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Prospective Observational Study of Common Organisms Causing Neonatal Sepsis and Its Antibiotic Sensitivity in Sick Neonatal Care Unit, Tiruppur

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Abstract

Background: Neonatal sepsis is a major cause of mortality and neurodevelopmental impairment among neonates. It contributes to nearly 30 % of neonatal deaths in developing countries. Increased prevalence of extended spectrum beta- lactamases (ESBLS) and methicillin-resistant Staphylococcus aureus (MRSA) and multiple drug resistant (MDR) strains is a cause of concern in neonatal intensive care units (NICU) worldwide. **Objectives**: To identify most common organism causing sepsis and also to analyse the most sensitive antibiotics against specific microorganism and to compare the different organism with different antibiotic sensitivities. **Materials and methods**: The study is based on a prospective analysis of all cases admitted to the neonatal intensive care unit (NICU) of Govt. Head Quarters Hospital Tiruppur, Tamil Nadu. The study was carried out from February to August 2019. **Results**: In our study out of 50 patients studied, Gram-negative organisms were isolated in 30 cases (60%), Gram-positive in 20 cases (40%). The most gram-negative organism which caused neonatal sepsis was Klebsiella Pneumonia 9 cases (45%) and of gram-positive organism was Staphylococcus Spp 10cases (50%). Amikacin and meropenem was the most sensitive antibiotic active against gram positive and gram-negative microorganisms respectively. **Conclusion:** Blood culture is the gold standard in diagnosis and treatment of neonatal septicaemia. Multiple antibiotic resistances among neonatal sepsis are currently one of the greatest challenges to the effective management of infections. Therefore, we suggest that surveillance of antimicrobial resistance is necessary.

Keywords

Neonatal sepsis, Gram positive and negative microorganisms, Antibiotics, Sensitivity.

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INTRODUCTION

Sepsis is a life-threatening condition that arises when the body's response to infection causes injury to its own tissues and organs [1]. According to the data from National Neonatal Perinatal Database 2002-03, incidence of neonatal sepsis was 30 per 1000 live births. Sepsis is one of the leading causes of neonatal mortality accounting for 18.6% neonatal deaths. Antibiotics should be re-viewed once the results of the cultures and sensitivity are available.

Neonatal sepsis is a clinical syndrome consisting of nonspecific symptoms and signs of infection accompanied by bacteraemia in the first 28 days of life [2,3]. Septicaemia has been classified as early onset septicaemia (EOS) and late onset septicaemia (LOS). The microorganisms most common associated with EOS include Group B Streptococcus (GBS), Escherichia coli, coagulase negative Staphylococcus species (CONS), Haemophilus influenza and Listeria monocytogenes and LOS is caused by CONS, S. aureus, E. coli, Klebsiella spp., Pseudomonas spp., Enterobacter. It contributes to nearly 30 % of neonatal deaths in developing countries [4].

Risk factors of EOS are[5, 6]Low birth weight (<2500gms) or preterm baby, Febrile illness in the mother within 2 weeks prior to delivery, Foul smelling and/or meconium stained liquor amnii, Prolonged rupture of membrane (>24 hours),Prolonged and difficult delivery with instrumentation. Risk factors for development of LOS include: [7,8] Poor hygiene, Low birth weight (LBW), Poor cord care, Prematurity, Bottle feeding, Superficial infection (pyoderma, umbilical sepsis), Pre lacteal feeding.

The organisms most frequently involved in early-onset Neonatal sepsis of term and preterm infants together are GBS and Escherichia coli, which account for approximately 70% of infections combined. Current epidemiological trends are showing a decrease in the frequency of early-onset GBS disease related directly to prenatal screening and treatment with intrapartum antibiotics (IPA) [9,10,11]. The use of intrapartum maternal prophylaxis for GBS has reduced the incidence of early-onset GBS disease by at least 80%; however, GBS remains one of the leading causes of EOS [12]. Complications involves Septic Shock, Acute respiratory distress syndrome (ARDS).

Diagnosis and management of sepsis are a great challenge facing neonatologists in NICUs. Clinical diagnosis of presentation is difficult due to nonspecific signs and symptoms. In addition, laboratory diagnosis is time consuming. This matter necessitates the initiation of empirical antibiotic therapy till the suspected sepsis is ruled out. Many studies suggest that resistance is directly associated with the selection of inappropriate antimicrobials, which leads to increased patients' mortality [13].

