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A Study of Current Trend of Sepsis Causative Organisms (Fungal and Bacterial) in Neonatal Blood Culture and their Drug Susceptibility Patterns at a Tertiary Care Hospital, Visakhapatnam, South India

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Background

Sepsis is one of the major causes of morbidity and mortality in new borns. it is the clinical manifestation of systemic infection during the first 28 days of life. It is classified as early onset (<72hrs) and late onset (>72hrs) of sepsis. By knowing the current spectrum of pathogens causing sepsis and their drug sensitivity pattern most cases of neonatal sepsis can be saved by prescribing appropriate drugs before culture report collected. Antibiotics may be lifesaving for the few infants who are truly infected. However, broad spectrum antibiotics increase colonization with drug resistant organisms and injudicious use of antibiotics increases antimicrobial resistance. In a critically ill neonate with negative blood culture Fungal sepsis should be suspected. Although Candida albicans has historically been most frequently isolated with good response to flucanazole but now a day's non albicans candida have emerged as one of the common pathogen. This change in trend may be due to resistance of candida species to azoles .According to pooled hospital data based on NNPD(national neonatal perinatal data) survey, the incidence of neonatal sepsis is around 30/1000 live births and this incidence is 1 to 8 cases in 1000 live births in United States[1.]

Materials and Methods

This is a descriptive study carried out in the NICU, Dept of Pediatrics, Andhra medical college, King George hospital, Visakhapatnam between April 2018- April 2019 (1 year). This study includes all neonates aged 0-28 days of life with presumptive diagnosis of neonatal sepsis admitted in our NICU. Babies >28 days of life or with other serious complications are excluded from this study. Neonates with suspected sepsis were investigated as per standard protocol and blood samples were collected with proper antiseptic precautions and sent to microbiology department of our institute where they do follow standard scientific procedure for blood cultures. As it provides a definitive diagnosis for neonatal sepsis and should be taken before starting antimicrobial therapy[3,4.] Parameters related to blood cultures such as bacterial versus fungal, gram positive/gram negative sensitivity and resistance pattern to various antibiotics were recorded and statistical analysis was done regarding frequency and percentages and the results were presented in tabular representation[5].

Results

Out of 1600 suspected neonatal sepsis blood cultures, 880 blood cultures positive for bacteremia and 60 for fungi .among bacterial organisms gram negative organisms accounts for 75.9% (668) and gram positive organisms are 24.1 % (212).

Organism Name	Number	Percentage
E.coli	289	32.9
Klebsiella	264	30.1
Staph Aureus	144	16.4
Pseudomonas	83	9.5
CONS	48	5.4
Proteus	22	2.4
MRSA	20	2.3
Acinetobacter	10	1.1
TOTAL	880	100%

Table 1: The common bacterial isolate in our study were E.coli (32.9%), Klebsiella(30.1%), Staphylococci Aureus (16.4%) and others such as Pseudomonas (9.5%),CONS (5.4%), and proteus & MRSA (2.3%), Acinitobacter (1.1%)

Organism Name	Number	Percentage
E.coli	289	43.2
Klebsiella	264	39.5
Pseudomonas	83	12.5
Proteus	22	3.2
Acinetobacter	10	1.6
Total	668	100(75.9%)

Table 2 : frequency of gram negative organisms isolated by blood culture of neonates with sepsis in the present study

Organism Name	Number	Percentage
Staph.aureus	144	67.9
CONS	48	22.6
MRSA	20	9.43
Total	212	100(24.1)

Table 3: frequency of gram positive organisms isolated by blood culture of neonates with sepsis in the present study

Antibiotic Sensitivity/resistance	E.coli S/R	Klebsiella S/R	Staph.aureus S/R	Pseudomonas S/R	Proteus S/R	Acinetobacter S/R	CONS S/R	MRSA S/R
Ampicillin	**28/200**	-/128	22/48	12/30	3/9	2/8	10/24	-/12
Amoxicillin	18/48	-/100	2/18	-/12	-/6	-/3	-/-	-/10
Amoxiclav	20/60	-/80	-/-	12/24	-/8	-/4	-/16	4/-
Amikacin	-/-	-/-	-/-	-/-	-/-	-/-	-/12	6/-
Azithromycin	-/-	30/-	58/-	-/-	-/-	-/-	18/12	12/-
Cefixime	76/78	**110/36**	24/14	14/14	-/-	-/-	-/-	-/6
Cefotoxime	32/18	2/36	-/14	14/-	-/-	-/-	-/-	6/-
Ceftazidime	118/62	84/28	18/-	24/12	-/-	-/-	-/-	-/-
Cefoxitine	-/-	15/32	54/42	14/-	-/-	-/-	14/13	8/-
Ceftriaxone	21/20	26/-	16/-	-/-	-/-	-/-	-/12	10/16
Cefpodoxime	10/40	40/38	-/24	16/16	-/6	-/4	-/16	-/-
Cefperozone+sulbactam	220/4	142/3	82/6	68/6	18/-	8/-	22/-	8/-

