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RESEARCH ARTICLE

AN OBSERVATIONAL STUDY OF BACTERIOLOGICAL PROFILE OF REFERRED NEONATES ADMITTED IN ATERTIARY CARE CENTER OF NORTH INDIA

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Abstract

A prospective observational study was conducted in a neonatal unit of referral teaching hospital of North India with an aim to study the bacteriological profile and sensitivity pattern of referred neonates. During this period of one year, incidence of culture positive sepsis was 34 % among which gram-negative bacilli predominated in both early onset and late onset sepsis. In early onset neonatal sepsis, predominant organism was Klebsiella pneumoniae followed by Staph aureus and Acinetobacter. In late onset sepsis, most common organism was again Klebsiella pneumoniae followed by Acinetobacter, Candida, Staph and E. coli. Sensitivity pattern of isolated organism and outcome of referred newborns are presented.

Introduction:-

Systemic infection is an important cause of neonatal mortality worldwide. The situationin low and middleand income country (LMIC) is still worse. There are 1.6 million neonatal deaths every year in the world with major contribution fromLMIC (1). The antibiotic use in South East Asia region is quite rampant and multidrug resistance is quite common. These antibiotics are being used for empirical treatment and often blood culture are not being done due to poor facility for blood culture and high cost of blood culture as well (2). The use of 3rdand 4th generation cephalosporin is quite common in peripheral centers. Even carbapenem and colistin is also being used for empirical treatment of neonatal sepsis in some settings. This prospective observational study was planned to evaluate the common organism and their sensitivity pattern.This study will guide us in making antibiotic policy for our institute and local area.

Materials and Methods:-

This study was conducted at pediatric emergency of Nalanda Medical College and Hospital, Patna Biharfrom March 2014 to February 2015.The written informed consent was obtained from parents or guardian before enrolling the neonate intothe study. The study is approved by institute ethics committee. In this prospective observational study, we enrolled one hundred and fifty neonates referred from adjoining areas. We analyzed the referral slip for antibiotic details. In case referral slip is missing or incomplete, we tried to get the information from parents or accompanying person. Our study did not involve any extra blood sampling or any extra investigation. The interview of parents or accompanying person was conducted in a separate room only after stabilization of neonate and treatment had been initiated.At admission, blood culture was sent to all neonates enrolled in the study. Those neonates who did not receive antibiotic prior to referral and at risk for sepsis were started on antibiotics as per hospital policy and blood

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was sent for culture and sensitivity. For empirical treatment of early onset neonatal sepsis (EONS), we started ciprofloxacin and Amikacin and for empirical treatment of late onset sepsis (LONS), Cefotaxime and Amikacin were started. In case blood culture was positive, the antibiotics were changed as per sensitivity pattern and repeat blood culture was sent after 5 days of sensitive antibiotic. We also analyzed the outcome of neonates. Sepsis was classified as early onset neonatal sepsis (EONS) and late onset neonatal sepsis (LONS) based on timing of culture positivity. EONS is defined as blood culture positivity within 72 hours of life. LONS is defined as blood culture positivity after 72 hours of life. All standard guidelines were followed during collection of blood sample from neonates (3,4). Based on birth weight and gestational age neonates are classified into SGA (small for gestational age), AGA (appropriate for gestational age), LGA (large for gestational age) based on Fenton's chart. ELBW (extremely low birth weight) is defined as weight< 1000 gram. LBW (low birth weight) is defined as weight < 2500 gram. Normal birth weight is weight between 2500 gram – 4000 grams. Extreme preterm is defined as gestation below 28 weeks, preterm is 28 weeks to < 37 weeks and term is ≥ 37 weeks. Illiterate means the parents were unable to write their names. Primary education is defined as educated up to 7th standard.Inclusion criteria was a neonate on antibiotic or risk of sepsis. Sepsis risk was defined as per our unit policy. We followed the baby till discharge or death.

Results:-

During our study period, two hundred and thirty-two neonates were brought to NICU. One hundred and sixty-two neonatessatisfied the inclusion criteria, but twelve parents refused to give consent.Finally, one hundred and fifty neonates were included in the study.