Antimicrobials used to treat sepsis in neonates usually include beta-lactams such as ampicillin, oxacillin, and cefotaxime; extended-spectrum beta-lactams such as piperacillin-tazobactam; and the carbapenem. Meropenem. These are bactericidal agents that inhibit the synthesis of the peptidoglycan layer of the bacterial cell wall [14].

OBJECTIVES

- To identify most common organism causing sepsis
- To analyse most sensitive antibiotics against specific microorganism
- To compare the different organism with different antibiotic sensitivities
- To analyse the data and draw the conclusion

MATERIALS

The study is based on a prospective analysis of all cases admitted to the neonatal intensive care unit (NICU) of Govt. Head Quarters Hospital Tiruppur, Tamil Nadu. The study was carried out from February to August 2019.

INCLUSION CRITERIA

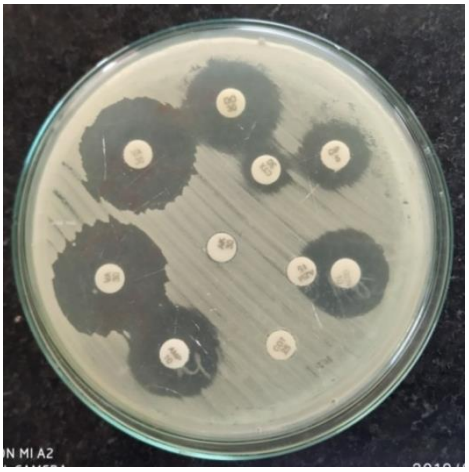
- Sepsis cases in the department of sick neonatal care unit (SNCU)
- Including both genders
- Patients admitted in the secondary care hospital

EXCLUSION CRITERIA

- Complicated cases are avoided
- Those patients who do not consent are excluded
- Patients above 28days are excluded

METHODS

The study was conducted in Govt. Headquarters hospital, Tiruppur, a 600 bedded multispecialty tertiary care hospital. The study procedure was conducted in the microbiology lab by taking the blood samples. The positive blood samples were taken for identifying whether the bacteria is gram positive or negative by gram staining method. By using different biochemical tests, the organisms were identified and antibiogram was done using appropriate antibiotics by Kirby-Bauer disc diffusion method.



ANTIBIOTIC SENSITIVITY& RESISTANCE PRODUCED BY MICROORGANISM

GROWTH OF MICROORGANISM

RESULTS

Total 50 patients with positive blood culture were studied during the study period. Among the culture positive cases, Gram-negative organisms were isolated in 30 cases (60%), Gram-positive in 20 cases (40%)

Fig. 1: Total of Gram Positive and Gram-Negative Cases

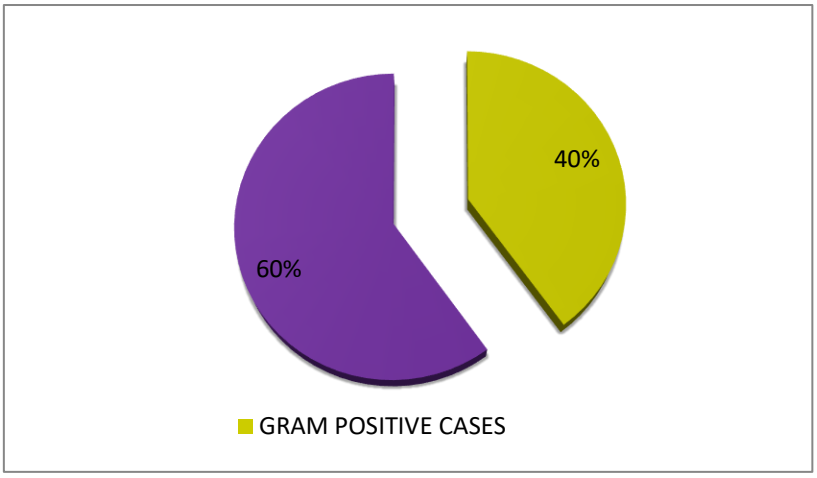


Table 1: Percentage of Gram-Positive Microorganism

Gram Positive microorganisms	No. of Microorganisms	Percentage
Staphylococcus Aureus	4	20%
Staphylococcus Spp	10	50%
Streptococcus Spp	2	10%
Enterococcus Faecalis	4	20%

