ORIGINAL RESEARCH:

Spectrum and antibiotic sensitivity pattern of bloodstream bacterial isolates from septicemic neonates in a tertiary care centre in Eastern India.

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Received:3rd August ,2018 Reviewed: 8th November,2018 Accepted :5th January,2019

ABSTRACT:

Objective: To determine the antibiotic sensitivity pattern of bacterial isolates from septic neonates so as to identify the most suitable policy for use of empirical antibiotics. ***Design:*** *Retrospective cross-sectional study*

Participants: *126 infants admitted between 1st September 2015 and 30th August 2016, for treatment of suspected sepsis* ***Method:*** *Reports of blood culture done by BacT/Alert® system and other relevant data pertaining to suspected*

cases of neonatal sepsis were collected from the case records and retrospectively analyzed.

***Results and outcome measures**:Commonest organism was E.coli. Resistance to ampicillin, gentamicin and cefotaxime was significant. Overall, 73% of all organisms were susceptible to either carbapenems or glycopeptides while 63% were susceptible to either piperacillin/tazobactam or an aminoglycoside (preferably netilmicin).*

***Conclusion:** Carbapenems and Glycopeptides rotated with Piperacillin/tazobactam and an Aminoglycoside (preferably netilmicin) may have to be empirically used in units with similar flora and sensitivity patterns.*

KEYWORDS: ***Newborn, Sepsis, Anti-Bacterial agents, Microbial Sensitivity tests.***

INTRODUCTION: Septicemia has been the second most frequent cause of death in newborns after perinatal asphyxia in as recent a time as 2002-03 in India, when an incidence rate of about 16% among hospital born neonates was estimated.[1] It is still one of the three most important causes of neonatal mortality in this country, the others being prematurity/low birth weight and birth asphyxia.[2] The pattern of organisms causing neonatal sepsis and that of their antibiotic sensitivity in developed countries [3, 4] differ substantially from those in the developing ones.[5-8] Regional variations are also seen within the geographical limits of developing nations. Having said that, it cannot be

overemphasized that empirical antibiotic therapy is an essential and life saving part of management of neonatal sepsis and any attempt at formalization of policy streamlining such practice requires a thorough knowledge of the regional spectrum of causative organisms as well as their antibiotic sensitivity patterns. This study was conceived with the above intention.

OBJECTIVE: To determine the antibiotic sensitivity pattern of bacterial isolates from septic neonates so as to identify the most suitable policy for use of empirical antibiotics.

METHODS: A retrospective cross-sectional study was conducted including 126 infants admitted between 1st September 2015 and 30th August 2016, for treatment of suspected sepsis to the NICU of RSV Hospital, Kolkata, a tertiary care hospital, providing level II neonatal intensive care services. Blood samples were collected for culture from all neonates either showing clinical signs of sepsis as described by Young Infants Clinical Signs Study Group[9] or born to mothers with risk factors for infection including prolonged rupture of membrane for more than 12 hours, fever, UTI, foul smelling and/or meconium stained amniotic fluid. Newborns with gross congenital anomalies and ongoing exposure to antibiotics for probable sepsis were excluded from the study. Aseptically collected samples of blood were cultured in a BacT/Alert® 3D system and were sub-cultured if indicated, onto specific media for isolation of

causative organisms. Isolated organisms were identified by colony characteristics, Gram staining and biochemical methods. Antimicrobial sensitivity tests were carried out following Kirby-Bauer's disc diffusion method modified as required according to current CLSI guidelines.[10] Demographic characteristics of the subjects as well as the blood culture and sensitivity results were collected from hospital records. Organization, descriptive representations and analysis of data were done using STATA® version 12SE for Windows® statistical software package. Categorical variables and blood culture results were tested for mutual independence using Pearson's χ^2 test.

RESULTS AND OUTCOME MEASURES: During the study period there were 19 (15%) culture positive cases among the 126 infants included in the study.