Demographic profile of neonates admitted to NICU consists of male -60 %, term - 65%, extremely low birth weight – 3 %, small for gestational age - 25%. Most of the parents (90%) were educated up to primary and majority of parents (92 %) are farmer or daily wage laborer. Demographic details are shown in table 1.

Table 1:- Demographic Profile.

Gender	Male	Female	Intersex
	60 %	40%	0
Gestational Age	Extreme Preterm	Preterm	Term
	3 %	32 %	65%
Birth Weight	ELBW	LBW	Normal weight
	3 %	37 %	60 %
Intrauterine Growth Status	SGA	AGA	LGA
	25%	75 %	00
Educational Status	Iliterate	Primay	Above primary
	06 %	90 %	04 %
Occupational status	Farmer	Labor	Others
Father	80 %	12%	08 %

Blood culture were sent to all babies who were enrolled in the study. Contaminant reported was 10 % (n=15). Culture positivity rate was 34 % (n = 51)sparing contaminant.Among the organism grown, gram negative bacilli predominated in both EONS and LONS. Rate of EONS was 10% (n=15) and rate of LONS was 24% (n=36).

In EONS growth, more than half of the organism were gram negative bacilli namely Klebsiella pneumoniae. Remaining was contributed by Acinetobacter baumannii and Staph aureus. Majority of Gram-negative bacilli were sensitive to Amikacin. Majority of Gram-positive bacteria was sensitive to Vancomycin. Details of culture is shown in figure 1 and sensitivity is shown in table 1A and 1B.

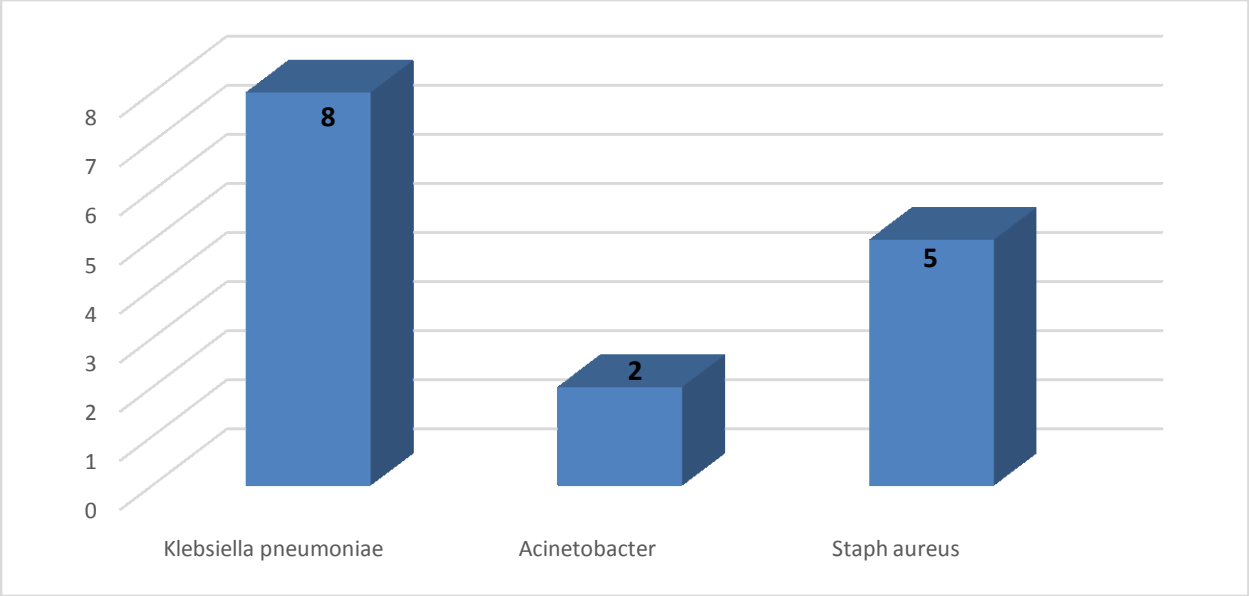

Figure 1: - Culture Pattern in EONS.

