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Bacterial agents and their antibiotic susceptibility in neonatal sepsis in high dependency NICU of Tertiary Care Hospital

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Abstract:- ***Background:*** *The type of bacterial flora causing neonatal sepsis varies in different parts of world and the emerging of resistance to various antibiotics has been a challenge currently faced by microbiologists and neonatologist's worldwide. The aim of this study was to isolate the bacteriological agent causing the neonatal sepsis and determination of their susceptibility to antibiotics.*

Methods: *In this study, neonates suspected of sepsis who were admitted to Neonatal Intensive Care Unit (NICU) were assessed. Neonates with positive blood culture and with clinical signs of sepsis were enrolled in the study. The other parameters included: age, sex, birth weight, gestation, type of infection, type of isolated pathogen along with their antibiotic sensitivity and the outcome of disease.*

Results: *1440 neonates with suspected sepsis were included in study, out of 1440 patients, blood cultures were taken from all patients, 180cultures (12.5%) were reported as positive. in 32 cultures (17.7%) gram positive microbes were isolated while in 148 cultures (82.2%) gram negative microorganisms were detected.The mostcommon microorganisms isolated were; Klebsiella pneumonia (33.05%), Acintobacter Spp. (17.01%), Pseudomonas (13.26%), Escherishia-coli (8.75%),Coagulase negative staphylococci (CONS) (11.94%), MRSA (6.59%), Enterobacter (4.44%), Citrobacter (4.37%) and Enterococcus(2.36%). All of the klebsiella and enterobacter strains were resistant to ampicillin and gentamicin. Acintobacter Spp., and Citrobacter, were multidrug resistant with their sensitivity to imipenem was 40 to 45 % while for tigicycline was near 90%.The sensitivity of K. pneumonia and enterobacter to imipenem was: 90 and 94%, respectively.61.66% of our patients were preterm, early and late-onset sepsis was seen in 71 and 29% of patients respectively. Mortality rate was high 61.76% among preterm patients with sepsis while as overall mortality rate was 37.77%.*

Conclusion: *In this study we found most common cause of bacterial sepsis was K. pneumoniae which was completely resistant to ampicillin and gentamicin. It therefore re-emphasis the need to change the empirical treatment of sepsis with ampicillin and gentamicin.*

Keywords: *Neonatal Sepsis, antibiotic susceptibility, Neonatal intensive care unit*

Introduction:

Neonatal sepsis continues to be major cause of mortality and morbidity in Neonates particularly in preterm infants. It is defined as a disseminated disease with positive blood culture during the first month of life[1].It is further classified into early onset presenting within first 3 days of birth and late onset from 4 to 28 days of postnatal life. Neonatal sepsis is more common in developing countries compared with developed countries[2].Spectrum of organisms which cause neonatal sepsis varies among different countries and geographical areas[3]. Mortality rate has been found to be highest with gram negative bacteria .The common

causes of neonatal sepsis are group B streptococci (GBS), Escherichia coli (E. coli) and Listeria monocytogenes among developed countries and Enterococci, group B streptococci (GBS), Escherichia coli (E. Coli) and coagulase- negative staphylococci (CONS) in developing countries [4]**.**Because of different pathogens causing neonatal sepsis, management depends on prior knowledge about the causative organisms and their sensitivity to antibiotics. The aim of our study was to detect bacterial pathogens responsible for early and late- onset neonatal sepsis and to determine their antibiotic sensitivity, gender variation, predisposition to low gestation and mortality rate of neonatal sepsis in our neonatal intensive care unit (NICU)

Materials and Methods:

