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Neonatal Septicemia and Drug Resistance; 2 Year Prospective Study

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A B S T R A C T

Neonatal sepsis is a worldwide problem with the prevalence at 1 to10 per 1000 live birth and one of the indicator for measuring the health status of a nation. According to WHO there are about 5 million neonatal death per year with 98% occurring in developing countries. Antimicrobial resistance is a growing threat worldwide. Blood culture is considered as the gold standard technique for diagnosis of neonatal septicemia. The main objectives includes, to know the various bacteria causing neonatal septicemia and their antibiogram. To detect drug resistance among the isolated bacteria. A Prospective study was done over a period of 2 year. Blood samples for culture were collected aseptically before starting antibiotic therapy and subcultures were performed. The isolates were identified by standard biochemical tests and antibiogram of the isolates were studied. Out of 360 cases 160 were bacteriologically positive, *Klebsiella* was the most common organism isolated (21%), followed by *Staphylococcus aureus* (20%) *Acinetobacter* (15%), *Pseudomonas* (13%). Maximum sensitivity was seen by Linezolid, Erythromycin for Gram positive organisms and Gram negative organisms were sensitive to Piperacillin/ Tazobactum, Imipenem, Levofloxacin, Meropenem. Knowledge of likely causative organism causing neonatal septicemia can help in instituting prompt and appropriate therapy which in turn reduce morbidity and mortality.

Introduction

Neonatal septicemia is an important cause of Neonatal morbidity and mortality. it is one of the indicator for measuring the health status of a nation. According to WHO estimates there are 5 million neonatal death a year with 98% occurring in developing countries. The incidence of neonatal sepsis varies from 11-24.5 /1000 live births in India. Neonatal deaths account for over a one-third of the global burden of child mortality.[1]

Neonatal sepsis can be divided into two main classes depending on the onset of symptoms namely Early-onset sepsis, which usually presents within the first 72 hours of birth and Late-onset sepsis, which usually presents 72

hours after birth.[2,3] The pattern of organisms causing neonatal sepsis has been constantly changing and indiscriminate use of antibiotics has resulted in the emergence of multidrug resistant and virulent organisms. Here lies the importance of microbiological investigation and determination of antibiotic susceptibility pattern of isolate.

Materials and Methods

The study group comprised of suspected cases of neonatal septicaemia in the neonatal intensive care unit for a period of 2 years admitted in SSIMS & RC, dvg. Neonates admitted with the clinical diagnosis of neonatal septicaemia are included in the study as per the criteria by Vergnano[4]. A detailed history of age, sex, birth weight, gestational age, and clinical symptoms of septicemia was recorded. Neonatal sepsis were suspected when any of the signs and systems or predisposing factors such as reduced activity, fever, refusal of feed, seizures, prolonged jaundice, birth asphyxia, umbilical sepsis, prematurity were noted in the newborn.

Exclusion criteria

Neonates already on antibiotics and with diagnosis of intra-uterine infection and congenital anomalies were excluded from the study.

Specimen Processing

Two samples of blood were collected from each case using aseptic precautions. About 2 ml of blood was added immediately into 20 ml of brain heart infusion broth with 0.025% sodium polyethanol sulphonate as anticoagulant. The bottles were incubated for seven days and subcultures were done appropriately. The organisms were isolated and identified by standard microbiological techniques as per CLSI guidelines[5]. Antibiotic sensitivity pattern was evaluated by Kirby Bauer's disc diffusion methods.

Results and Discussion

Totally 360 neonates who were suspected to have septicemia on clinical basis were included in the study. Among these 160 neonates had definitive septicemia as they were bacteriologically positive. Among these 100 cases (62.5%) were Gram-negative organisms & 60 cases (37.5%) were Gram-positive organisms.

Among the 100 Gram negative organism, commonest was Klebseilla (33%), followed by Acinetobacter (24%), Pseudomonas(22%), E.coli (11%), citrobacter(6%), Enterobacter (3%), Proteus (1%). Among the 60 Gram positive organism, *Staphylococcus aureus* were (53%) the most common followed by coagulase negative staphylococcus (33%)(CONS), Enterococci (13%), pathogenic role of CONS was confirmed by isolation of same organism with similar antibiotic susceptibility pattern from two blood samples collected from two different sites.

Male babies were more(63%) affected by neonatal septicemia than female babies(37%) in culture proven cases. This could be explained on the basis of genetic factors. Preterm babies 115(72%) were more affected by septicemia than full term babies 45(28%) as shown in fig 2.