(Table 1)

Among the 19 pathogenic bacteria isolated, about 74% (n=19) were Gram negative organisms. Predominant among those were *E. coli* (42%, n=19) and *Klebsiella sp*. (22%, n=19). *Staph. aureus* (11%, n=19) and *Staph. epidermidis* (16%, n=19) were the Gram positive isolates. As regards antibiotic sensitivity of the flora, Gram negative bacteria were highly (85%, n=14) resistant to cefotaxime. Ampicillin susceptibility was found to be 29 % (n=14). Only 50 % (n=14) of the entire Gram negative group were susceptible to Aminoglycosides as well as Piperacillin/tazobactam although the figure was slightly better (75 %)

for *E. coli* alone. Best overall susceptibility of the Gram negative flora were to Chloramphenicol (79 %, n=14), followed by Carbapenems (64 %, n=14). As for the Gram positive organisms, half of the *S. aureus* and all of the *S. epidermidis* were resistant to ampicillin. 50% (n=2) of *Staph. aureus* and all of *Staph. epidermidis* were methicillin resistant but were uniformly susceptible to vancomycin, teicoplanin and linezolid. Azithromycin and clindamycin susceptibility stood at 60% (n=5). Overall, 100 %, (n=5) were susceptible to netilmicin, glycopeptides and linezolid. Gentamicin resistance was 50 % (n=2) among *S. aureus* and 100 % (n=3) among *S. epidermidis.*

(Table 2)

DISCUSSION: Our analysis showed a blood culture yield of 15.1 %(n=126) and an overall incidence rate for sepsis of 31.7 per 1000 live births. In this study, early onset sepsis was encountered more often than late onset sepsis, male preponderance prevailed among afflicted (male: female=1.4:1) and prematurity was associated with culture positivity in a statistically significant manner. The causative organisms were mostly Gram negative and *E.coli* was the commonest one. Among Gram positive flora, *S.epidermidis* was most commonly isolated followed by *S.aureus*. With regard to antibiogram of the isolates, very steep resistance to ampicillin and third generation cephalosporins and significant resistance to aminoglycosides were noted among Gram negative

organisms. As for the Gram positive flora, susceptibility to penicillins, macrolides as well as cephalosporins were found to be dwindling.

This was a purely retrospective analysis done without controls. Hence, although prematurity has been linked with increased vulnerability to sepsis, there might have been a selection bias involved. Coagulase negative staphylococci could very well have been contaminant growths since we analyzed cases where only single cultures were taken and response to antibiotics could not have been detected retrospectively.

Similar incidence rates for neonatal sepsis and associations of culture positivity were reported in recent Indian studies.[6, 11-13] Contrary to our findings, many workers reported *Klebsiella sp*. as the commonest isolate.[1, 7, 8] Our overall scenario may reflect a principally nosocomial source but such findings are not uncommon and similar scenarios among hospital born neonates in the developing world were recently found and analyzed by Zaidi et al.[7] In our study, 73% (n=19) of all organisms were susceptible to either carbapenems or glycopeptides providing the highest coverage. The figure for Piperacillin/tazobactam and aminoglycosides (preferably netilmicin) was close (63%, (n=19)). Reports from Pakistan [14] and JIPMER, Pondicherry [15] submit that carbapenems and glycopeptides may have to be escalated to the first line of attack in places where significant antibiotic resistance prevails. While we find ourselves in the same boat, our study also indicates that antibiotics with

susceptibility patterns almost similar to those with broadest spectrum coverage can usually be found. We have to utilize that opportunity and although not studied here, rotation between such antibiotics can always minimize the selection of resistant strains in the long run.

CONCLUSION: Carbapenems and glycopeptides can sometimes appear to be the only antibiotics with decent coverage of bloodstream isolates from septic neonates thus making them candidates for empirical use in rotation with other antimicrobials with almost similar effectiveness (Pipearacillin/Tazobactam and Netilmicin in our study).

DECLARATIONS:

Contributors: Saugata Bhattacharyya- Determination of study design and methodology, analysis of the collected data, literature search and preparation of manuscript. Tapabrata Chatterjee- Conceptualization, collection of data and revision of the manuscript.

Competing and conflict of interests: None

Funding- None

REFERENCES:

1. *National neonatal-perinatal database: report for 2002-2003. New Delhi: National Neonatology Forum NNPD Network; 2005.*

2. *Age profile of neonatal deaths. Indian Pediatr. 2008 Dec;45(12):991-4.*

3. *Stoll BJ, Gordon T, Korones SB, Shankaran S, Tyson JE, Bauer CR, et al. Early-onset sepsis in very low birth weight neonates: a report from the National Institute of Child Health and Human Development Neonatal Research Network. J Pediatr. 1996 Jul;129(1):72-80.*

