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Short Report:

Increasing Trends of Methicillin Resistant Coagulase Negative *Staphylococcus* in Neonatal Septicaemia - A Study in a Tertiary Care Hospital, Mysore, South India

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Abstract:

Introduction: Neonatal septicaemia is one among the leading causes of neonatal mortality in India. For the last 20 years CoNS has been identified as a major cause of neonatal septicaemia in NICU. Different studies show 70-75% of CoNS as resistant to methicillin. Material and methods: Blood samples from neonatal septicaemia cases during Dec 2007 to Dec 2010 were processed & isolates were identified. CoNS were biotyped & methicillin resistance was detected using cefoxitin 30 µg disk. Results: Of 2256 blood samples from neonatal septicaemia cases, 587(36.98%) were CoNS. Staphylococcus epidermidis 234(39.86%) was the commonest isolate. Methicillin resistance was noted in 286 (48.72%). MRCoNS prevalence during 2008, 2009 & 2010 were 41.57%, 47% and 57.36% respectively. Conclusion: Our study showed increased trends of MR-CoNS in neonatal septicaemia leading to increased usage of vancomycin & other glycopeptides, resulting in emergence of multidrug resistant strains, thus narrowing the treatment options in neonates.

Key Words: Neonatal septicaemia; Coagulase Negative Staphylococcus; Methicillin resistance

Introduction:

Neonatal septicaemia is one among the leading causes of neonatal mortality in India. The spectrum of organisms causing neonatal septicaemia is quiet different in developed countries in comparison with developing countries like India. Also there exists regional variation in the spectrum of organisms causing sepsis. For the last 20 years Coagulase negative Staphylococci (CoNS) has been identified as a major cause of neonatal septicaemia in Neonatal Intensive Care Unit (NICU). The increasing recognition of pathogen potential CoNS and emergence of drug resistance among them demonstrates the need to identify and determine the prevalence of CoNS. Data from the world wide SENTRY study showed that, independent of geographic origin, 70-75% of CoNS are nowadays resistant to methicillin. Similarly the rate of multidrug resistant CoNS is in increased trend. On this account vancomycin has been widely used and it

is the major cause for the emergence of glycopeptide resistant

On this basis in the present study an attempt has been made to evaluate the prevalence of Methicillin resistant Coagulase negative Staphylococci (MR-CoNS) in neonatal septicaemia in our hospital.

Materials and Methods:

This study was carried out in the department of Microbiology, Mysore Medical College & Research Institute, Mysore. Samples were received from Cheluvamba hospital NICU over a period of 3 years from December 2007 to December 2010.

Cases included in our study were neonates less than 28 days with clinical diagnosis of septicaemia. Infections within 7 days of birth were considered early onset septicaemia (EOS) and infections between 7 to 28 days were late onset septicaemia (LOS).⁵ Blood samples were subjected to further processing in our Microbiology lab according to standard methods.⁶

All the samples were processed for blood culture and isolates were initially identified by colony morphology, Gram stain, catalase, oxidase, slide coagulase, tube coagulase test (read after 4-24 hours). Gram negative isolates were further identified by standard biochemical reactions and antibiotic susceptibility pattern was studied.

In babies whom CoNS was isolated in blood culture, a repeat sample was taken and reconfirmed for the isolate. Biotyping of CoNS was done by the following panel of tests – fermentation of mannose, xylose, sucrose, maltose, lactose, novobiocin sensitivity, urease, nitrate reduction test, ornithine decarboxylase test.

The antibiotic susceptibility of the isolates was determined by disk diffusion method on Muller Hinton agar using antibiotics at the specific absolute concentration using HiMedia disks. Methicillin resistance was determined using cefoxitin $30\mu g$ disk.

Results:

A total of 2256 blood samples received from NICU to the department of Microbiology were processed for aerobic culture. 1587 samples were positive for blood culture. Among 1587 isolates, 1425 were from EOS and 162 from LOS. CoNS 587(36.98%) was the most common pathogen isolated in both EOS 523(36.70%) and LOS 64(39.50%) cases. *Staphylococcus epidermidis* 234(39.86%) was the commonest CoNS species.

