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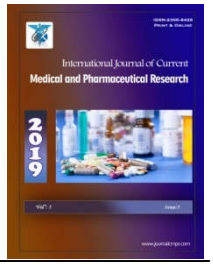

Research Article

# BACTERIAL ISOLATES OF NEONATAL SEPSIS AND ANTIBIOTIC RESISTANCE PATTERN IN A LEVEL III NEONATAL INTENSIVE CARE UNIT IN EASTERN INDIA: A 4 YEARS REPORT

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**ABSTRACT**

**Objectives:** This study was undertaken to investigate the distribution of etiological agents and antimicrobial resistance pattern among the blood culture-positive cases of neonatal sepsis admitted to a level III neonatal care unit in a teaching hospital Kolkata, Eastern India for the period of 4 years (2014 – 2017).

**Methods:** Blood culture was done for all babies admitted with clinical sepsis or with positive sepsis screen by automated BACTEC 9050 system. In positive cases, identification of organism was done followed by antimicrobial sensitivity testing by Kirby Bauer disc diffusion method using Clinical Laboratory Standard Institute Guidelines. Multi-drug resistance (MDR) was defined as presence of resistance to at least three of the five antibiotic groups in case of gram negative bacteria. Chi-squared test was performed to test association between different groups.

**Results:** Out of 4781 cases of clinical neonatal sepsis, 415 (8.68%) were culture positive. In 240 (69%) cases, the pathogens belonged to the family Enterobacteriaceae. Gram-positive cocci account for 38 (11%) cases of positive blood culture cases. Klebsiella is the foremost infectious agent with positive in 187(54%) of all bacterial isolates . Enterobacteriaceae positive babies had 90 (36.9%) death which is significantly higher than that associated with others. Klebsiella tops the list of MDR organisms with highest mortality.

**Conclusions:** Gram-negative pathogens and more specifically Klebsiella account for a substantial disease burden of neonatal sepsis in form of antibiotic resistance , multidrug resistance and mortality in a neonatal intensive care unit .



## INTRODUCTION

Neonatal sepsis remains the major cause of mortality and morbidity among neonates worldwide in spite of great advances in neonatal care. South Asia alone accounts for 3.5 million cases out of 6.9 million cases of neonatal sepsis per year. In India the incidence of neonatal sepsis is 30/1000 live births.[1,2] Considering the fact that 27 million birth every year in this country, which is one-fifth of global live births, India claims a huge burden of neonatal sepsis cases in the global scenario. More than one fourth of neonatal deaths occur in India and neonatal sepsis alone contributes to 19% of all neonatal deaths here is actually.[3] Lack of antenatal care, unhygienic and unsafe delivery practices, prematurity and low birth weight contribute to the high morbidity and mortality in neonatal sepsis.[4] Hence this topic really deserves paramount significance. Infections are routinely treated with antimicrobial agents, the effectiveness of which depends on the sensitivity of the causal organisms. But recently the rising resistance to the antimicrobial agents in developing countries including India is heralding an emerging medical crisis that needs urgent attention.[5] It is estimated that India has the highest neonatal mortality due to neonatal sepsis caused by bacteria resistant to first-line antibiotics. Approximately one fifth of neonates with sepsis die in the hospital and the mortality rise to 50% for those with culture-proven sepsis.[6] Overuse of multiple and broad spectrum antibiotics empirically without proper blood culture facility , ignorance on the prevailing flora and absence of adherence to strict antibiotic protocol in neonatal intensive care units have increased the incidence of antibiotic resistance and even multi drug resistance. In a recent multi-center Indian cohort study from North India, organisms showed a high degree of antimicrobial resistance to the high end antibiotics like extended-spectrum cephalosporins and carbapenems. [7] In a diverse country like India with high birth rate, periodic microbial isolates at neonatal intensive care unitsand their antimicrobial sensitivity may always differ not only in relation to different places and population, but also periodically in a single place. But in reality there is dearth of this surveillance data here in this country where majority of neonatal death due to sepsis occur. In this context this study was undertaken to investigate the distribution of etiological

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agents and antimicrobial susceptibility patterns among the blood culture-positive cases of neonatal sepsis from a level III neonatology unit of a large tertiary-care teaching hospital in Kolkata, Eastern India, over a period of 4 years with a view to gather valuable information regarding rising anti-microbial resistance (AMR) pattern among causative organisms of neonatal sepsis in eastern India. This will help to formulate an antibiotic stewardship programme with proper knowledge of prevailing bacterial flora which can be the only answer to this emerging problem of antimicrobial resistance even in newborn.