Cephalexin	-/-	18/22	14/-	-/-	-/-	-/-	-/-	-/-
Ciprofloxacin	70/28	-/24	28/14	12/-	-/-	-/-	-/-	14/6
cotrimoxazole	18/22	32/21	-/-	-/14	-/-	-/-	-/12	-/-
Clindamycin	-/-	14/22	18/32	-/-	-/-	-/-	-/-	8/8
Gentamycin	190/8	**136/22**	38/20	62/-	14/-	9/-	20/-	-/12
Imipenem	74/10	100/8	22/-	24/-	10/-	4/-	10/-	12/-
levofloxacin	-/-	38/12	-/-	21/-	-/-	-/-	14/-	-/-
Linezolid	-/-	-/-	42/34	-/-	-/-	-/-	14/-	14/2
Meropenem	118/6	52/-	24/-	22/-	10/-	4/-	-/-	-/-
Ofloxacin	38/2	48/24	48/-	18/-	-/-	-/-	18/12	10/-
Piparacillin+tazobactem	218/4	48/18	42/-	64/4	16/-	8/-	14/-	8/-
Tetracycline	-/-	-/-	78/4	-/-	-/-	-/-	18/10	6/-
Tigecycline	-/-	-/-	42/24	-/-	-/-	-/-	10/-	10/-
tiecoplanin	-/-	-/12	70/12	16/-	-/-	-/-	18/-	6/6
tobramycin	32/2	28/14	72/14	12/-	-/-	-/-	20/-	8/2
vancomycin	-/-	-/14	94/4	18/-	-/-	-/-	32/-	12/8

Table 4: shows antibiogram (sensitivity/resistance pattern) of all bacterial organisms.

Antibiotics	**Staph Aureus**	**CONS**	**MRSA**
Ampicillin	22(15.2%)	10(20.8%)	-
Cefotoxime	-	-	6(30.0%)
Ceftazidime	18(12.5%)	-	-
Ceftriaxone	16(11.1%)	-	10(50.0%)
Cefperazone+sulbactam	82(56.9%)	24(50.0%)	8(40.0%)
Ciprofloxacin	28(19.4%)	-	14(70.0%)
Clindamycin	18(12.5%)	-	8(40.0%)
Gentamycin	38(26.3%)	20(41.6%)	-
Linezolid	42(29.1%)	14(29.1%)	14(70.0%)
Meropenem	24(16.6%)	-	-
Ofloxacin	48(33.3%)	18(37.5%)	10(50.0%)
Pipzo	42(29.1%)	14(29.1%)	8(20.0%)
Tigecycline	42(29.1%)	10(20.8%)	10(50.0%)
Tiecoplanin	70(48.6%)	18(37.5%)	6(30.0%)
Vancomycin	94(65.2%)	38(79.1%)	12(60.0%)

Table 5: Shows antibiotic sensitivity pattern among gram positive bacterial isolates in the present study .65.2%(94/144), 56.9%(82/144) and 48.6%(70/144) of Staph Aureus isolates were found sensitive to Vancomycin, Cefperazone+Sulbactam and Tiecoplanin respectively .about 70%MRSA strains were sensitive to Linezolid and Ofloxacin and 79.1% CONS were found to be sensitive to Vancomycin.

Antibiotics	Staph aureus	CONS	MRSA
Ampicillin	48(33.3%)	24(50.0%)	12(60.0%)
Cefotoxime	14(9.7%)	-	-
Ceftazidime	-	-	-
Ceftriaxone	-	12(25.1%)	16(80.0%)
Cefperazone+sulbactam	6(4.1%)	-	-
Ciprofloxacin	14(9.7%)	-	6(30.0%)
Clindamycin	32(22.2%)	-	8(40.0%)
Gentamycin	20(13.8%)	-	12(60.0%)
Linezolid	32(22.2%)	-	2(10.0%)
Meropenem	-	-	-
Ofloxacin	-	12(25.1%)	-
Pipzo	-	-	-
Tigecycline	24(16.6%)	-	-
Tiecoplanin	12(8.3%)	-	6(30.0%)
Vancomycin	4(2.7%)	-	8(40.0%)

Table 6: Shows antibiotic resistance pattern among gram positive bacterial isolates in the present study 33.3% of Staph Aureus, 60% MRSA were found to be resistance to Ampicillin and 40% of MRSA found be resistance even to Vancomycin also.