Table 1A:- Sensitivity Pattern of gram-positive EONS organism (n=5).

Antibiotic	Sensitive (%)	Resistant (%)
Methcillin	01(20)	04(80)
Vancomycin	05(100)	----
Clindamycin	04(80)	1(10)
PiperacillinTazobactam	04(80)	1(20)
Linezolid	05(100)	00
Ciprofloxacin	05(100)	00

Table 1B:- Sensitivity Pattern of gram-negative EONS organism.

Antibiotic	Sensitive (%)	Resistant (%)
Amikacin	08(80)	02(20)
Meropenem	10(100)	00
Colistin	10(100)	00
Ciprofloxacin	02(20)	08(80)
Cefotaxime	04(40)	06(60)
Cefoperazone-sulbactam	05(50)	05(50)
Piperacillintazobactam	07(70)	03(30)

Late onset organism was predominated by multidrug resistant bacteria and fungus. More than two – third of bacteria were multidrug resistant. Fungal growth was also noted in LONS which were resistant to first line antifungal drugs. Details of growth is shown in figure 2 and sensitivity pattern is shown in 2A and 2B.

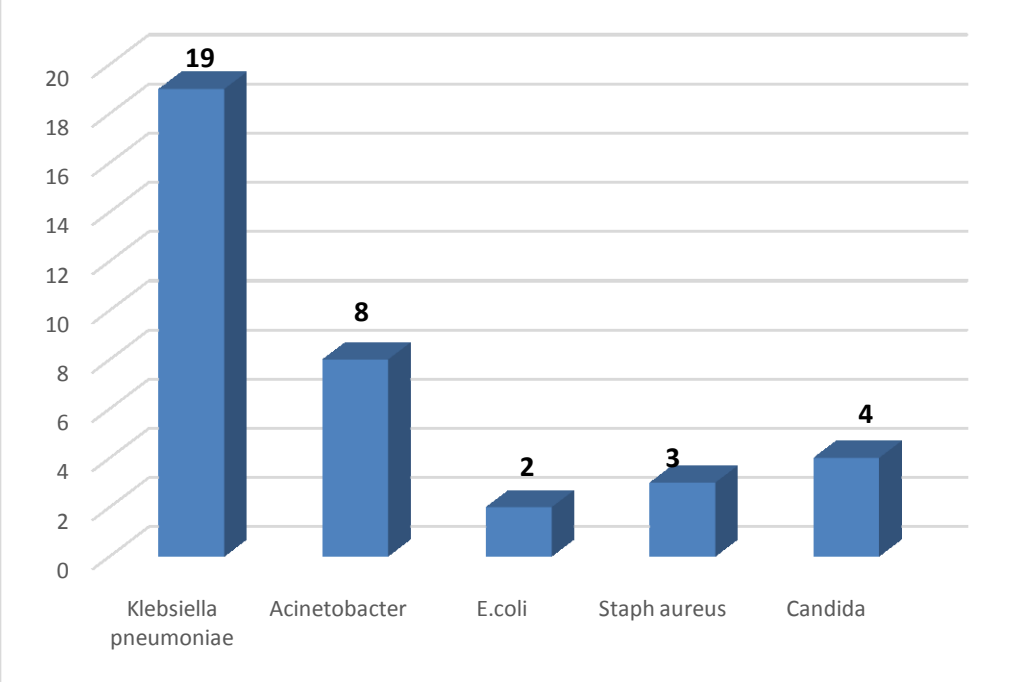

Figure 2: -Culture Pattern in LONS.

Table 2A:- Sensitivity Pattern of gram-positive bacteria in LONS (n=3).

Antibiotic	Sensitive (%)	Resistant (%)
Methcillin	0(0)	3(100)
Vancomycin	03(100)	00
Clindamycin	03(100)	0(0)
Piperacillin-Tazobactam	02(67)	01(33)
Linezolid	03(100)	00

Table 2B:- Sensitivity Pattern of gram-negativebacteria and fungus in LONS (n= 33).