## MATERIALS AND METHODS

It was a retrospective study of analysis of all blood cultures positive sepsis cases obtained from neonates admitted to the level III Neonatal intensive care unit of a tertiary care teaching hospital in Kolkata , eastern India , over a period of 4 years , from July 2014 to .December 2017. This level III Neonatal Intensive care unit ( NICU) was a referral unit with high admission rate of 1600-1800 babies annually including both intramural and extramural babies . All the newborn who were admitted to the said neonatal unit during the study period and got treatment for sepsis were included in the study . Babies with lethal congenital anomalies and malformations, diagnosed cases of inborn errors of metabolism and babies with surgical emergencies were excluded as per the study protocol.

Informed consent was obtained from both the parents or the legal guardians when each baby was enrolled with the diagnosis of clinical sepsis. Blood culture was performed for all neonates with suspected clinical sepsis. Clinical sepsis was suspected when the baby presented with a set of clinical signs as per the Young Infant Study Algorithm.[6]Alternatively clinical sepsis was also suspected even in absence of clinical symptoms but in the presence of perinatal risk factors with positive sepsis screen .A positive septic screen again was defined as the presence of two of the five parameters: total leucocytic count <5,000/cmm, immature neutrophil to total neutrophil (I/T) ratio >0.2, absolute neutrophil count <1,800/cmm or as per Manroe chart for term and Mouzinho's chart for very low birth weight babies ,micro ESR >15 mm 1st h, C-reactive protein(>1mg/dL). The opinion of two independent clinicians was taken for confirming the case as clinical sepsis by the clinical symptoms suggestive of sepsis or the sepsis screen being positive in case of presence of risk factors only. Clinical sepsis with perinatal risk factors and positive sepsis screen was relevant for only early onset sepsis , i.e occurrence of sepsis at or before 72 hours of life. Clinical sepsis defined by presence of clinical symptoms was relevant for both early and late onset sepsis i.e occurrence of sepsis after 72 hours of life .Isolation of a recognised pathogen from blood, in cases of neonatal clinical sepsis on the basis of clinical features or perinatal risk factors, along with treatment with appropriate type and duration of antibiotic therapy was known as blood culture positive sepsis.

The study unit was following an antibiotic policy which was being periodically reviewed as per the guideline of the unit infection -control team comprising of one microbiologist , one neonatologist and one nurse practitioner. During the study period, according to the protocol, antibiotics was used initially empirically in case of clinical sepsis. For empirical use, the first line of antibiotics used was Inj piperacillin-tazobactam and aminoglycoside combination, the second line of antibiotics being a combination of fluoroquinolone - aminoglycoside and the third line being carbapenem for management of clinical sepsis in the unit. The choice of antibiotics and its escalation in case of clinical deterioration was decided by the consultant doctor on call . After the start of antibiotics future course was decided by the availability of blood culture results and clinical course. However if the blood culture was positive, the antibiotics was chosen as per the sensitivity pattern. The researchers regularly recorded details of the antibiotics administered and the clinical course of the baby namely the survival or mortality and bacteriological report of the blood culture .

