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BLOODSTREAM INFECTIONS AND ANTIMICROBIAL PROFILE IN PEDIATRIC PATIENTS WITH ASSOCIATED RISK FACTORS IN A TERTIARY CARE HOSPITAL

Clinical Microbiology

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ABSTRACT

Background- Blood stream infections are very common (up to 20–50 %.) in the pediatric age group in developing countries. The choice of empirical antimicrobial requires the knowledge of the epidemiology of common pathogens which constantly changes necessitating periodic review to their sensitivity profile to formulate an antibiotic policy. **Method-** This retrospective observational cross sectional study was conducted in Tezpur Medical College & Hospital, Tezpur, Assam from October 2020 to September 2021 among 138 samples from Pediatric cases (Day one to 14 yrs of age) with clinically suspected sepsis. **Result-** Out of 138 studied blood samples 36% (50/138) were culture positive. Out of 50 positive cases, 45(90%) of were in Neonatal group and 5(10%) were the non-neonatal group .Isolates were Gram positive cocci 56% (28/50), Gram negative bacilli 36% (18/50) and Candida albicans 8% (4/50). Isolates were Staphylococcus aureus 50% (25/50), Klebsiella pneumoniae 26% (13/50), Acinetobacter species 8% (4/50), Enterococcus species 4% (2/50), Coagulase negative Staphylococci 2% (1/50) and Escherichia coli 2% (1/50). S. aureus were sensitive to Vancomycin 100%, Linezolid 84%, Clindamycin 80%, Gentamicin 60%, Amikacin 60%, Cotrimoxazole 44%, Doxycycline 44% and Ampicillin 24%. MRSA among S. aureus was 28% (7/25). Only one of the isolates of CoNS, 1/2 (50%) was resistant to Ampicillin, Cotrimoxazole and Doxycycline whereas it showed 100% sensitive to vancomycin, Linezolid, Clindamycin, Gentamicin and Amikacin., All Gram positive isolates in this study were 100% sensitive to vancomycin. Klebsiella pneumoniae were found to be resistant to Cefuroxime 100%, but susceptible to meropenem 100% and imepenem 100% followed by amikacin 77%, gentamycin 69%. All of Gram-negative bacilli were susceptible to meropenem and imipenem. Maternal risk factors were PROM (Premature rupture of membrane) 17(37.7%), MSAF (Meconium stained amniotic fluid) 15 (33.3%), Prolonged labour12 (26.6%) and UTI 6(13.3%). Maternal febrile illness3(6.6%) and foul smelling liquor 3(6.6%). Among neonatal risk factors low birth weight 26(57.7%), Prematurity (42.2%), Perinatal asphyxia 17(37.7%) and Mechanical ventilation 3(6,6%). Patients were presented with refusal to feed 46.6% (21) ,Jaundice37.7% (17) Respiratory distress31.1% (14) and Convulsion28.8% (13). **Conclusion**- S. aureus and Klebsiella pneumoniae, were the leading cause of pediatric sepsis and resistant to multiple antibiotics. Risk factors identified were Premature Rupture of Membrane, Meconium Stained Amniotic fluid, Prolonged labour, LBW , Prematurity and Perinatal asphyxia .Commonest presentation were Refusal to feed, Jaundice and Respiratory distress.

KEYWORDS

Blood culture, Pediatrics Sepsis, Antibiogram, Risk factor

INTRODUCTION

Blood stream infections are very common in the pediatric age group and these are one of the common causes of morbidity and mortality in neonates and children[1]. In developing countries, the rate of blood stream infections in children is about 20–50% and it is estimated that one in five neonates is suffering from blood infection[2,3].. Blood stream infection is caused by a variety of Gram-positive as well as Gram-negative bacteria, and sometimes yeasts[4].. From region to region the spectrum of causative organisms varies and changes over times. This is due to the changing pattern of lifestyle and changes in antibiotic use[5].

Several risk factors have been identified both in the neonates and children, which make them susceptible to infections. The risk factors for neonatal septicemia include premature rupture of membrane, prolonged rupture of membrane, prematurity, maternal urinary tract infection, poor maternal nutrition, low birth weight, birth asphyxia and congenital anomalies (Meremkwer *et al.,* 2005)[6]. While in children are serious injury, chronic antibacterial therapy, malnourishment, chronic medical problems, and immuno-suppressants therapy constitutes the risk factors for septicemia. Polymicrobial sepsis occurs in high risk patients and is associated with catheters, gastrointestinal diseases, neutropenia and malignancy[6].