Neonatal sepsis is a life threatening emerging infection in the developing countries and it is estimated about 5 million neonatal death occur every year worldwide. The invasive procedures in the postnatal period and inadequate hand washing before and after handling babies also contributes to the neonatal sepsis in intensive care units. In the present study, males were more affected than females (fig1). This is comparable to the other

studies by Begum S *et al.,*[7] and Shrestha N J *et al.,*[8]. The reason for male preponderance is unknown, but this could be due to sex-dependent factors[9]. The synthesis of gamma globulins is probably regulated by X–linked immunoregulatory genes and as males are having one X chromosome, they are more prone for neonatal septicemia than females[10].

In the present study preterm babies (72%) are more involved than term (28 %) babies as in fig 2, this could be due to the immaturity of immune system in preterm babies as compared to term babies.

Higher incidence of many complications of labour and resuscitation are more common in preterm babies than full term neonates. Premature babies are relatively immuno-compromised and immuno-inexperienced. These factors predispose them to infection.

Khatua *et al.,*[15] observed that out of 92 babies with neonatal septicemia 58 were preterm in 56.52%. Vinodkumar C. S. *et al.,* in their study stated that Preterm babies were highly significantly more susceptible to infection than term babies (61.9% vs 40.4%;P<0.001).[16]

The organisms causing neonatal septicaemia differ from area to area and also change with respect to time even in the same area, which may be due to different life conditions.[21]

Gram negative bacterial isolates (63%) were more than Gram positive isolates (37%) in our study. This is in contrast to developed countries, where Gram positive bacteria were more commonly reported. This was in concordance with National Neonatal Perinatal Database (NNPD) (2003)[6], Aletayeb S M H *et al.,*[9] and Sundaram V *et al.,*[11].

In this study, the most frequent isolate was *Klebsiella pneumoniae* 22 (35.4%) in both EOS and LOS. This was in accordance with other Indian studies NNPD 2003[6], Kumar G D *et al.,*[12], Roy I *et al.,*[14] and Kayange N *et al.,*[13]. The second most common Gram negative organism in the present study was Acinetobacter followed by *Pseudomonas aeruginosa*. *Staphylococcus aureus* was the commonest Gram positive organism and was second most common organism among all isolates. Among the isolates, a considerable percentage (12%) was CONS as pathogen, which could be due to immature immune system development, and a large population of premature and debilitated infants. Jyothi P *et al.,* stated in their study that Gram negative bacteria accounted for (55.7%) of cases and Gram positive (44.3%) of cases. *Klebsiella Spp, Acinetobacter Spp and Coagulase negative Staphyloccous (CoNS)* were most common organisms isolated.[17]

Desai K J *et al.,* (2011) showed that Gram negative were (67.85%) and Gram positive were (28.57%). Klebsiella species and *Staphylococcus aureus* were the most common Gram negative and Gram positive organisms accounting for (47%) and (25%) of the isolates respectively.

All the Gram positive isolates were 100% sensitive to vancomycin,96% to Linezolid,80% Gentamicin, Gram negative organisms isolated were more sensitive to Amikacin, Levofloxacin, Imepenem, Pipercillin tazobactum, Meropenem.

Table.1 Microbial Profile of Neonatal Septicemia

Bacterial isolates	No. of isolates
Klebsiella	34
Acinetobacter	23
Pseudomonas	22
E.coli	12
Citrobacter	5
Others	4
Staphylococcus aureus	32
CONS	20
Enterococcus Spp	8

Table.2 Pattern of sensitivity in Gram positive bacteria

Antibiotics	*Staphylococcus aureus*	Cons	*Enterococcus*
Penicillin	50%	45%	37%
Erythromycin	65%	75%	75%
Gentamicin	80%	60%	86%
Cefoxitin	53%	70%	-
Cotrimaxozole	71%	80%	25%
Linezolid	96%	100%	100%
Doxycycline	84%	60%	62%
Amikacin	68%	80%	64%

Table.3 Pattern of sensitivity in Gram negative bacteria

	Klebsiella n=33	*Acinetobacter* n=24	*Pseudomonas* n=22	*Ecoli* n=11	*Citrobacter* n=6	Others n=4
Amikacin	69%	66%	50%	72%	66%	80%
Gentamicin	54%	63%	60%	63%	50%	75%
Ceftazidime	48%	51%	72%	54%	50%	88%
Cefotaxime	51%	48%	72%	45%	66%	88%
Cefepime	66%	63%	70%	54%	50%	90%
Meropenem	72%	66%	45%	72%	83%	100%
Pipercillin/ tazobactum	80%	75%	81%	90%	83%	80%
Imepenem	82%	81%	95%	90%	83%	100%
Levofloxacin	78%	70%	72%	63%	66%	75%

Fig.1 Distribution of neonatal septicemia cases according to gender in culture proven cases