FIG.2:

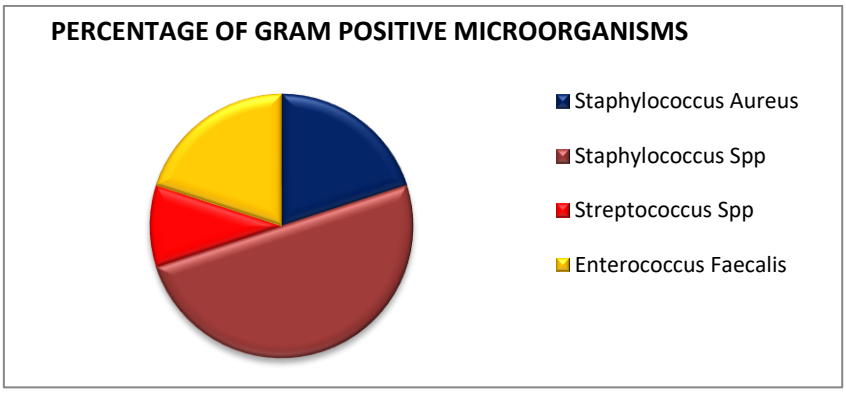


TABLE 2: PERCENTAGE OF GRAM-NEGATIVE MICROORGANISM PRESENT

Gram Negative Microorganisms	No. Of Microorganisms	Percentage
Proteus Mirabilis	5	25%
Klebsiella Pneumoniae	9	45%
Enterobacter Aerogenes	2	10%
Pseudomonas Aerugenosa	2	10%
Citrobacter Freundi	1	5%
Proteus Vulgaris	1	5%
E.coli	4	20%
Citrobacter Spp	3	15%
Klebsiella Oxytoca	3	15%

Fig.3: Percentage of Gram-Negative Microorganisms

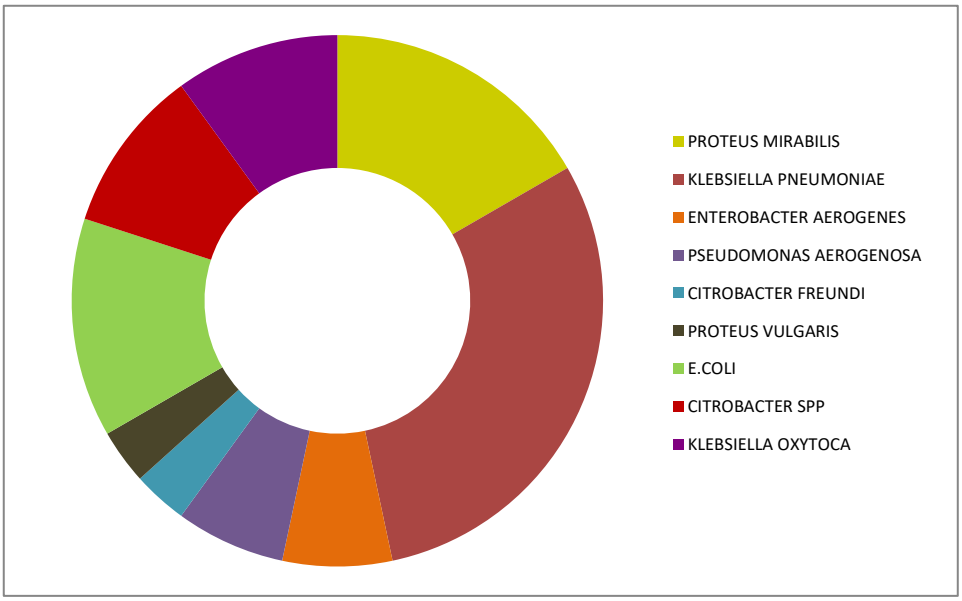


Table 3: Distribution of Risk Factors in Early Onset Sepsis and Late Onset Sepsis (50cases)

RISK FACTOR	EOS	LOS
Maternal Fever	9	0
Maternal UTI	9	0
Prolonged Rupture of Membrane	12	0
Foul Smelling Liquor	5	0
Very Low Birth Weight	0	11
Preterm Babies	0	4