Children with septicemia present with fever, difficulty in breathing, tachycardia, malaise, refusal of feeds or lethargy[7]. Septicaemia may have serious consequences like shock, disseminated intravascular coagulation, multiple organ failure, etc. Therefore timely detection and identification of blood stream pathogen is important (Bailey and Scott's Diagnostic Microbiology)[8] . Though clinical assessment using symptoms and sign is a useful guide for the provisional diagnosis of septicemia ,bacteriologic culture to isolate the offending pathogen remains the mainstay of definitive diagnosis of septicemia[1].

The choice of empirical antimicrobial requires the knowledge of the epidemiology of common pathogens which constantly changes, necessitating periodic review and their sensitivity profile to formulate an antibiotic policy. The present study was designed and implemented to determine the etiology of blood stream infections in pediatric patients and to examine antibiotic susceptibility patterns of the isolated organisms and to correlate associated risk factors.

MATERIALS AND METHODS

This retrospective observational cross sectional study was conducted in the Department of Microbiology in collaboration with the Department of Pediatrics, Tezpur Medical College & Hospital, Tezpur, Assam from October 2020 to September 2021. A total 138 samples from Pediatric cases with clinically suspected sepsis were studied. Under aseptic precautions, single blood samples were collected from each patients. 1 – 2 ml of blood was collected in BacT/ALERT Pediatric FAN blood culture bottles. Blood culture bottles were placed in the BacT/ALERT blood culture instrument as soon as possible after arrival in the Microbiology laboratory. The blood culture bottles are incubated in The BacT/ALERT automated blood culture system and a positive result is signaled immediately upon detection of carbon dioxide production in the blood culture bottle. Positive blood culture bottles are uploaded according to BacT/ALERT instrument operation protocol and subcultures done onto blood agar and Mac Conkey's agar plates and incubated aerobically at 35-37°C. Plates were examined for the growth of bacteria. All positive cultures were identified by their characteristic appearance on their respective culture media, Gram staining reaction and were confirmed by the pattern of biochemical reactions using the standard methods (Mackie and MacCartney)[9]

The antibiotic susceptibility test was done by Kirby-Bauer disk diffusion method. Zone sizes were measured and interpreted according to Clinical and Laboratory Standard Institute CLSI standards[10]. The antimicrobial discs used were from HiMedia Lab Ltd. Staphylococcus aureus ATCC 23235 and Escherichia coli ATCC 25922 were used as quality control strains. Antimicrobial discs were used for determination of sensitivity by disc diffusion test were AMP-

Ampicillin, GEN- Gentamicin, AK- Amikacin, COT- Cotrimoxazole, DOX- Doxycycline, CD- Clindamycin, LID- Linezolid, VAN- Vancomycin for Gram positive bacteria and AMC- Amoxy-clavunate, PIT- Piperacillin + Tazobactum, CAZ- Ceftazidime, CTR- Ceftriaxone, CXM- Cefuroxime, IMP- Imipenem, MER- Meropenem, GEN- Gentamicin, Ak- Amikacin, LEV- Levofloxacin, COT- Cotrimoxazole for Gram negative bacteria.

The different clinical manifestations and the risk factors associated with both neonatal and maternal causes in all positive cases were collected from departmental record book.

RESULTS AND OBSERVATIONS

A total of 138 blood samples from paediatric cases with suspected history of sepsis were received to the department of microbiology during the period from October 2020 to September 2021. Out of which 36% (50/138) were culture positive, while 64% (88/138) were sterile.

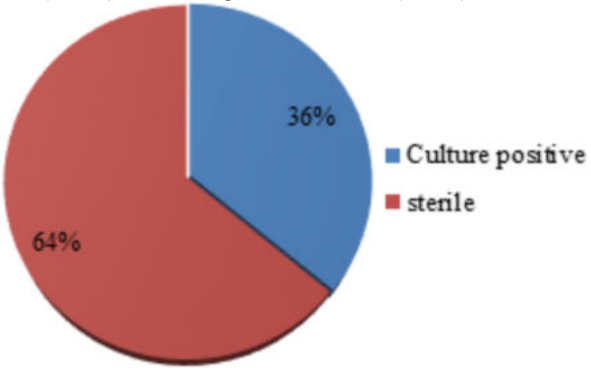


Fig 1: Culture results of blood stream infections

Fig 2 shows age and sex wise distribution of culture positive samples. Neonatal group (between 0 to 1month) of patients constituted 90% (45). In the non-neonatal group (beyond 1 month of age) only 10 % (5). further d non-neonatal group was further divided as between 1months -5yrs (2), 6-10 years (2) and 11-14yrs (1). Out of 50cases 60%(30/50)were male and 40%(20/50)were female.