Table 1: Showing frequency of isolates in neonatal sep- ticaemia							
		E	OS	LOS			
Isolates		No	%	No	%		
CoNS		523	36.70	64	39.50		
Klebsiella species		276	19.36	44	27.16		
Escherichia coli		189	13.26	-	-		
Staphylococcus aureus		153	10.73	21	12.96		
Acinetobacter species		125	8.70	4	2.46		
Candida species		112	7.85	20	12.34		
Pseudomonas species		57	4.00	4	2.46		
Enterobacter species		49	3.43	6	3.70		
Enterococci species		29	2.03	4	2.46		
Total		1425		162			

Table 02: Showing frequency of species of Coagulase negative Staphylococci

CONS species	N=587	%					
Staphylococcus epidermidis	234	39.86					
Staphylococcus haemolyticus	84	14.31					
Staphylococcus hominis	65	11.07					
Staphylococcus capitis	58	9.88					
Staphylococcus cohnii	46	7.83					
Staphylococcus simulans	34	5.79					
Staphylococcus xylosus	29	4.94					
Untyped	37	6.30					

Table 3: Antibiotic susceptibility pattern										
Isol-	Percentage susceptible (%)									
ates	A	E	Cd	Ak	G	Cf	Co		Lz	т
n=					_			(30µg)		1 (10μg)
587	(1048)	(15 µB)	(246)	(3048)	(1048)	(5 48)	(2048)	(3048)	(3048)	(1046)
MSCo										
NS	2.15	4.30	4.83	60.75	34.40	65.59	44.08	8.45	89.17	45.32
n=301										
MR-										
CoNS	0	4.19	8.74	16.78	5.24	14.68	11.18	8.39	60.19	29.13
n=286										
NT -4 7	Note: MC CoNC = mathicillin congitive CoNC A=amnicillin									11:

Note: MS-CoNS = methicillin sensitive CoNS, A=ampicillin, Ak=amikacin, Co=cotrimaxazole, E=erythromycin, G=gentamycin, C=chloramphenicol, Cd=clindamycin, Cf=ciprofloxacin, Lz=linezolid, T=tetracycline.

Methicillin resistance was seen in 286(48.72%) of CoNS isolates. Also we noted increasing methicillin resistance over years. MRCoNS prevalence during 2008, 2009 & 2010 were 41.57%, 47.0% and 57.36% respectively. Methicillin resistant CoNS were mostly sensitive to linezolid 58(20.27%), amikacin 48(16.78%), ciprofloxacin 42(14.68%) and were totally resistant to ampicillin 100%.

Discussion:

The infections in neonates are most frequent and habitually more seriously associated with high mortality. CoNS is increasingly being implicated as a significant nosocomial pathogen, so many reviewers have emphasised the need for species identification. Species identification is important in monitoring the reservoir and distribution of CoNS involved in nosocomial infections.

CoNS are further gaining importance due to increase in resistance rates to betalactam antibiotics and multiresistance. MR-CoNS have become the predominant pathogen in hospitalised patients with the number of infections increasing dramatically.⁸

MRCoNS are the source of resistance gene to other Gram positive cocci including *Staphylococcus aureus* in hospital settings.⁴

In our study an attempt was made to retrospectively analyse the trends of occurrence of MRCoNS in neonatal septicaemia cases. In our study CoNS was the commonest isolate, 36.98% followed by Klebsiella species, 22.45% and *Escherichia coli*, 19.45%. This is in concordance with the reports of Shahsenam Gheibi et al ⁵, reported causes of neonatal septicaemia as CoNS from EOS – 48.8%, LOS – 69.8% followed by Klebsiella, *Escherichia coli & Staphylococcus aureus*. However Nalini et al ⁹ have reported predominance of Gram negative septicaemia, 58.5% over Gram positive cocci, 41.5%. Gupta B et al ¹⁰ in their study over a period of 4 yrs reported an increase in incidence of neonatal septicaemia caused by CoNS from 20% to 35%.

Shubra Singh et al ³ have reported common CoNS species as *Staphylococcus epidermidis* 40%, *Staphylococcus haemolyticus* 12% which is similar to that seen in our study of *Staphylococcus epidermidis* 39.86% and *Staphylococcus haemolyticus* 14 31%

Of the 587 CoNS isolates 286 (43.72%) were methicillin resistant. Amit Jain et al 11 reported 66% MR-CoNS from neonatal septicaemia.

In our study there was an increase in prevalence of MR-CoNS over a period of 3 yrs from 41.57% to 57.36%. Many other authors also have reported increasing trend of CoNS in neonatal sepsis. ¹²⁻¹⁴ MR-CoNS also showed increased resistance even to non betalactam antibiotics thereby narrowing the therapeutic options. Periodic surveillance of the causative agents and their antibiotic profile is essential for effective management of neonatal septicaemia. Appropriate antibiotic therapy would minimise the risk of severe morbidity and mortality besides decreasing the emergence of multidrug resistant organisms by rational antibiotic use.⁵

Conclusions:

In view of the above facts that in our study we have noticed an increase in prevalence of MR-CoNS in neonatal septicaemia and increase in their resistance pattern, it is necessary to periodically review the strategy of antibiotic usage.

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