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Research Article

DISCRIMINATE USE OF CARBAPENEMS AND POLYMYXINS: SALVAGER OF LIFE IN FIRST FEW DAYS

Manali H. Shah* and Summaiya A. Mullan

Department of Microbiology, Government Medical College, Surat

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ABSTRACT

Neonatal septicemia is one of the most important cause of morbidity and mortality of neonates. Gram negative bacilli are one of the most important cause of neonatal septicemia being Klebsiella species the most common. Reports of multi resistant bacteria causing neonatal sepsis in developing countries are increasing. So this study will show predominant organisms causing septicemia and their antibiotic susceptibility testing. It was a retrospective study conducted in tertiary care hospital of India for period of 6 months. Samples sent by clinicians to the laboratory were included in the study. Blood culture samples were processed as per standard guidelines and organisms were identified using different biotyping methods. Antibiotic susceptibility was studied by Kirby-bauer disc diffusion method according to CLSI guidelines 2016. 60 isolates were obtained from 131 neonatal blood culture samples. Amongst them, half of isolates were Klebsiella pneumoniae accounting for the most common organism isolated. On antibiotic susceptibility testing, most of gram negative bacilli isolates showed multi drug resistance with complete sensitivity only to Polymyxins. The study emphasize upsurging resistance and importance of judicial use of Polymyxins and Carbapenems.

INTRODUCTION

Septicemia is a life threatening condition in which there is bacterial blood stream infection with presence of fever. Neonatal septicemia is one of the most important cause of morbidity and mortality of neonates.

Neonatal septicemia is divided into early onset (≤7 days of life) and late onset (>7 days of life) septicemia. Early onset septicemia leads to more complications and deaths. Gram negative bacilli are one of the most important cause of neonatal septicemia being Klebsiella species the most common.

Klebsiella pneumoniae is known for causing severe community as well as nosocomial infections. Multi drug resistance in bacilli is a burning issue nowadays. Mechanism of this resistance can be various like through transposon, plasmid mediated or genetic. (Khajuria *et al 2014*)

Multi drug resistance to an organism can be defined as resistance to at least three different group of drugs. Carbapenems used to be drug of choice in multi drug resistance. But recently resistance to these novel drugs have also been rapidly increasing, that may be due to inappropriate and broad spectrum use of them (Ali *et al 2012*).

So conditions have arrived where for survival of life, as in neonates, one needs to give more higher antibiotics to treat the infection and save the life. The only available option remains colistin (Kaur *et al 2016*), which gives very good sensitivity in vitro and vivo both. So a big question arises whether colistin is an only drug for first few days of life and whether it is to be given broad spectrumly or reserved for multi drug resistance cases.

This study was designed to document gaining resistance towards the commonly used antibiotics and appropriate use of the higher ones.

MATERIAL AND METHODS

It was a retrospective study conducted in tertiary care hospital of India catering 1000 beds, for period of 6 months (April 2016 to September 2016). Blood culture samples from Neonatal Intensive Care Unit, were processed according to standard guideline CLSI 2016. Blood samples were inoculated into Brain heart infusion broth. The samples were incubated at 37°C and sub cultured for three consecutive days. Subculture was done on Mac Conkey agar (aerobically) whereas partially anaerobically on Chocolate agar and human blood agar.

Corresponding author:* **Manali H. Shah
Department of Microbiology, Government Medical College, Surat

Identification of bacteria was done by different biotyping methods including colony morphology, gram staining, motility and different biochemical reactions appropriate for different organisms which included Citrate utilization test, Triple sugar iron test, Urease test, Methyl red test, Voges proskauer test, Indole test, Catalase test, Coagulase test, Bile esculin hydrolysis test, Sugar fermentation test, arginine dehydrolase test, ornithine decarboxylase test, lysine decarboxylase test etc.

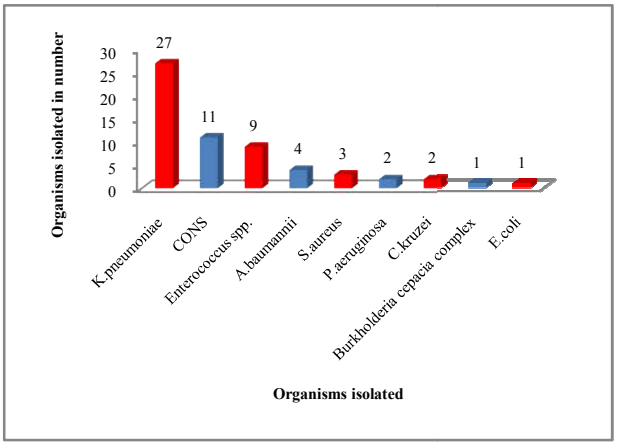
Isolation of the organism was followed by antibiotic susceptibility testing which was done on Muller hinton agar using Kirby bauer disc diffusion method. Quality control was done by comparing inoculums to 0.5 McFarland standard. Panel of drugs tested for different organism as well as interpretation of results were according to Clinical and Laboratory Standards Institute (CLSI) Guidelines 2016 (Ghotaslou *et al* 2017).