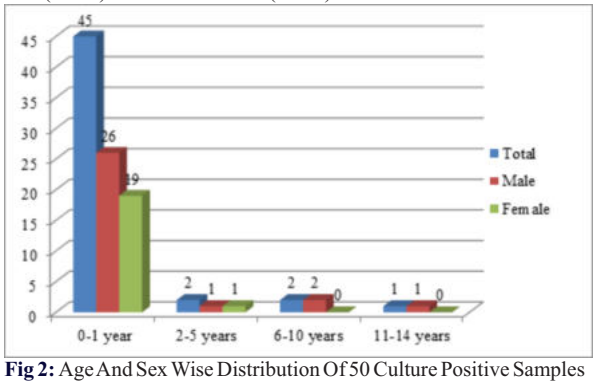
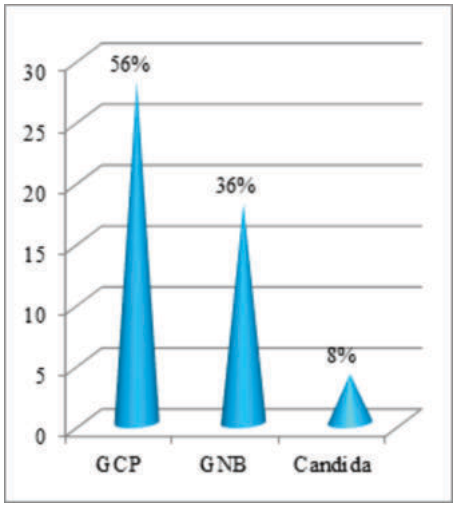


Fig 2: Age And Sex Wise Distribution Of 50 Culture Positive Samples



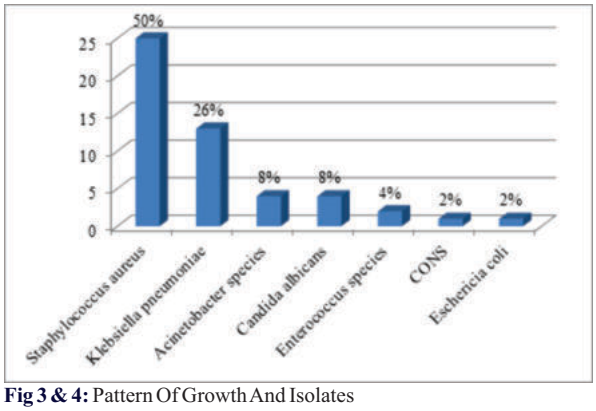


Fig 3 & 4: Pattern Of Growth And Isolates

The most common isolate in this study was Gram positive cocci which accounts for 56% (28/50), followed by Gram negative bacilli were 36% (18/50) and Candida albicans 8% (4/50) (Fig 3). Among Gram positive cocci, the predominant isolate was *Staphylococcus aureus* 50% (25/50) followed by Enterococcus species 4% (2/50) and *Coagulase negative Staphylococci 2%* (1/50). Among Gram negative bacilli, the predominant isolate was *Klebsiella pneumoniae* 26% (13/50) followed by Acinetobacter species 8% (4/50) and *Escherichia coli* 2% (1/50) (Fig 4).

Table 1: Demographic Characteristic Of Culture Positive Cases Neonatal Group

	TOTAL (45)	Early Onset Sepsis 29 (64.4%)	Late Onset Sepsis 16 (35.5%)
GENDER			
MALE	26(57.7%)	17 (37.7%)	9 (20%)
FEMALE	19(42.2%)	12(26.6%)	7(15.5%)
GESTATION			
PRETERM	19 (42.2%)	13(28.8%)	6(13.3%)
TERM	26(57.7%)	16(35.5%)	10(22.2%)
BIRTH WEIGHT			
<2500	28(62.2%%)	19(42.2%)	9(20%)
2500 or more	17 (37.7%)	10(22.2%)	7(15.5%)
PLACE OF DELIVERY			
INBORN	34 (75.5%)	24(53.3%)	10(22.2%)
OUTBORN	11 (24.4%)	5(11.1%)	6(13.3%)
MODE OF DELIVERY			
LSCS	29 (64.4%)	18(40%)	11(24.4%)
SVD	16(35.5%)	11 (24.4%)	5(11.1%)