***Microbiological Methods:*** 1ml blood for culture was drawn from a peripheral vein and Automated BACTEC 9050 system using Peds Plus Vial was used for blood culture. After the blood culture was found positive, Gram stain was performed and subculture was done on appropriate media based on the Gram stain, like Mac Conkey agar and 5% sheep blood agar (Biomerieux, la balme les Grottes, France) for Gram negative and positive organisms respectively. Bottles were incubated in the system for upto 7 days, at the end of which all the negative bottles were sub cultured once on blood agar before discarding. Identification was done by conventional methods and confirmed by mini API analyzer using ID32E kit for Enterobacteriaceae, ID32GN for non fermenters, ID32 Staph and Rapid ID32 Strep for Gram positive organisms (BioMérieux, Marcy l'Etoile, France). Antimicrobial susceptibility testing was done by Kirby Bauer disc diffusion method and selection of antibiotics for susceptibility testing for each isolated bacteria was done using Clinical and Laboratory Standard Institute (CLSI) guidelines[8]for interpretation as resistant (R), intermediate sensitive (IS) and sensitive (S). In Kirby-Bauer method, small discs containing different antibiotics or impregnated paper discs, were dropped in different zones of the cultureplate ,resulting in zones of bacterial lysis according to the susceptibility. The diameter of the lysis zone in millimeter for each antibiotic disc has been converted to Minimum Inhibitory Concentration (MIC) in µg/ml, based on known linear regression curves. Resistance to a group of antibiotic was defined as non-susceptibility ("R" or "IS" report on disc-diffusion test).

Multi-Drug Resistance Further the gram-negative pathogens were classified based on their resistance to various antibiotic classes. Multi-drug resistance was calculated based on the method adapted from Sievert *et al* due to theabsence of universally accepted criteria.[9] Multidrug resistance was defined for as resistance to any three of five antibiotic classes like Aminoglycoside (Gentamicin, Amikacin, Netilmicin), carbapenem (Imipenem, Meropenem), extended-spectrum cephalosporins (Cefotaxime, Ceftriaxone, Ceftazidime), fluoroquinolones (Ciprofloxacin, Levofloxacin, Ofloxacin), piperacillin (Piperacillin, Piperacillin-Tazobactam).

***Statistical Analysis:*** For statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS 20.0.1 and Graph Pad Prism version .Chi-squared test was performed to test association between mortality with incidence of antibiotic resistance .P-value $\leq$ 0.05 was considered for statistically significant.

## RESULTS

During the study period, 4781 babies with clinical sepsis were treated and blood culture was drawn for them. Positive blood culture was found in 415(8.68%) cases and of which 348 cases (7.21%) were found to be bacterial sepsis. Blood culture for fungal sepsis was positive for 7 cases. The fungal sepsis cases were not considered further in this study.

There was dominance of gram-negative bacteria causing neonatal sepsis in infants in this center. The number of various isolates along with frequency , incidence of death among culture positive cases were depicted in table 1. More than two third of the pathogens belonged to the family Enterobacteriaceae (*Klebsiella spp, Escherichiacoli, Enterobacter spp* and *Serratia spp*) accounting for 241 (69.2%) cases of all bacterial infections. Gram-positive cocci account for only 38 cases , i.e. , 11 % of the total bacterial infections. *Klebsiella* spp was the foremost infectious agent with 187 (53.7%) of the total culture positive bacterial infections followed by *E. coli spp* in 48 (13.7%), *Acinetobacter spp* in 40 (11.5%) and *Pseudomonas spp* in 29 (8.3 %) cases. Apart from bacterial pathogens, 67 cases were observed to be infected with *Candida* (data not shown).

**Table 1** Bacterial pathogens of neonatal sepsis and associated mortality

| Organism | No. of cases[a] ,n=348 | Death (case fatality rate )[a] |
|---|---|---|
| Klebsiella spp | 187 (53.7%) | 72 (38%) |
| Escherichia .coli | 48 (13.7%) | 17 (35.4%) |
| Serratia spp. | 05(1.4%) | 01(20%) |
| Enterobacter spp. | 01(0.2%) | 00(0) |
| Acinetobacter spp. | 40 (11.5%) | 11 (27.5%) |
| Pseudomonas spp. | 29 (8.3%) | 08 (27.5%) |
| Staphylococcus spp. | 34 (9.7%) | 03 (8.8 %) |
| Enterococcus spp. | 04 (1.1%) | 01 (25%) |

[a]:expressed as number ( %)