Fig.4: Distribution of Risk Factors In Eos And Los

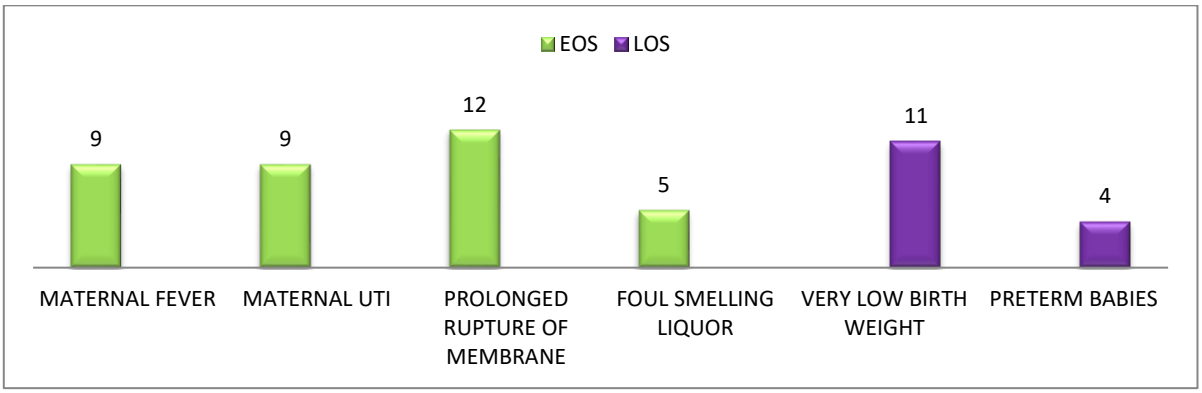


Table 4: Number Of Antibiotic Sensitivity and Resistant Cases

ANTIBIOTICS	SENSITIVITY	RESISTANT
Cefotaxim	19	31
Ciprofloxacin	26	24
Ampicillin	14	36
Gentamycin	25	25
Amikacin	37	13
Doxycycline	19	31
Vancomycin	13	37
Cotrimoxazole	16	34
Azithromycin	14	36
Erythromycin	12	38
Norfloxacin	21	29
amoxiclav	7	43
Meropenem	30	20
Piperacillin tazobactam	30	20

FIG.5:

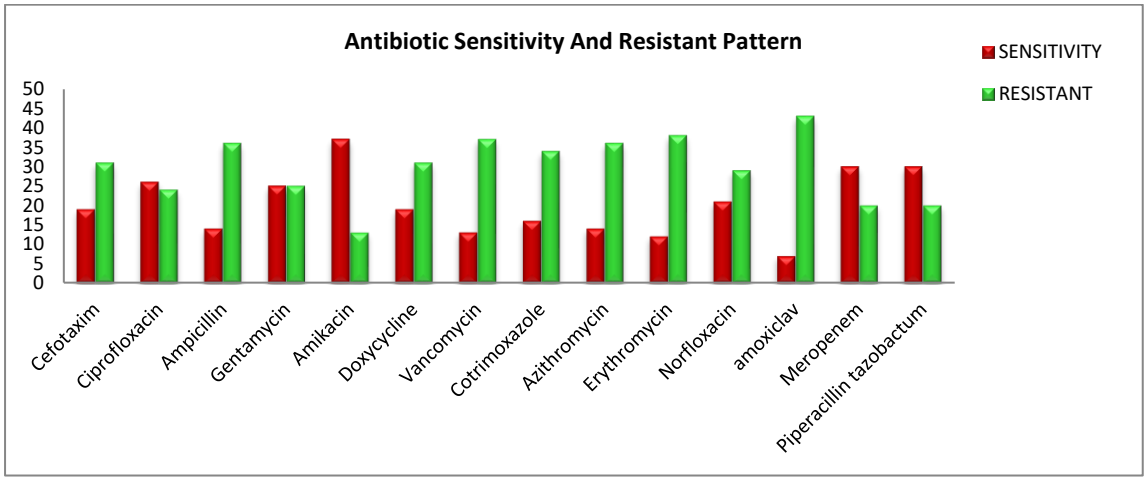


Table 5: Sensitivity Level Of Staphylococcus Species

ANTIBIOTICS	SENSITIVITY LEVEL (In mm)