This study was conducted in NICU SKIMS-MC Over a period 24 months (from December 2015 to November 2017), 1440 neonates with clinical signs and symptoms suggestive of sepsis admitted to NICU SKIMS-MC were assessed with inclusion criteria of respiratory distress, poor feeding, fever, hypothermia, lethargy, signs of gastrointestinal or central nervous system involvement with a positive blood culture. Exclusion criteria were chromosomal disorders, multiple congenital malformations and neonates suspected of any metabolic disorder. Neonates were divided into two groups according to timing of clinical signs as early onset (clinical signs of sepsis from birth to 3days) or late-onset (clinical signs of sepsis from 4 to 28 days) infections. Neonates were also classified into low birth weight (birth weight< 2500 gms) and normal birth weight (birth weight 2500 gms) and as per the gestational age into term (gestational age 37 weeks) and pre-term (gestational age< 37 weeks)**.**

The investigations panel included; Electrolytes, blood sugar (BS), complete blood count (CBC), C - reactiveprotein (CRP), Cerebrospinal fluid analysis and Urine analysis. Blood culture were obtained aseptically from peripheral veins (2.5 ml for each blood culture). Blood samples were inoculated into the Nutrient broth culture media **(**Trypticase Soy Broth) and incubated for one week at 37 C[5]and were checked for daily evidence of bacterial growth. From positive cultures subcultures were obtained on solid media (Blood agar and McConkey agar) and were incubated in 37 C for 24 to 48 h. The grown ofbacteria were identified by gram stain, colony morphology and standard biochemical tests[5]. Antibiotic susceptibility testing was performed as per the Clinical and Laboratory Standards Institute guidelines with their concentrations per disk (μg) comprised: Penicillin (10), ampicillin (10), ceftriaxone (10), gentamicin (10), amikacin (10), ciprofloxacine (30), vancomycin (30), and imipenem (10). Statistical analysis was done by SPSS version 15.

Results:

1440 neonates with suspected sepsis were included in study, blood cultures were taken from all patients, and 180 cultures (12.5%) were reported as positive. Out of all positive cultures,in 148 cultures (82.22%)gram negative microbes were isolated while in 32 cultures (17.7%) gram positive microbes were isolated**.** The most common microorganisms isolated were; Klebsiella pneumonia (33.05%), Acintobacter Spp. (17.01%), Pseudomonas (13.26%), Escherishia-coli (8.75%), Coagulase negative staphylococci (CONS) (11.94%), MRSA (6.59%), Enterobacter (4.44%), Citrobacter (4.37%) and Enterococcus (2.36%). Whileall of the klebsiella and enterobacter strains were resistant to ampicillin and gentamicin. Acintobacter Spp., and Citrobacter, were multidrug resistant with their sensitivity to imipenam was 40 to 45 % while for tigicycllin was near 90%.The sensitivity of K. pneumonia and enterobacter to imipenem was: 90 and 94%, respectively. 61.66% of our patients were preterm, early and late-onset sepsis was seen in 71 and 29% of patients respectively.

Table 1: Type and number of bacterial isolates in neonates with sepsis based on the sepsis onset.

Microorganism	**Early-onset**	**Late-onset**	**Total**
Klebsiella pneumoniae	41	18	59
Acinetobacter spp.	23	7	30
Pseudomonas aeruginosa	17	6	23
E. coli	10	5	15
CONS	14	7	21
MRSA	8	4	12
Enterobacter spp.	6	2	8
Citrobacter spp.	5	3	8
Enterococcus	3	1	4
Total	**127(70)**	**53(30)**	**180**

There was no significant correlation between gestational age and type of pathogens in this study (P = 0.137). Similarly, no significant relationship was found between birth weight and type of neonatal sepsis. There were 111 (61.66%) neonates with low birth weight and 69 newborns (38.33%) with normal birth weight. Mortality rate was high 61.76% among preterm patients with sepsis while as overall mortality rate was 37.77%.Considering sex preponderance there were more cases of sepsis in male neonates compared with female neonates (110 male and 70 female with 1.6:1 ratio). The mortality rate was 37.77% (68 cases: 40 male neonates and 28female neonates) in this study. The mortality was higher among male neonates 58.82% compared to female neonates 41.17%

Table 2: Treatment outcome (No. of cases) according to sex, birth weight and type of sepsis.