In this study total 113 babies died among 348 blood culture positive cases, the case fatality rate being 32.4%.Enterobacteriaceae group alone accounted for total 90(79.6%) death . *Klebsiella* spp predominated the neonatal sepsis infections and caused highest number of deaths , as high as 72 (63.7%) followed by17(15.0%) death by *E.coli*. *Acinetobacter* accounted for 11(9.7%) deaths while for 08(7.07%) deaths *Pseudomonas* was the causal organism. Gram positive pathogens (*Staphylococcus aureus* and *Enterococcus* sp.) were responsible for only 4(3.5%) of total deaths. *Candida* was accounted for 15 casesthough are not included in our study.Case fatality rate of sepsis due to different organisms has been also depicted in table 1 which showed *Klebsiella* spp and *Escherichia coli* sepsis carried almost equal high case fatality rate of 35-39% followed by *Acinetobacter* spp and *Pseudomonas* spp ( 27.5% each ). The case fatality rate of staphylococcus spp was as low as 8% where Enterococcus had higher case fatality rate of 25%.

The antibiotic resistance pattern of gram positive organisms like *Staphylococcus spp* and *Enterococcus* spp has been shown in table 2 where as the resistance pattern of various gram negative organisms like *Klebsiella spp , Escherichia coli , Serratia spp , Enterobacter spp , Pseudomonas spp* and *Acinetobacter spp* has been depicted in table 3 . Gram-positive cocci exhibited 100% sensitivity to amikacin, netilmicin, vancomycin and linezolid. But more than 90% of these organisms were resistant to ampicillin and approximately 80% of them were resistant to fluoroquinolones. A quarter of them were resistant to carbapenems and more than 65% were resistant to cephalosporin.

Gram negative organisms as a whole were found resistant to ampicillin in 82.9% of cases , cefotaxime in 55% of cases , piperacillin-tazobactum to 42% of cases, aminoglycosides to 39-42 % of cases and fluoroquinolones excepting ofloxacin to 45 % of cases. Gram negative organisms showed less resistance and better susceptibility pattern for ofloxacin (27.8%), carbapenems (20-21%) , colistin (1.9%) and cefoxitin (1.3%)

**Table 2** Antimicrobial resistance in Gram positive organisms

| Antimicrobials | Isolates tested (n) | Isolates resistant (n) | Resistance ( %) |
|---|---|---|---|
| Ampicillin | 32 | 30 | 94 |
| Penicillin G | 33 | 33 | 100 |
| Amoxyclav | 35 | 16 | 47 |
| Ampicillin.Sulbactam | 25 | 18 | 72 |
| Imipenem | 34 | 7 | 21 |
| Meropenem | 34 | 9 | 26 |
| Co.trimoxazole | 30 | 20 | 67 |
| Cefoxitin | 33 | 22 | 67 |
| Cefotaxime | 33 | 20 | 60 |
| Gentamicin | 36 | 4 | 12 |
| Amikacin | 36 | 0 | 00 |
| Netilmicin | 36 | 0 | 0 |
| Ciprofloxacin | 36 | 26 | 72 |
| Levofloxacin | 36 | 29 | 80 |
| Ofloxacin | 36 | 21 | 58 |
| Erythromycin | 33 | 26 | 79 |
| Vancomycin | 35 | 0 | 0 |
| Teicoplanin | 31 | 1 | 32 |
| linezolid | 33 | 00 | 0 |