Cefotaxime	26
Ciprofloxacin	30.2
Ampicillin	28.5
Gentamycin	28.2
Amikacin	28.5
Doxycycline	31.57
Vancomycin	25.7
Cotrimoxazole	29.4
Azithromycin	26.6
Erythromycin	27
Norfloxacin	28
Amoxiclav	30

FIG.6:

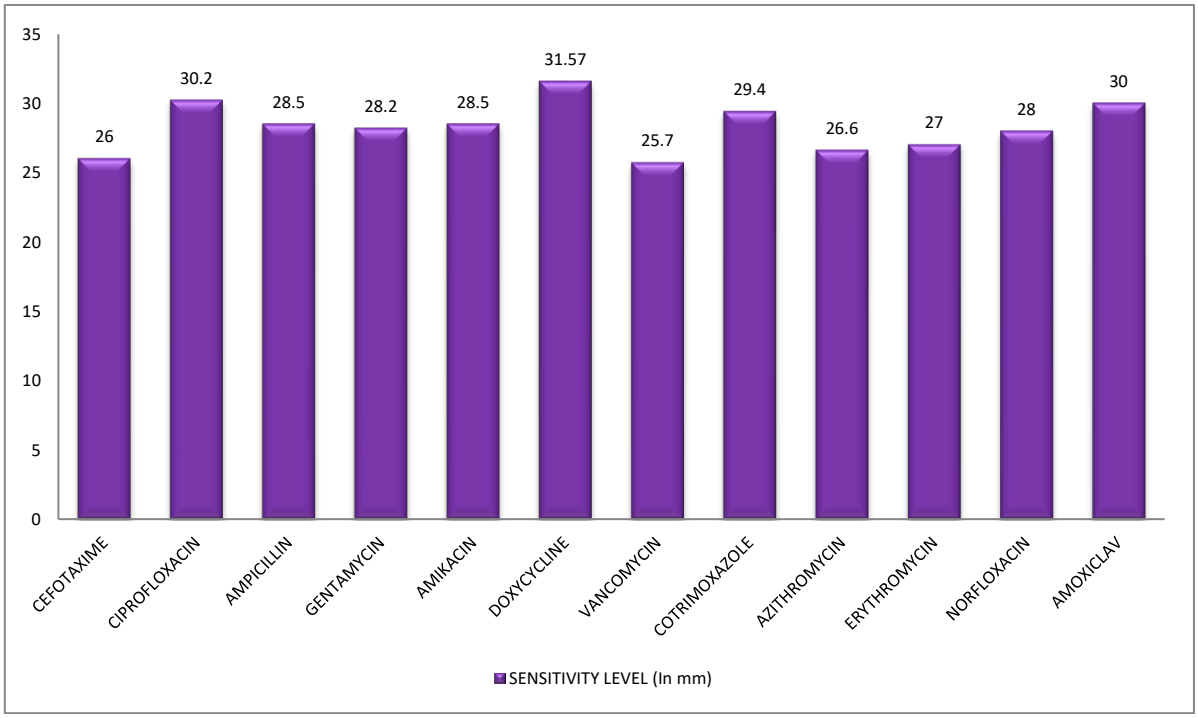


Table 6: Sensitivity Level of Klebsiella Pneumoniae

ANTIBIOTICS	SENSITIVITY LEVEL (In mm)
Cefotaxime	21
Ciprofloxacin	26.6
Ampicillin	28
Gentamycin	28.6
Amikacin	24
Doxycycline	25.6
Vancomycin	28
Cotrimoxazole	22
Piperacillin Tazobactam	25.7
Erythromycin	27
Norfloxacin	23
Amoxiclav	25
Meropenem	30.1