Outcome		**Male/Female**	**Weight < 2.5**	**Weight > 2.5**	**LOS**	**EOS**
Death	68	40/28	42	26	19	49
Recovery	112	70/42	69	43	34	78
Total	**180**	**110/70**	**111**	**69**	**53**	**127**

There was no significant correlation between mortality rate and type of causative pathogen, early or late-onset sepsis . However, significant relationship was observed between gestational age and mortality rate in this study (P = 0.2).

Discussion:

In our study, the prevalence of neonatalsepsis documented with positive blood culture was 12.5%.This

incidence however is much lower compared to prevalence of positive blood cultures in Rahman et al.[6] study whose prevalence was (62.8%) and Bhttacharjee et al.[7] study with prevalence of (48%). The lowprevalence of our study had different reasons like antibiotic administration to mother or neonate, difficulty in taking bloodsamples, blood culture technique (Bansal et al)[8]or sepsis due to viral or fungal pathogens(Agnihotri et al)[9]and improper diagnosis because of some similarities in clinical presentation of sepsis with other diseases like metabolic disorders (Lund et al)[10]. In our study, early onset sepsis was more common than late-onset sepsis (71 and 29%).This finding was similar to the results of the Vinodkumar et al[11] study which reported prevalence of early onset neonatal sepsis of 73%. However in contrast to our study, a study done by Kuruvilla etal[12] reported higher prevalence of late-onset sepsis compared with early-onset as (77.1 versus 22.9%). This difference may bebecause of delayed referralsto that health center. Neonatal sepsis with gram negative bacteria was more common than gram positive bacteria in our study and these results match with some of other studies (Isaacs and Royal[13]; Sundaram et al[14]). This could be because of colonization of gram negativebacteria in the skin of the neonates and the personnel of neonatal ICU and by use of more invasive procedures. In our study K. Pneumoniae was the most common microorganism isolated from the blood cultures. This finding was consistent with the results of Kumar et al[15], but was different to results of (Gheibi et al[16]) which showedthe CONS as the most common isolated bacteria. No GBS colonies were isolated from cultures as showen by (Ahmed et al[17]; Aurangzeband Hameed[18]). This could be because of weak virulence or low colonization of pregnant mothers with GBS.A large chunk of gram negative and gram positive bacteria, were resistant to one or more type of antibiotics which was in pattern to similar studies (Lund et al., 2002[10]; Vinodkumar et al., 2008[11]). Nowadays antibiotic resistance is widespread and a global problem that has caused ineffectiveness of current empirical treatment to gram negative bacteria. As we observedin our study, all of klebsiella and enterobacters were completely resistant to current empirical treatment of (ampicillin+ gentamicin) and these were among the most common cause of bacterial sepsis.Antibiotic resistance causes many difficulties while managingsepsis such as increase in mortality rate, increase in duration of hospitalization and off course treatment expenses. So it becomes mandatory to reevaluate the antibiotic treatment protocol continuously (Goossen)[19].In our study male to female ratio in sepsis was 1.6 to 1 which was close to the results of Mosayebi et al[20]study. The reason for higher male gender susceptibility to sepsis is largely unknown but may be related to sex – dependent factors (Llorens,)[21].In our study mortality rate in sepsis with gram negative bacteria was 55.76% which was higher compared with the study by Khassawneh et al.[22]which reported30.9%. According to our study results, we canconclude that gram negative bacteria were the main cause of early and late-onset neonatal sepsis in our ICU and K. pneumoniae was the most common pathogen isolated.Many of the isolated bacteria were resistant to the usual first line antibiotics and the mortality rate due to neonatal sepsis was high compared withthe other studies. So it is imperative to change and reconsider the empirical antibiotic therapy in our hospital NICU.

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