Table 1 shows the demographic characteristics of the neonatal patients, Out of 45 culture positive newborn cases Early onset sepsis (i.e sepsis occurring within 72 hours of birth) is 29 (64.4%) while late onset sepsis (beyond 72hrs of birth) is 16(35.5%). Male 57.7% (26) and female35.5% (19), Term babies constituted57.7% (26) against preterm baby 42.2% (19). Majority of the babies were low birth weight 62.2% (28). Most of the babies 34(75.5%) were born in our hospital itself. Normal delivery among culture positive cases were only 16(35.5%), rest 64.4% (29) were conducted by LSCS.

Table 2: Risk Factor For Neonatal Sepsis:

Features	Cases	Percentage
MATERNAL RISK FACTORS		
Meconium Stained Amniotic Fluid (MSAF)	15	33.3%
Premature Rupture of Membrane(PROM)	17	37.7%
Urinary Tract Infection	6	13.3%
Febrile illness (UTI)	3	6.6%
Foul smelling liquor	3	6.6%
Prolonged labour	12	26.6%
NEONATAL RISK FACTORS		
Low birth weight	26	57.7%
Prematurity	19	42.2%
Perinatal asphyxia	17	37.7%
Mechanical ventilation	3	6.6%

Table 2 shows the risk factor for neonatal sepsis which is further divided into maternal and neonatal risk factors. Among Maternal risk factors majority of cases were associated with PROM (Premature

rupture of membrane) 17(37.7%) followed by MSAF (Meconium stained amniotic fluid) 15 (33.3%), Prolonged labour12 (26.6%) and UTI 6(13.3%). Maternal febrile illness and foul smelling liquor 3(6.6%) each. Among neonatal risk factors low birth weight was 26(57.7%), Prematurity (42.2%), Perinatal asphyxia 17(37.7%) and Mechanical ventilation 3(6,6%).

Table 3: Clinical Feature Of Newborn Sepsis

CLINICAL FEATURE	TOTAL	EOS	LOS
Refusal to feed	21(46.6%)	12 (26.6%)	9 (20%)
Jaundice	17(37.7%)	5 (11.1%)	12(26.6%)
Respiratory distress	14 (31.1%)	11 (24.4%)	3(6.6%)
Convulsion	13 (28.8%)	10 (22.2%)	3(6.6%)
Lethergy	4(8.8%)	3 (6.6%)	1(2,2%)
Cyanosis	2((4.4%)	0	2 (4.4%)
Hypothermia	4 (8.8%)	1(2.2%)	3(6.6%)
Abdominal distension	3 (6.6%)	0	3(6.6%)
Vomiting	2 (4.4%)	0	2 (4.4%)
Fever	1 (2.2%)	0	1(2.2%)
Pus from umbilicus	1 (2.2%)	0	1 (2.2%)
Skin pustule	2 (4.4%)	0	2 (4.4%)
Shock	2 (4.4%)	1 (2.2%)	1 (2.2%)
Bleeding	1 (2.2%)	0	1 (2.2%)

Majority of the babies presented with refusal to feed 46.6% (21) followed by Jaundice37.7% (17) Respiratory distress31.1% (14) and Convulsion28.8% (13). Jaundice is more in late onset group. Fever is found only in on 1(2.2%) baby while hypothermia found in 4 (8.8%) babies. 3 (6.6%babies presented with abdominal distension, all are late onset and later diagnosed as Necrotizing Enterocolitis. Convulsions were mostly perinatal asphyxia except 2 cases of hypoglycaemia. Other clinical features presented were lethergy4 (8.8%), Cyanosis2(4.4%), Vomiting 2(4.4%), Pus from umbilicus1(2.2%), Skin pustules2(4.4%), Bleeding 1(2.2%) and shock 2(4.4%)

Table 4: Non Neonatal Group (1MONTHS -14YR)