FIG.7

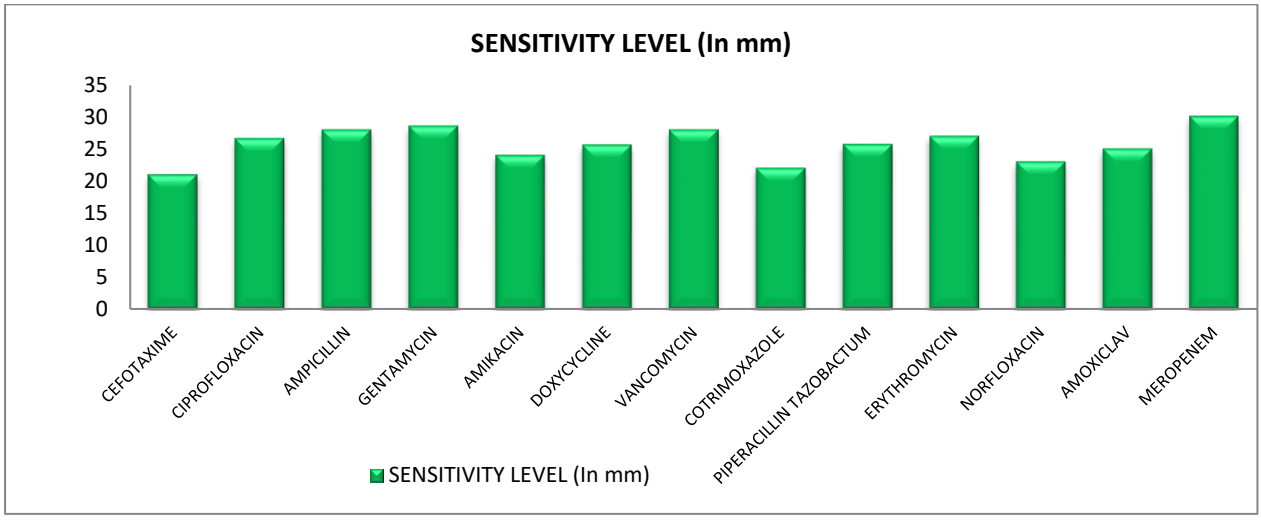


Table 7: Distribution Of Different Antibiotics Against Gram Positive Microorganisms

MICRO ORGANISMS	ANTIBIOTICS													
	CTX	NX	CIP	AMP	COT	MRP	PIT	AMC	AK	E	DO	VA	AZM	GEN
Staphylococcus Aureus	3	2	4	2	2	1	2	0	2	0	3	3	3	2
Staphylococcus Species	7	5	5	7	5	0	0	1	9	2	7	7	5	5
Streptococcus Species	0	0	0	1	0	0	0	0	2	1	1	1	1	1
Enterococcus Faecalis	1	0	4	0	1	1	1	2	4	0	2	1	3	4

FIG.8:

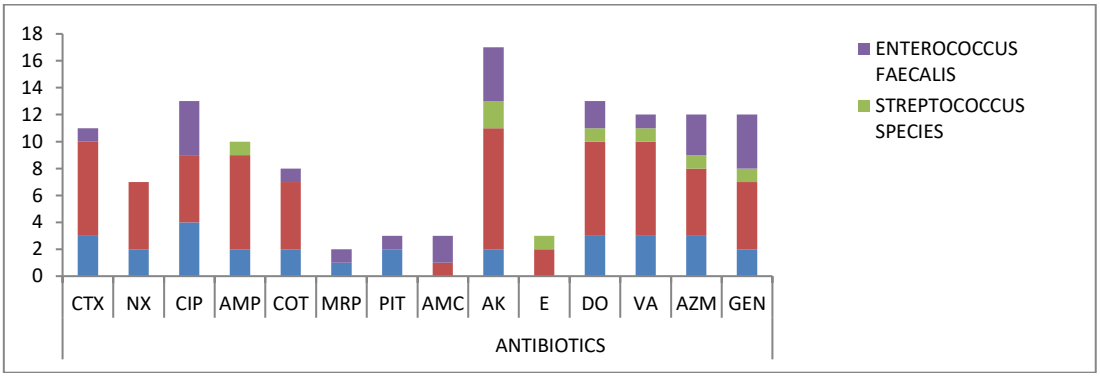
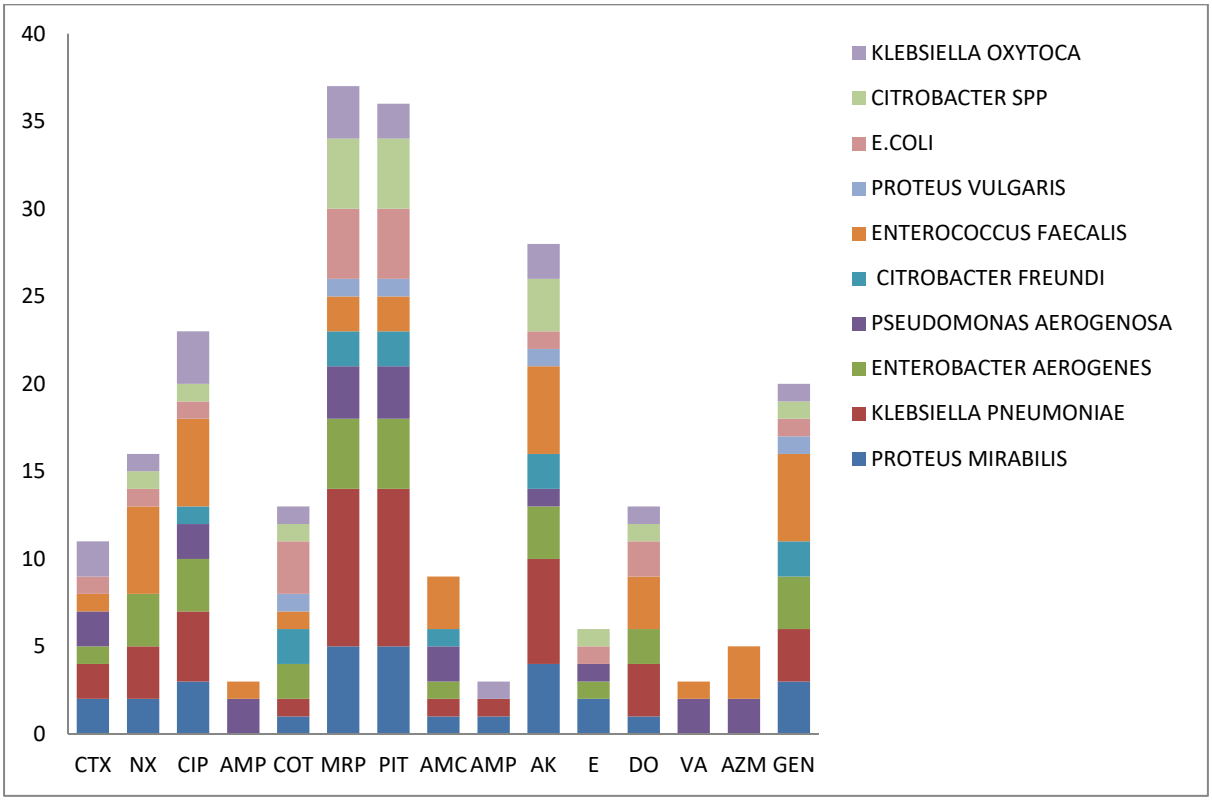


Table 8: Distribution of Different Antibiotics Against Gram Negative Microorganisms

ANTIBIOTICS	CTX	NX	CIP	AMP	COT	MRP	PIT	AMC	AK	E	DO	VA	AZM	GEN
Proteus Mirabilis	2	3	3	1	1	5	5	1	4	2	2	0	0	4
Klebsiella Pneumonia	2	4	3	1	1	8	8	1	7	0	1	0	0	3
Enterobacter Aerogenes	0	1	1	0	1	2	2	0	1	0	0	0	0	1
Pseudomonas Aerugenosa	1	0	1	1	0	2	2	1	1	1	0	1	1	0
Citrobacter Freundi	0	1	1	0	1	1	1	1	1	0	0	0	0	1
E.Coli	1	1	1	0	2	4	4	0	1	0	1	0	0	2
Proteus Vulgaris	0	0	0	0	1	1	1	0	1	0	0	0	0	1
Citrobacter Spp	0	0	0	0	0	3	3	0	2	1	0	0	0	0
Klebsiella Oxytoca	2	1	3	1	1	3	2	0	2	0	1	0	0	1

(CTX-Cefotaxime, NX-Norfloxacin, CIP-Ciprofloxacin, AMP-Ampicillin, COT-Cotrimoxazole, MRP-Meropenem,PIT-Piperacillin-Tazobactam,AMC-Amoxiclav,AK-Amikacin,E-Erythromycin,DO-Doxicycline,VA-Vancomycin,AZM-Azithromycin,GEN-Gentamycin)

Fig.9: Distribution of Antibiotics Against Gram Negative Microorganisms



DISCUSSION

Sepsis in neonates refers to generalised bacterial infection documented by positive blood culture in the early weeks of life and is one of the four leading causes of neonatal mortality and morbidity in India. Neonatal sepsis continues to be a major problem for neonates in neonatal intensive care unit around the world.