**Table 3** Antimicrobial resistance in Gram negative organisms

| Antimicrobials | Isolates tested (n) | Isolates resistant (n) | Resistance (%) |
|---|---|---|---|
| Ampicillin | 305 | 253 | 82.9 |
| Amoxyclav | 308 | 236 | 76.8 |
| Ampicillin.Sulbactam | 307 | 98 | 31.9 |
| Piperacillin-tazobactum | 306 | 130 | 42.3 |
| Imipenem | 307 | 65 | 21.1 |
| Meropenem | 307 | 62 | 20.1 |
| Co.trimoxazole | 309 | 146 | 47.2 |
| Colistin | 307 | 6 | 1.9 |
| Cefoxitin | 307 | 4 | 1.3 |
| Cefotaxime | 307 | 171 | 55.7 |
| Gentamicin | 307 | 137 | 44.6 |
| Amikacin | 307 | 120 | 39.1 |
| Netilmicin | 307 | 125 | 40.7 |
| Ciprofloxacin | 305 | 139 | 45.5 |
| Levofloxacin | 305 | 135 | 44.2 |
| Ofloxacin | 305 | 85 | 27.8 |
| Erythromycin | 307 | 01 | 0.3 |
| Vancomycin | 307 | 01 | 0.3 |
| Teicoplanin | 307 | 01 | 0.3 |
| linezolid | 307 | 14 | 4.5 |

The study has also noted the presence of multidrug resistance in case of gram negative organism. *Klebsiellaspp* topped the list of MDR organisms with 88 cases followed by *Acinetobacter spp with* 20 cases, *Escherichia coli* with 14 cases and *Pseudomonas spp* with 7 cases(Table 4).We have also observed more death in case of MDR organisms .Fifty babies died among 129 babies who were positive for MDR gram negative bacteria with and the case fatality rate was 38.7% . In comparison,58 babies died among175 babies positive for non MDR gram negative bacteria case fatality rate being 33.1%. Though not statistically significant, we have found this increasing trend of mortality among MDR positive organisms. ( p=0.31).We have found the case fatality has been

increased in the MDR group in comparison to the overall case fatalityin case of *Acinetobacter spp* and *Pseudomonas spp* (Table 1 and table 4) . The incidence of MDR was highest in *Acinetobacter spp* ( 50%) followed by *Klebsiella spp* ( 47%), *Escherichia coli* (29%) and *Pseudomonas spp* ( 24%). Overall 129 isolates showed MDR among 304 gram negative culture positive cases, the incidence being 42.4%.

**Table 4** Association of MDR organism with mortality

| MDR Organism | MDR (n,%) | Death | Case fatality rate |
|---|---|---|---|
| Klebsiella spp | 88(68.2% | 33 | 37.5 % |
| Escherichia coli | 14 (10.8%) | 06 | 42.8 % |
| Serratia spp | 00 (0) | 00 | 0 |
| Acinetobacter spp | 20 (15.5%) | 08 | 40% |
| Enterobacter spp | 00 (0) | 00 | 0 |
| Pseudomonas spp | 07(5.4%) | 03 | 42.8 % |
| Total | 129 | 50 | 38.7% |

MDR: multi drug resistance

## DISCUSSION

The spectrum of microbial etiology of neonatal sepsis varies from region to region , varies in different hospitals of the same region. [2]The comparative analysis of bacterial isolates reported from different parts the country has been depicted in Table 5.[7,10-18]While studies from Chennai and Rajasthan.[12,13] reported pre-dominance of *Klebsiella spp*as the causal organism as also found in the present study, studies from Delhi.[7] reported *Acinetobacter spp*. Interestingly, reports from Punjab, Himachal Pradesh and Karnataka.[11,14,15] showed *Staphylococcus aureus* as the main pathogen which is less common in our study. Our analysis revealed members of Enterobacteriaceae as the most prevalent group of organisms with *Klebsiella spp* as the lead causal organism. Systematic analysis by Le Doare and colleagues included results from eleven neonatal units: three in Africa, one in the Middle East, one in South East Asia, and six in Asia.[19] In all areas, *Klebsiella spp* was the predominant pathogen, accounting for 49.8% of allgram negative bacilli, followed by other Enterobacteriaceae which corroborates our finding.

Two earlier reports from the same unit during 2007 to 2014 had shown *Acinetobacter spp* as the most common causal organism .[4,18] The authors found that Non-fermenting gram-negative bacteria (NFGNB) dominated the neonatal sepsis infections including certain rare organisms . In present study, *Acinetobacter spp* (12%) has been outnumbered by *Klebsiella spp* and *Escherichia Coli* which account for 67% of all bacterial infections. Both *Acinetobacter spp* and *Pseudomonas spp* (NFGNB) have been found associated with 20% of the bacterial neonatal sepsis cases in the present study as compared to 23.6% as reported by Vishwanathan *et al*. in 2014.[18]. One organism or group of organisms may be replaced over a period of time in critical areas like neonatal intensive care units ( NICU) which has been also reflected in previous studies like by Roy *et al*. [2]That is why on going surveillance and review of antibiotic policy is required for prevention of emergence of antimicrobial resistance.