Total number of culture positive cases	5	Male 3 Female 2
Diagnosis	Septic Arthritis of hip joint with cerebral palsy	1
	Post operative case of Congenital Heart Disease with Pneumonia	1
	Multiple intramuscular and subcutaneous abscess with Hb E disease	1
	Right upper limb thigh abscess	1
	Pneumonia with severe PEM.	1
Presentation	Fever	5
	Pain	3
	Difficulty in breathing	3
	Cyanosis	2
	PEM	4
	Hypotension	2
Organism detected	Staph Aureus	5

Table 4 shows different parameters for cases beyond 1moth to 14 years. Total number of cases was 5, out of which 3 were male and 2 were female. Diagnoses were different in all cases as shown in the table. All 5 cases presented with high fever. Weight for age is normal for one case only, other 4 were having protein energy malnutrition. Pain and difficulty in breathing in 3 cases. Cyanosis and hypotension are associated with 2 cases. Staph aureus is detected in blood culture of all 5 cases.

Table 5: Antimicrobial Susceptibility Pattern Of Gram Positive Bacterial Isolates From Blood Culture

Antibiogram pattern (%)								
Organism isolated	**AK**	**CD**	**AMP**	**COT**	**DOX**	**LID**	**VAN**	**GEN**
Staphylococcus aureus	60	80	24	44	44	84	100	60
Enterococcus species	0	0	0	0	50	100	100	0
CONS	100	100	0	0	0	100	100	100

Table 6: Antimicrobial Susceptibility Pattern Of Gram Negative Bacterial Isolates From Blood Culture

Antibiogram pattern (%)											
Organism isolated	**AK**	**COT**	**GEN**	**PIT**	**CTR**	**CXM**	**AMC**	**IMP**	**MER**	**LEV**	**CAZ**
Klebsiella pneumoniae	77	23	69	54	31	0	62	100	100	23	31
Escherichia coli	100	100	100	0	0	0	0	100	100	0	0
Acinetobacter species	25	0	25	0	0	0	0	100	100	25	0

Antimicrobial Susceptibility Test

The antibiotic susceptibility pattern of Gram positive organisms and Gram negative organisms were detailed in the table 5 and 6 respectively.

Susceptibility patterns of Gram-positive bacteria (n = 28) isolated from the blood cultures of suspected BSI against 8 antibiotics were presented in Table 5. Gram-positive isolates produced wider variations in their susceptibility patterns. Isolates of *S. aureus* were sensitive to antibiotics such as vancomycin 100%, Linezolid 84%, Clindamycin 80%, Gentamicin 60%, Amikacin 60%, Cotrimoxazole 44%, Doxycycline 44% and Ampicillin 24%. Among the 25 isolates of *S. aureus*, 7 were with a zone of inhibition ≤ 21 mm (16.2 to 19.5 mm)), in the cefoxitin disc diffusion assay and were extrapolated as methicillin-resistant *S. aureus* (MRSA). The percentage of MRSA among *S. aureus* was 28% (7/25). Only one of the isolates of CoNS, 1/2 (50%) was resistant to Ampicillin, Cotrimoxazole and Doxycycline whereas it showed 100% sensitive to vancomycin, Linezolid, Clindamycin, Gentamicin and Amikacin. In case of *Enterococci* species 4% (2/50) of the isolates were resistant against Ampicillin, Cotrimoxazole, Clindamycin, Gentamicin and Amikacin whereas it showed 100% sensitive to vancomycin, Linezolid and 50% to Doxycycline. Overall all Gram positive isolates in this current study were 100% sensitive to vancomycin.

The extent of antimicrobial resistance by Gram negative organisms are shown in Table 6. All of these Gram-negative isolates were 100% susceptible to meropenem and imepenem. All the isolates of *Klebsiella pneumoniae* were found to be resistant to Cefuroxime 100%, and on the contrary, all were susceptible to meropenem 100% and imepenem 100% followed by amikacin 77%, gentamycin 69%. Similarly, isolate of Acinetobacter species had shown 100% resistance to Amoxy-clavunate, Piperacillin + Tazobactum, Ceftazidime, Ceftriaxone, Cefuroxime and Cotrimoxazole whereas Imipenem and Meropenem showed 100% susceptibility followed by 25% sensitive to Gentamicin, and Levofloxacin. 100% of *E. coli* were susceptible to meropenem, imipenem, amikacin, gentamycin and Cotrimoxazole. Altogether, it is clear from the results that all of Gram-negative bacilli respectively were susceptible to meropenem and imipenem.