RESULT

Total 60 isolates were obtained from 131 neonatal samples. Amongst them Klebsiella pneumonia (45%) was the most common organism isolated followed by Coagulase Negative Staphylococcus (18%), Enterococcus spp. (15%), Acinetobacter baumannii (7%), Staphylococcus aureus (5%), Pseudomonas aeruginosa (3%), Candida krusei (3%), Burkholderia cepacia complex (2%) and Escherichia coli (2%).

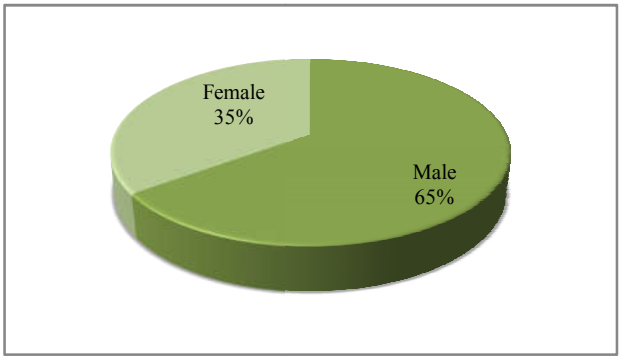
Growth on 1st subculture was predominant than 2nd subculture whereas male preponderance was seen amongst the isolates. 92% samples showed early onset septicemia (<7 days of neonatal age), whereas only 8% showed late onset septicemia (>7 days).

Half of the isolates were Klebsiella pneumonia accounting for the most common organism isolated in early onset septicemia. Sensitivity of these showed multi drug resistance with total resistance to Cephalosporins, Piperacillin, Aminoglycosides and to some extent carbapenems. They were 100% sensitive to Colistin and Polymyxin B (Chakkarapani *et al* 2014, Eren *et al 2017)*. They also showed 15% ESBL (Extended spectrum beta lactamase) positivity.

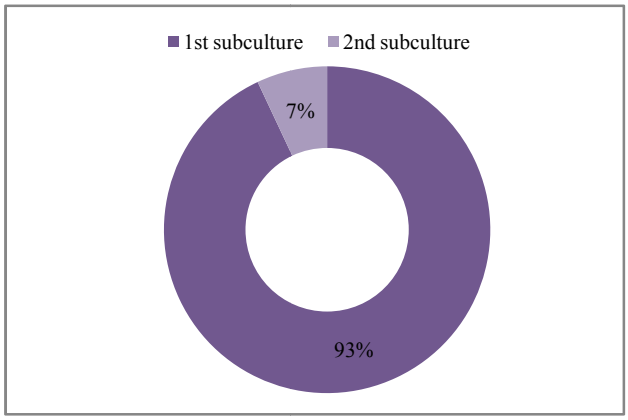


Graph 1 Organisms isolated from the samples

Coagulase negative staphylococci and Staphylococcus aureus were completely sensitive to Vancomycin, Daptomycin and Linezolid while totally resistant to Penicillin. Macrolides showed 20-30% sensitivity.



Graph 2 Male preponderance amongst the isolates



Graph 3 Predominant growth on 1st subculture

Table 1 Antibiotic susceptibility of Klebsiella pneumoniae

Drugs	% Sensitivity of isolates
Colistin	100
Polymyxin B	100
Ertapenem	82
Doripenem	78
Imipenem	45
Piperacillin-tazobactum	41
Aztreonam	15
Piperacillin	0
Ampicillin-sulbactum	0
Cefazoline	0
Cefepime	0
Ceftriaxone	0
Cefotaxime	0
Cefuroxime	0
Ceftazidime	0
Amikacin	0
Netilmicin	0

All Coagulase negative staphylococci isolates were Methicillin resistant. Tetracyclines showed 100% sensitivity to all gram positive cocci.

Sensitivity of Enterococcus spp. showed 30-40% susceptibility to Penicillin and Ampicillin. Whereas 80-85% sensitivity for Glycopeptides (Vancomycin, Teicoplanin). Sensitivity to Daptomycin was 56% while there was total resistance to Pristinamycin (Quinupristin /dalfopristin). 11% isolates were Vancomycin resistant Enterococcus.

Acinetobacter baumannii was completely sensitive to Polymyxin B and Colistin whereas 70-80% resistant to ureidopenicillins, cephalosporins, quinolones, aminoglycosides and carbapenems. Sensitivity of Pseudomonas shows 100 %

sensitivity to Polymyxin B and Colistin whereas around 40-50% sensitivity to carbapenems and ureidopenicillins.

DISCUSSION

In present study, most common isolate obtained was Klebsiella pneumonia which was completely sensitive to Polymyxins only (Jin *et al 2010)*. Sensitivity of carbapenemes is also decreasing which used to be a drug of choice in multi drug resistant bacteria (Zakariya *et al* 2012, Mumbula *et al 2015)*. As shown in the Table: 1, sensitivity of Ertapenem and Doripenem is 70-80% while that of Imipenem and Piperacillin-tazobactum which are preferred drugs in clinics, is only 40-45%. Which means it is not even effective in 50% of patients. Moreover, rest all group of drugs including, Aminopenicillins, Cephalosporins, Aminoglycosides were total resistant to the organism.