According to our study mortality associated with Enterobacteriaceae is significantly higher than the same associated with other groups (Table 1).Within this group, *Klebsiella spp* was found to be most lethal causing death in about 38 % cases infected with it. (Table 1). *Klebsiella spp* is closely followed by *Escherchia coli* in terms of lethality with 35.4% mortality rate (Table 1), though it is placed lower in MDR list. This is consistent with earlier observations and this mortality has been attributed to K1 capsular antigen present is some strains.[18] K1 antigen is a polysialic acid that impairs opsonophagocytic killing. They report that babies infected with K1 antigenic strains have increased morbidity and mortality compared to babies infected with other strains. Other virulence factors linked to neonatal sepsis include complement resistance mediated by O-lipopolysaccharide and a group of surface proteins which aid in binding and invasion of brain endothelium.[20]

We have found some differences in commonest isolates in NICU (Table 5) which may be attributable to variation of microbial spectrum from region to region and in different hospitals of the same region and often one organism or group of organisms may be replaced by others over a period of time. In absence of strict antibiotic policy for neonatal sepsis, use of different antibiotics at different centers may give rise to emergence of separate resistant flora at various centers.

Significantly, *Klebsiella spp* has shown pre-ponderance in multidrug resistance in this study (Table 4 ) followed by *Acinetobacter spp* and *Pseudomonas spp*. The rise of MDR Gram-negative bacteria (GNB) is of greatest concern in the neonatal population and with very limited therapeutic options.[19]A positive correlation between MDR and mortality was observed. Antimicrobial resistance among the Enterobacteriaceae represents a major problem in both healthcare-associated and community-acquired neonatal infections.[21]

The antimicrobial resistance pattern of gram positive organisms has clearly indicated that Ampicillin being resistance in 90 % of cases , could never be recommended as first line empirical antibiotic. Aminoglycosides rather would be better choice with resistance rate of 0-12 % . Gram positive organisms exhibited better sensitivity to vancomycin and linezolid (100%) and can be used selectively when definitive organism is detected . Our study result corroborated the finding of the previous studies like by Marwah *et al*, who reported 100% sensitivity to vancomycin and linezolid in S. aureus strains from a tertiary care centre in Northern India.[15]

For gram negative organism ,colistin was found to have least resistance (0%) followed by carbapenems ( 20%) and ofloxacin ( 27%)among all fluoroquinolones. Indiscriminate use of these reserve drug has to be avoided. Third generation cephalosporin like cefotaxime has also been ineffective with documented resistance in 55 % of cases. Hence piperacillin-tazobactam or aminoglycoside which showed resistance in and around 40 % of cases, can be used empirically as initial antibiotics. The observation was quite similar to a few reports published from North India .[10,11,15] However after blood culture report is available the target should be to shift to monotherapy with narrowest spectrum sensitive antibiotic. India being the world's largest consumer of antibiotics for human health in 2010 at 12.9 x 109 units (10.7 units per person), irrational overuse of antibiotics is always a possibility which has driven the problem of antibiotic resistance .[22]

In India presently the sick newborn care is going through the phase of rapid expansion with introduction of a number of sick newborn care units , but rapid blood culture facility is still beyond the reach of most of the units. In absence of proper detection of organisms and documentation of susceptibility by rapid blood culture method at neonatal care units, the misuse of antibiotics and even the reserve drugs like carbapenems and

colistin is creating the upsurge of deadlier MDR pathogens. Hence blood culture facility should be availed to the all neonatal units especially at the peripheral units to curb undue reliance on unyielding parameter like C-reactive protein to escalate and continue antibiotics at situation while actually they are not warranted.