4. *Stoll BJ, Holman RC, Schuchat A. Decline in sepsis-associated neonatal and infant deaths in the United States, 1979 through 1994. Pediatrics. 1998 Aug;102(2):e18.*

5. *Ahmed AS, Chowdhury MA, Hoque M, Darmstadt GL. Clinical and bacteriological profile of neonatal septicemia in a tertiary level pediatric hospital in Bangladesh. Indian Pediatr. 2002 Nov;39(11):1034-9.*

6. *Sundaram V, Kumar P, Dutta S, Mukhopadhyay K, Ray P, Gautam V, et al. Blood culture confirmed bacterial sepsis in neonates in a North Indian tertiary care center: changes over the last decade. Jpn J Infect Dis. 2009 Jan;62(1):46-50.*

7. *Zaidi AK, Huskins WC, Thaver D, Bhutta ZA, Abbas Z, Goldmann DA. Hospital-acquired neonatal infections in developing countries. Lancet. 2005 Mar 26-Apr 1;365(9465):1175-88.*

8. *Zaidi AK, Thaver D, Ali SA, Khan TA. Pathogens associated with sepsis in newborns and young infants in developing countries. Pediatr Infect Dis J. 2009 Jan;28(1 Suppl):S10-8.*

9. *Clinical signs that predict severe illness in children under age 2 months: a multicentre study. Lancet. 2008 Jan 12;371(9607):135-42.*

10. *Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing. Twenty second Informational Supplement M100-S22. Wayne, PA, USA2012.*

11. *Jyothi P, Basavaraj MC, Basavaraj PV. Bacteriological profile of neonatal septicemia and antibiotic susceptibility pattern of the isolates. J Nat Sci Biol Med. 2013 Jul;4(2):306-9.*

12. *Shah AJ, Mulla SA, Revdiwala SB. Neonatal sepsis: high antibiotic resistance of the bacterial pathogens in a neonatal intensive care unit of a tertiary care hospital. J Clin Neonatol. 2012 Apr;1(2):72-5.*

13. *Tallur SS, Kasturi AV, Nadgir SD, Krishna BV. Clinico-bacteriological study of neonatal septicemia in Hubli. Indian J Pediatr. 2000 Mar;67(3):169-74.*

14. *Mahmood A, Karamat KA, Butt T. Neonatal sepsis: high antibiotic resistance of the bacterial pathogens in a neonatal intensive care unit in Karachi. J Pak Med Assoc. 2002 Aug;52(8):348-50.*

15. *Zakariya BP VBB, Harish B N, Arun Babu T, Joseph NM. Risk factors and outcome of Klebsiella pneumoniae sepsis among Newborns. Curr Pediatr Res. 2012;16(2):115-8.*

Table 1: Culture results with respect to patient characteristics

Characteristics	Culture Positive	Culture Negative	*p*-value*
Less than 72 hours old	14	60	0.151
More than 72 hours old	5	47	
Term infants	2	92	0.000
Preterm infants	17	15	
Male babies	11	54	

Female babies	8	53	0.551

*Derived from Pearson's χ^2 test, where a *p*-value <0.05 was considered as statistically significant.

Table 2: Percent isolates susceptible to various antibiotics

	CPM	FLQ	CMB	PCL	PLXN	GLCN	AMG	CPHN3
E. coli	88	50	75	88	75*	88	75	25
K.pneumoniae	100	50	50	100	100	100	50	None
K. oxytoca	None	None	None	100	100	None	None	None
A. baumanni	None	None	None	None	100	100	None	None
S. epidermidis	None#	None	None	100	Not tested	Not tested	100$,£	None
S. aureus£	50	Not tested	50	100	Not tested	Not tested	50	50

*this includes 25% *E. coli* which were resistant to colistin but susceptible to polymyxin-B

#only 33% was sensitive to Imipenem; $all were resistant to gentamicin; £all were sensitive to netilmicin.

CPM=Carbapenems (Meropenem, Imipenem & Doripenem), FLQ=Fluoroquinolones (Ciprofloxacin, Ofloxacin), CMB=Combinations (Piperacillin/Tazobactam, Ampicillin/Sulbactam), PCL=Phenicols (Chloramphenicol), PLXN=Polymyxins (Colistin, Polymyxin-B), GLCN=Glycylcyclines (Tigecycline), AMG=Aminoglycosides (Gentamicin, Amikacin, Netilmicin), CPHN3=3rd generation cephalosporins (Cefotaxime, Ceftriaxone).