Gram negative organism= 29		
Antibiotic	Sensitive (%)	Resistant (%)
Amikacin	10(34)	19(56)
Meropenem	16(55)	13(45)
Colistin	29(100)	------
Ciprofloxacin	07(24)	22(76)
Cefotaxime	12(41)	17(59)
Cefoperazonesulbactam	18(62)	11(38)
Piperacillintazobactam	20(69)	09(31)
Fungus =4		
Fluconazole	0(0)	3(100)
Amphotericin	3(100)	0(0)

We also analyzed the referral slip to know about the antibiotic usage prior to referral. We found that more than half (n= 78, 52 %) of the babies had already received antibiotic when they reach our tertiary care center. Most common antibiotic was cefotaxime. Antibiotic usage pattern prior to referral is shown in figure 3 below.

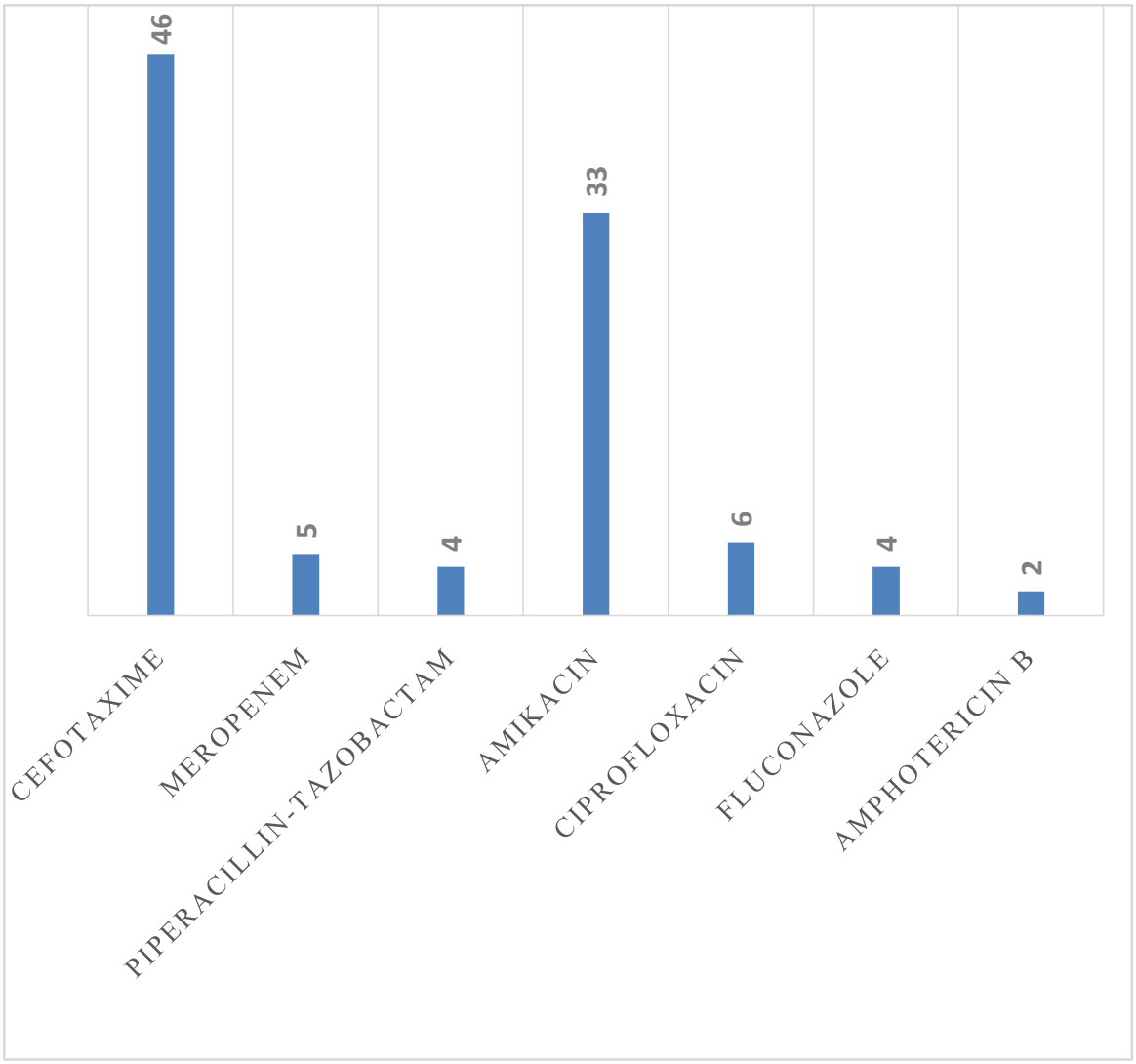

Figure 3: -Antibiotic usage pattern prior to referral(%)

We followed the neonate till discharge or death. Mortality rate in our study was 39 % (n=57). Around 1/4th of neonates was discharged to home. Around 1/5th of neonates was referred back to nearby hospital for antibiotic completion. Remainingparents left against medical advice (LAMA) due to poor prognosis or financial constraints. Outcome details are depicted in figure 4 below.

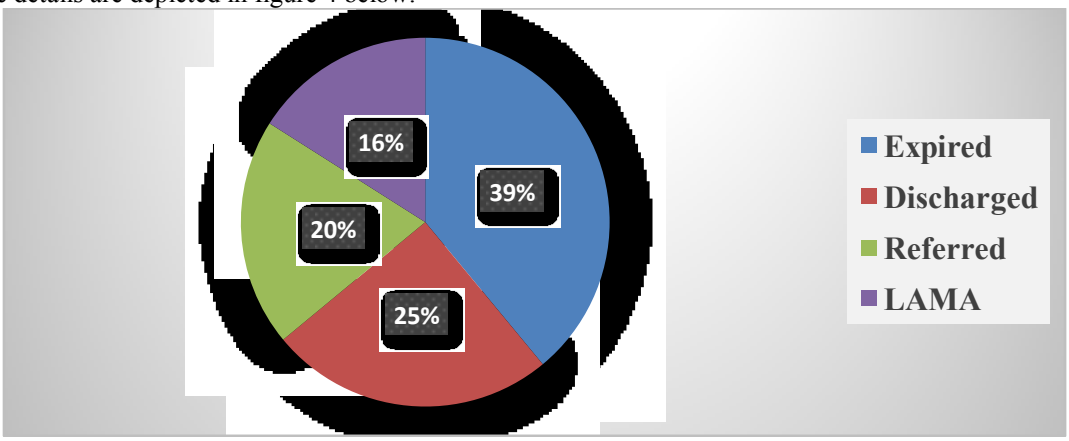

Figure 4:- Final outcome.

Discussion:-

In our setting blood culture positivity is higher as compared to other tertiary care centers (5). Majority of culture positive cases were LONS as we included outborn neonates referred from other centers. Our finding is quite different from study done at Chandigarh where EONS was common.The spectrum of bacteria in our setting is different from western data where gram positive bugs predominate (6). Gram negative bacilli predominate in developing countries with klebsiella pneumoniae being most common. (7). Recent data from developing countries has shown the growth of Staph aureus (8-10). In EONS, resistance to Ciprofloxacin and Methicillin is worrisome as these antibiotics are first line drugs.In LONS, resistance to ciprofloxacin and Amikacin is quite problematic as these are the first line antibiotic in LONS. Growth of resistant fungus is marker of poor neonatal care.

Conclusion:-

Our study provides renewed focus on antibiotic policy and need for antibiotic stewardship. The emerging resistance of bacteria and fungus to common antibiotics and common antifungals forces clinician to use higher antibiotics. It will lead to increase in resistance and emergence of new resistance. Emergence of panresistant bacteria and fungus in our setting is not extremely hard to see. There is immediate need to change of antibiotic policy and conservative use of antibiotics in neonates.

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