Antibiotics	E.Coli	Klebsiella	Psudomonas	Proteus	Acinetobacter
Ampicillin	28(9.6%)	-	12(14.4%)	3(13.6%)	2(20.0%)
cefotoxime	32(11.0%)	2(0.7%)	14(16.8%)	-	-
ceftizidime	118(40.8%)	84(31.8%)	24(28.9%)	-	-
ceftriaxone	21(7.2%)	26(9.8%)	-	-	-
ciprofloxacin	70(24.2%)	28(10.6%)	12(14.4%)	-	-
Cefperazone+ sulbactam	220(76.1%)	142(53.7%)	68(81.9%)	18(81.8%)	8(80.0%)
Clindamycin	-	18(6.8%)	-	-	-
Gentamycin	190(65.7%)	136(51.5%)	62(74.6%)	14(63.6%)	9(90.0%)
Linezolid	-	42(15.9%)	-	-	-
Meropenem	118(40.8%)	52(19.6%)	22(26.5%)	10(45.4%)	4(40.0%)
Ofloxacin	38(13.1%)	48(18.1%)	18(21.6%)	-	-
Pipzo	218(75.4%)	48(18.1%)	64(77.1%)	16(72.7%)	8(80.0%)
Tigecycline	-	-	-	-	-
Ticoplanin	-	-	16(19.2%)	-	-
Tobramycin	32(11.0%)	28(10.6%)	12(14.4%)	-	-
Vancomycin	-	-	18(21.6%)	-	-

Table 7: Shows antibiotic sensitivity pattern among gram negative bacterial isolates in the present study. Cefperazone and Sulbactam, Piperacillin /Tazobactem and Gentamycin were the three most effective antibiotics for all gram negative organisms mentioned in the present study.

Antibiotics	E.coli	Klebsiella	Pseudomonas	Proteus	Acinetobacter
Ampicillin	200(69.2%)	128(48.4%)	30(36.1%)	9(40.9%)	8(80.0%)
cefotoxime	150(51.9%)	88(33.3%)	-	-	-
ceftizidime	62(21.4%)	28(10.6%)	12(14.4%)	-	-
ceftriaxone	98(33.9%)	82(31.0%)	-	-	-
ciprofloxacin	28(9.6%)	14(5.3%)	-	-	-
Cefperazone+ sulbactam	4(1.3%)	3(1.1%)	6(7.2%)	-	-
Clindamycin	-	32(12.1%)	-	-	-
Gentamycin	8(2.7%)	22(8.3%)	-	-	-
Linezolid	-	34(12.8%)	-	-	-
Meropenem	6(2.05%)	-	-	-	-
Ofloxacin	2(0.6%)	24(9.09%)	-	-	-
Pipzo	4(1.3%)	18(6.8%)	4(4.8%)	-	-
Tigecycline	-	-	-	-	-
Ticoplanin	-	12(4.5%)	-	-	-
Tobramycin	2(0.6%)	14(5.3%)	-	-	-
Vancomycin	-	14(5.3%)	-	-	-

Table 8: Shows antibiotic resistance pattern among gram negative bacterial isolates in the present study .we found that most of the gram negative organisms are resistant to Ampicillin and Cefotoxime and Ceftriaxone.

Organism	No of isolates	Percentage
Candida.albicans	33	55.1%
Candida.parapselosis	14	24.4%
Candida. glabrata	10	16.3%
Candida.tropicalis	2	4.0%
others	1	

Table 9: Shows characterization of various fungal species isolated from blood culture

Organism	Amphotericin	Flucanazole	Isolates
Candida.albicans	31(96.2%)	26(81.4%)	33
Candida.parapselosis	14(100%)	12(83.3%)	14
Candida. glabrata	9(93%)	3(25.0%)	10
Candida.tropicalis	2(100%)	1(50.0%)	2

