Resistance to macrolides, fluroquinolones increasing whereas the less used antibiotics like tigycycline, tetracycline, daptomycine, lincomycin show good sensitivity. Resistance is also increasing in gram negative organisms. The resistance in gram negative cases are higher than the positive cases. Ampicillin resistance in 95% isolates. Increased resistance was also noticed against amikacin and gentamycin, which are commonly used for empirical therapy. According to our antibiogram of our hospital, higher generation ciprofloxacin, β-lactamase inhibitor combinations, carbapenems, tigycyclines, nalidixic acid, ticarcillin were effective against Gram-negative bugs. But resistance in previous studies are much less to conventional antibiotics [3, 10, 13]. The drug treatment given according to the protocol showed marked improvement in the outcome of patient. All cases in our study were positive for high senstive quantitative CRP (>1gm/dl). This shows hs C-reactive protein is a very good septic screen marker, other screening markers also should be looked for.

CONCLUSION

Blood culture is the gold standard in diagnosis and treatment of neonatal septicemia. Multiple antibiotic resistances among neonatal sepsis is a great headache for the clinicians now a days. Slow progress in development of newer drugs and rapidity in resistance development are major areas of concern.

Abundant use of precious antibiotics by doctors as well as common men who use medication without consulting physician rather consulting medicine storekeepers is the primary cause of rampant misuse. Paucity of abundant knowledge and specific guidelines for treatment of several infections make situation even worse. It is observed that some people demand antibiotics or stealthily use them for minor viral problems. Wise use of antibiotics should be done or there will be no drugs available in the future for treatment. There is a need of wide pan India studies on emerging resistance of antibiotics as well as very strict antibiotics policy. Each and every hospital must have its own local antibiogram mentioning empirical therapy options.

We conclude that higher generation cephalosporins with β-lactamase inhibitor combination is best for empirical treatment. Vancomycin should be added to cover Gram-positive ones. Reserve drugs should be kept for delay in improvement. Strict hand washing and isolation of sepsis patients will help decrease the emergence of nosocomial strains. Other possible strategies to reduce the load of neonatal sepsis like barrier nursing, promotion of clean deliveries, exclusive breast feeding, rationalization of admissions to and discharge from neonatal units should be adapted for fighting antibiotics resistances. Decrease in the CONS isolates can be done by proper skin treatment before collection of blood, reducing the duration of central and peripheral blood lines.

KEY MESSAGES

Antibiotics resistance is a big hazard for our society. Our study sends strong message that due to rampant injudicious use and epigenetic variations, a very large number of contemporary antibiotics are becoming resistant in course of time. This will trigger havoc in recent future as there are very less number of new antibiotics discovered now a day. Strict and judicious regulation of use of antibiotics is the very necessity for every clinician.

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