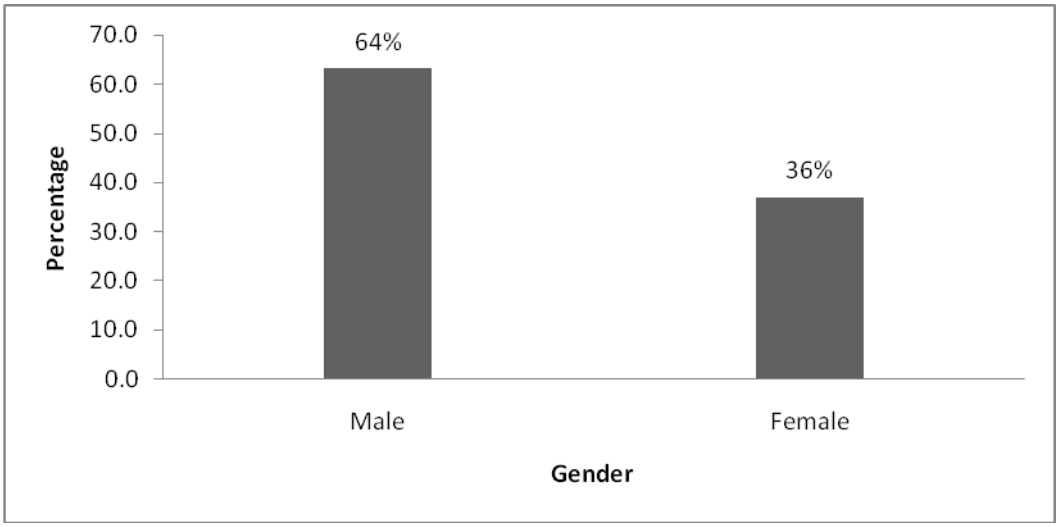
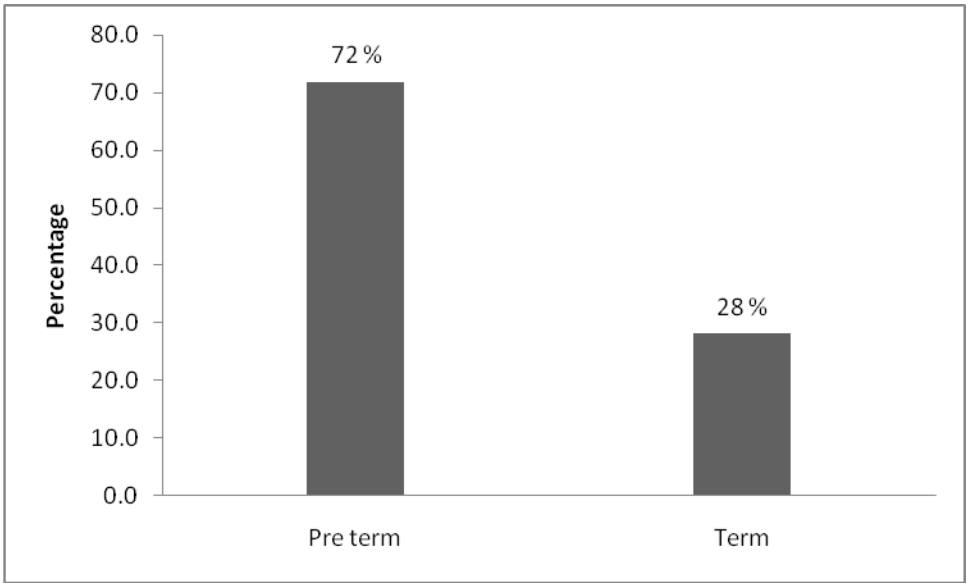


Fig.2 Distribution of neonatal septicemia cases according to gestational age i.e., maturity in culture proven cases



From our study we noticed that Gram negative bacteria were more commonly the cause of septicemia in neonates, and *Klebsiella pneumoniae* was the predominant pathogen. We also noticed that these Gram negative bacteria were resistant to routinely used antibiotics, hence their resistant pattern should be considered essential before deciding the empirical treatment. The higher antibiotics such as Meropenem should be reserved for multi-drug resistant Gram negative bacteria, whereas Linezolid and Vancomycin should be reserved for drug resistant Gram positive isolates.

The positive blood culture with antibiotic sensitivity of the isolated organism is the best guide to antimicrobial therapy, as resistance to antibiotics is a worldwide problem that causes ineffectiveness of empirical treatment. More

so, strict infection control practices combined with judicious use of antibiotic therapy are the main solutions to this problem. However, it will be important to continue the surveillance of neonatal septicaemia in order to closely follow changes in trends and identify risk factors, to obtain information for empiric antibiotic therapy and to act rapidly in case of major changes in susceptibility patterns.

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