We have not isolated the culture positive cases into early or late onset sepsis , because the earlier data has already shown there is not much differences in the isolates specially in the Indian scenario.[3,7,18]

infection control policy to effectively curtail spread of these resistant organisms. Early bacterial detection by rapid and automated blood culture techniques at NICU can speed-up the diagnosis and facilitate targeted therapy to decrease the burden of antimicrobial resistance.

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**Table 5** Bacterial isolates of neonatal sepsis reported from various clinical centres of India

| Period | State | Culture positive cases | Commonest isolate | Other isolates | Antibiotic susceptibility | Reference |
|---|---|---|---|---|---|---|
| 2010-2013 | Haryana | 336 | Pseudomonas | E.coli Staphlyococcus aureus | Gram negative bacteria were sensitive to piperacillin tazobactam and carbapenems. Gram+ve organisms were most sensitive to linezolid and vancomycin. | (10) |
| 2012-2013 | Himachal Pradesh | 188 | Staphylococcus aureus | CONS Klebsiella pneumonie | Gram –ve showed high resistance to 3rd gen. cephalosporins and aminoglycosides. | (11) |
| 2013-2014 | Delhi | 1047 | CONS | Acinetobacter, Staphylococcus aureus, Klebsiella pneumonie | Acinetobacter exhibited more than90% resistance to 3rd gen cephalosporins. Approximately 50% were MRSA and 22% of entrococcus were vancomycin resistant. | (2) |
| 2010-2011 | Tamil Nadu | 110 | Klebsiella pneumonie | Staphylococcus aureus | 56% of MRSA with all sensitive of vancomycin.ESBL was found in 70.9% of Klebsiella and 57.1% of E.coli | 12) |
| 2014 | Rajasthan | 239 | Klebsiella pneumonie | Enterococcus, Streptococcus faecalis | 22% Kebsiella were reisistant to al antibiotics tested. | (13) |
| 2012-2014 | Karnataka | 180 | Staphlyococcus aureus | CONS Klebsiella , Enterococcus, Pseudomonas | Gram +ve organisms were sensitive to vancomycin(97%),linezolid(91%) and least sensitive to ampicillin(31.5%). | (14) |
| 2011-2014 | Delhi | 840 | Acinetobacter | Klebsiella, E.coli | High rates of MDR in acinetobacter (82%),klebsiella(54%),E.coli(38%). MRSA in 38% | (7) |
| 2008-2012 | Punjab | 167 | Staphylococcus aureus | Klebsiella, Acinetobacter | High resistance observed in staph isolates to oxacillin(51%) but sensitive to aminoglycosides(86%),vancomycin & Linezolid(100%) | (15) |
| 2014-2016 | Kerela | 126 | Staphylococcus aureus, | Klebsiella, Pseudomonas | Not studied | (16) |
| 2015 | Karnataka | 197 | Klebsiella | CONS, Staphylococcus aureus, | MRSA incidence was 71.43% & ESBL 96.05% incidence. | (17) |
| 2007-2010 | West Bengal | 186 | Acinetobacter | Burkholderia | Most common MDR phenotype (approx 60 %) was resistant | (18) |
| 2014-2017 | West Bengal Kolkata | 348 | Klebsiella | E.coli, Acinetobacter | Ampicillin shows resistance in almost 93% organisms,while carbapenems in approx 20 %.colistin showed least resistance. | This Study |

MDR: multi drug resistance, CONS: coagulase negative staphylococcus, ESBL: extended spectrum b-lactamase, MRSA: methicillin resistance staphylococcus aureus

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## CONCLUSION

We conclude by saying that gram negative pathogens belonging to Enterobacteriaceae were more prevalent and more lethal with more MDR organisms compared to others in neonatal sepsis and MDR were associated with more neonatal deaths than susceptible ones. Finally it is to be noted that despite recent advances in health care, morbidity and mortality due to neonatal sepsis and increasing trend in MDR organisms remains a major cause of concern in neonates. There is need for strict adherence to hand hygiene practices, periodic surveillance of pathogens, and a need to implementantibiotic stewardship programme in neonatal care units under definite

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