Our study has been conducted and carried out in SNCU, Govt. Head Quarters Hospital Tiruppur for a 6 months' time period. This study was conducted for identifying most common microorganisms causing neonatal sepsis and its antibiotic sensitivity. A similar study was conducted by Samuel EK Acquah et.al.[15] in Tamale Teaching Hospital also focused on the susceptibility of bacterial etiological agents and commonly used antimicrobial agents in neonatal sepsis.

The present study is an attempt to closely monitor the microorganisms causing neonatal sepsis and to identify the most sensitive antibiotic. In fig.1, a total number of 50 patients were analysed. Based on the type of microorganisms, the cases were categorized into gram positive and gram-negative cases. Out of these cases, gram positive cases were 20(40%) and gram-negative cases were 30(60%).

Fig.2 shows the classification of gram-positive microorganisms. Similar classification were made by Hardik V Vania et al[16] in a study conducted in north India. From the present study, staphylococcus species is the most predominant in gram positive organisms followed by klebsiella pneumoniae in gram negative organisms (fig.3). Similar results were made by Indrajit Gupta et. Al [17] and Ayman El Badawyet. al. [18] which showed klebsiella pneumoniae (40%) followed by CONS (20%).

Neonatal sepsis is broadly divided into two types according to age of onset: Early onset sepsis and Late onset sepsis. Fig.4 shows the risk factors that contributed to early onset sepsis and late onset sepsis. Among these, most neonates with early onset sepsis was with premature rupture of membrane while in case of late onset sepsis was very low birth weight and preterm infants as like in the study of Jun-Ho Wu et.al. from Taiwan [19] .

The analysis also showed the sensitivity and resistance of antibiotics towards the microorganism causing neonatal sepsis (Fig.5) and found out that, Amikacin is the most sensitive and Amoxiclav is the least sensitive antibiotic. When comparing with the study of Chandra Madhur Sharma et al [20], maximum isolates were sensitive to either Cefotaxime or Amikacin and a low susceptibility to commonly used antibiotics like Ampicillin and Gentamicin is a cause for concern.

Antibiotic resistance is a widespread problem. In the present study too, a large number of gram positive and gram-negative bacteria exhibited variable resistance to commonly used antibiotics. Among these amoxiclav showed more resistance. In contrast

to our study, Ashwini D et.al [21] noticed an increasing resistance of Erythromycin against most of the gram-positive isolates.

The most common gram-positive microorganism causing neonatal sepsis is staphylococcus species and its antibiotic sensitivity is shown in fig.6 based on sensitivity level. These data shows, Doxycycline (31.57mm) has more sensitivity and Cefotaxime (26mm) has the least sensitivity.

The most common gram-negative microorganisms causing neonatal sepsis is klebsiella pneumonia and its antibiotic sensitivity is given in table 5 based on sensitivity level. These data show Meropenem (30.1mm) has more sensitivity and Cefotaxime (26mm) has the least sensitivity.

Consistent with other studies, Amikacin showed maximum sensitivity against gram positive microorganisms (fig.7) while in case of gram-negative microorganisms, Meropenem and Piperacillin-Tazobactam showed highest sensitivity which showed in fig.9.

Recent study of Preeti Mallikarjunappa et al [22] and Shwetha nayak et al [23], Meropenem 18 (94.7%) and Imipenem 12 (63.15%) were highly sensitive for gram negative organisms.

CONCLUSION

It is evident from the study that gram positive organism, Staphylococcus species is the leading cause of neonatal sepsis followed by klebsiella Pneumoniae, a gram negative microorganism. Most of them are resistant to multidrug antibiotics.

Moreover, majority of neonates with early onset sepsis were term babies. In contrast, late onset sepsis affected mainly preterm and very low birth weight babies.

Amikacin, doxycycline and ciprofloxacin are the most sensitive antibiotics for gram positive organisms whereas meropenem and piperacillin-tazobactam are for the gram negative organisms causing neonatal sepsis.

Most of the organism has developed resistance to the commonly used antibiotics such as amoxiclav and erythromycin.

Moreover, an antibiotic policy should be formulated in the hospital. Antibiotic should be used depending on the antibiotic sensitivity pattern of the isolates.

CONFLICT OF INTEREST

None

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