DISCUSSION

Culture positivity in our study was 36% which is close to studies done by Wasihun et al (28%)[11] and Rashmi P et al (26.5%)[12,] but some studies showing very low positivity rate like Jatsho J et al (14%)[13] The difference in positivity may be due to different criteria for sending blood culture from patient.

In our study we found male preponderance (60%) which is similar to Rashmi P et al (64.5%.)[12,] Jatsho J et al (52.3%)[13] and Tallur et al[14.]

Majority (75.5%)of the culture positive cases were inborn patient which is similar to Jatsho J et al (86.4%)[13] but some study found low number of inborn sepsis patient like 59.1% in Rashmi P at al[12] This may be late arrival of complicated cases to our hospital.

Mode of delivery was found to be LSCS in 64% of cases which is more than Jatsho J et al (50%)[13] and Rashmi P et al (39.3%)[12]. This may be due to more number of complicated deliveries were conducted by LSCS.

In our study majority of cases (64%) were early onset sepsis (EOS)which is similar to Galhotra S et al (82.4%)[15]. Prevalence of higher EOS than Late onset sepsis(LOS) has been reported by various authors like Jai NK et al (68%)[16] and Vinodkumar CS et al(73%)[17]. However Kuruvilla et al[18]had reported a lower rate of EOS (22.9%) than LOS (77.1%). This could be due to the fact that they defined EOS as <48 h and LOS as >48 h.[24]

The risk factors for sepsis were identified by different studies differently. Our study reveals commonest maternal risk factors associated were PROM (37.7%) MSAF (33.3%) and prolonged labour (26.6%) while Rashmi et al[12] found MSAF, UTI and PROM as commonest associated risk factor. Neonatal commonest risk factor associated is LBW (57,7%), prematurity (42.2%), perinatal asphyxia. (37.7%) Which is similar to Jatsho J et al[13] LBW (59.1%) prematurity (52.2%) and perinatal asphyxia (31.8%).

Presentation of sepsis varies depending on severity of disease and immune status of newborn. In our study Refusal to feed, Jaundice and Respiratory distress were commonest presentation while Galhotra S et al[15] found Hypothermia and Respiratory distress as commonest presentation.

In the present study Gram positive and Gram negative organisms accounted for 56 % and 36 % respectively, which is in concordant with that of Mikulska *et al.,* (2014) (55% and 45%)[19]. Among Gram positive organism, *Staphylococcus aureus found* (50 %), which was similarly observed in Wasihun *et al.* (28%)[11]and among Gram negative organisms, *Klebsiella pneumonia* (26 %) were the most common isolates, similarly was observed in Premalatha *et al.,* (2014) 36.36% study[20]. In this study, the proportion of MRSA was 20 %. The occurrence of MRSA is more common because of indiscriminate use of higher antibiotics as an emergency empirical therapy. Vancomycin remains the drug of choice for the Gram positive bacterial isolates. *Klebsiella pneumonia*e was more sensitive to imipenem (100%), meropenem (100%), amikacin (77%), gentamicin (69%) and amoxy-clav (62%) and resistant to cephalosporins and levofloxacin, which is similar to study by Premalatha *et al.,* (2014) [20]. All Gram negative isolates were 100% imipenem and meropenem, so was observed in Premalatha *et al.,* (2014) study [20].

CONCLUSION:

In conclusion, it is evident from this study that among Gram positive organisms *S. aureus* and among Gram-negative organisms *Klebsiella pneumoniae*, are the leading cause of paediatric sepsis. Also the most challenging observation was the resistance pattern of these isolates to multiple antibiotics. The main forces driving the increase in antimicrobial resistant bacteria are the inappropriate use of antibiotics. Specific antibiotic utilization strategies like antibiotic restriction, combination therapy and antibiotic escalation and de-escalation may help to decrease or prevent the emergence of resistance. Risk factors associated with blood stream infection were Premature Rupture of Membrane,,.Mecnium Stained Amniotic fluid and prolonged labour .Neonatal commonest risk factor associated is LBW , prematurity perinatal asphyxia. Presentation of sepsis varies depending on severity of disease and immune status of newborn. In our study Refusal to feed, Jaundice and Respiratory distress were commonest presentation

Recommendation

Continuous monitoring of paediatric septicaemia and formulation of appropriate antibiotic policy is the need of the hour for surveillance and control of infection in the hospital.

Conflict of Interest- None,

Disclaimer- Nil

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