Table 10: Shows antifungal suspceptability of candida isolates

Discussion

Emergence of increased antimicrobial resistance is due to Lacking of health system based ongoing surveillance of infections and tracking of antimicrobial resistance, information provided in the current paper will help practitioners stay vigilant for any change and institute appropriate practice modalities. Removal of antibiotic from the therapeutic regimen may lead to reversal of microbial resistance into susceptible phenomena have been described in the literature with serious public health ramifications as one study

mentioned that chloroquine once again became highly effacaious in Malawi,12 years after it was withdrawn from use because of rate of treatment failures in more than 50% cases.in the context of worldwide threat of microbial resistance our country condition is considered more stark than any other place. Most newborn units in our country are facing the problem of overwhelming resistance to all antibiotics particularly to cephalosporins[4.] Antimicrobial therapy can be made specific on positive culture and sensitivity reports. However, this would be known only after two to three days in a best institutions. Hence every treating unit should adapt a suitable policy based on spectrum of etiological agent and drug sensitivity and must be periodically reviewd and modified.

During the study period , out of 1600 newborn babies who had been primarily diagnosed as neonatal sepsis, culture confirmed sepsis (880/1600) are bacterial and (60/1600) are fungal. Out of 880 bacterial organisms isolated,75.9% (668/880) were gram negative and 24.1% (212/880) were gram positive which was in agreement with vaniya HV vd al study[6] (51%), shrestha et al study[7](44%), shahian at al study[8] (43%) and thakur s at al study[9](42%). Where as in meher at al study[1], they found culture positivity in 22.1% cases and jyothi p et al[16] found 92% culture positivity. in our study out of 1600 newborns suspected neonatal sepsis, 1136(71%) are outborn, 464(29%) are inborn which was in agreement with shamiya NK et al study[7] (outborn-75%, inborn-25%).

In our study, predominance of gram negative organisms is comparable with studies reported by Rahman[17] et al most common pathogen isolated is E.coli (32.9%), klebsiella(30.1%), staph aureus (16.4%) and pseudomonas(9.5%) but klebsiella was the predominant organism isolated in neonatal sepsis in studies reported by Vaniya HV[6] et al, Shrestha[7] et al, Jyothi[15] et al and Aletaveb[18] et al. whereas pseudomonas and staph aureus were the predominant isolate in studies done by Bhet[19] et al and Shahian[7] et al.

The analysis of antibiogram of our study revealed decreased sensitivity among gram negative isolates against commonly used antibiotics such as ampicillin, amoxicillin, amoxyclav and cefotaxime and ceftriaxone. This finding was in agreement with vaniya[6] et al study.

Gram negative isolates in our study were found most sensitive to cefperazone+salbactum, piperacillin+tazobactum and to gentamicin. This is in contrary to vaniya et al study where these isolates were most sensitive to ciprofloxacin and oflaxacin.

Gram positive organisms are most sensitive to tobramyin, vancomycin, cefperazone+salbactum where as MRSA isolates of our study were found most sensitive to ofloxacin, linezolid, vancomycin and tigecycline in jyothi[15] et al and vaniya[6] et al studies, found that gram positive isolates are most sensitive to linezolid.

In our study, we found overall very few isolates were sensitive to cefotaxime, ampicillin, amoxyclav and ceftriaxone. Among 60 fungal isolates, 33 are found to be candida albicans (55.1%) and remaining 44.9% are non-candida albicans, this was in comparison to study conducted by Agarwal[12] et al(13.6%) and Rani et al (11%)[13].

Combination of various risk factors (prematurity, low birth weight, prolonged antibiotic use, ventilator support and total parental nutrition) is known to be strongly associated with development of candidiasis[11]. Most of the fungal isolates are sensitive to amphotericin B compared to flucanazole[14]. This substantiates the need of prophylactic antifungal used in a setup where continuous upsurge in the incidence of fungal infection[10].

Conclusion

This study revealed gram negative organisms constituted major cause of neonatal sepsis and most of the organisms are resistant to commonly used antibiotics such as ampicillin, cefotaxime and ceftriaxone. Even for vancomycin at the same time in fungal isolates there was good correlation

between the virulence traits and antifungal agent flucanazole, so amphotericin B or newer azoles (voriconazole) are better alternatives[14]. Therefore we suggest an appropriate drug policy should be formulated in the hospital depending upon the antibiogram pattern. Unnecessary or excessive use of antibiotics should be discouraged at all levels. Institute should implement a surveillance program on antibiotic resistance. It is recommended to sensitize local hospitals regarding the common isolates and their drug sensitivity pattern to prevent emergence of drug resistance.

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