This is a matter of concern for treating a neonatal patient having infection with Klebsiella pneumonia, all primary line of drugs have developed resistance towards the organism and only choice left is higher drugs like Polymyxins and Carbapenemes. Day by day resistance to Carbapenemes is also increasing which again decreases resources of treatment to only Polymyxins.

If in future, faulty practice of empirical therapy with Polymyxins continues, then the era will rise where even Polymyxins will also become resistant to Klebsiella pneumoniae and there will not be any effective treatment available against this organism as no other drug higher than this is presently available for its treatment.

The present study shows similar results with Jaspal Kaur study, Chakkarapani *et al* (2014) and Khajuria *et al* (2014).

CONCLUSION

As neonatal septicemia is a grevious condition, it has become a big challenge to treat it in the era of multi drug resistance organisms. Carbapenemes were the effective drugs but resistance developed to them leads to one and only treatment option available for physicians and that is ”Polymyxins” (Colistin, Polymyxin B). Studies has shown good compatibility and effectiveness of these drugs in neonates with tolerable adverse effects. So for prevention of further multi drug resistance as well as resistance to Colistin, one should use antibiotics with crucial care, in appropriate dose and in appropriate patient (Karabinis *et al 2004)*. As these are higher drugs, their use should be limited to MDR patients only or else no treatment would be available for saving a newborn’s life. Moreover, strict infection control practices should be followed which would definitely prevent infections and drug resistance.

Limitations

As it was a retrospective study, we could not correlate our findings with clinical history of patients. Isolates of Vancomycin resistant Enterococci have not differentiated into species due to lack of facilities.

Also we have not assessed infection control practices and more importantly antibiotic practice of the neonatal intensive care units, which plays a major role in spread of multi drug resistance infection. Moreover, we have done antibiotic susceptibility testing of Polymyxins by disc diffusion method as MICs were not available due to limited resources.

References

1. Ali S, Abbasi SA, Mirza IA, Khan IU, Fayyaz M, Hussain A, Satti L. Outbreak of multidrug-resistant Klebsiella pneumoniae sepsis in Neonatal Intensive Care Unit. *Gomal Journal of Medical Sciences* 2012; 10(1):154-7.
2. Chakkarapani A, Amboiram P, Balakrishnan U, Ninan B, Sekar U. Pattern and Antimicrobial Susceptibility of Carbapenem Resistant Organisms in Tertiary Care Neonatal Intensive Care Unit, India. *J of Clin Neo* (2014), 3(4):200-4.
3. Eren Çağan, Evrim Kıray Baş, Hüseyin Selim Asker. Use of Colistin in a Neonatal Intensive Care Unit: A Cohort Study of 65 Patients. *Med Sci Monit*, 2017; 23: 548-554.
4. Ghotaslou R, Ghorashi Z, Nahaei M. Klebsiella pneumoniae in neonatal sepsis: A 3 year study in the paediatric hospital of Tabriz, Iran. *Jpn. J. Infect. dis* 2017; 60:126-8.
5. Jin Y, Shao C, Li J, Fan H, Bai Y, Wang Y.2015 Outbreak of Multidrug Resistant NDM-1-Producing Klebsiella pneumoniae from a Neonatal Unit in Shandong Province, China. Plos one., 10(3):e0119571.
6. Karabinis A , Paramythiotou E, Mylona-Petropoulou D, Kalogeromitros A, Katsarelis N, Kontopidou F, Poularas I, Malamou-Lada H. Brief Report: Colistin for *Klebsiella pneumonia*. Associated Sepsis. *Clinical Infectious Diseases* 2004; 38:e7-9.
7. Kaur J, Sheemar S, Chand K, Chopra S, Mahajan G. Outbreak of Carbapenemase-Producing Klebsiella pneumoniae Blood Stream Infections in Neonatal Intensive Care Unit. *Int. J. Curr. Microbiol. App. Sci* (2016), 5(1): 727-33.
8. Khajuria A, Praharaj A, Kumar M, Grover N, Aggarwal A. Multidrug resistant NDM-1 metallo-beta-lactamase producing *Klebsiella pneumoniae* sepsis outbreak in a neonatal intensive care unit in a tertiary care center at central India. *Ind J of Path Micro* (2014), 57(1): 65-8.
9. Mumbula EM, Kwenda G, Samutela MT, *et.al*. Extended Spectrum -Lactamases Producing Klebsiella pneumoniae from the Neonatal Intensive Care Unit at the University Teaching Hospital in Lusaka, Zambia. *Jour of Med Sc &Tec*. 2015, 4(2); 85-91.
10. Zakariya BP, Vishnu Bhat B, Harish B N, Arun Babu T, Joseph NM. Risk factors and outcome of Klebsiella pneumoniae sepsis among Newborns. *Curr Pediatr Res* 2012; 16 (2): 115-118.

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