ORIGINAL RESEARCH PAPER

Paediatrics

KEY WORDS:

TO STUDY BLOOD CULTURE POSITIVE SEPSIS AND ANTIMICROBIAL SENSITIVITY PATTERN IN NEONATAL SEPSIS, IN NEONATAL INTENSIVE CARE UNIT

Dr. Rohit M Bhandar — Professor, Department Of Paediatrics, M R Medical College, Kalaburagi.

Dr. Sharan Deshmukh — Assistant Professor , Department Of Pediatrics , M R Medical College , Kalaburagi

Dr. Vijay kumar B.T — Post Graduate, Department Of Paediatrics, M R Medical College, Kalaburagi

Dr. Kumar Angadi — Associate Professor, Department Of Paediatrics, M R Medical College, Kalaburagi

ABSTRACT

Background And Objectives: Septicemia continues to be a major cause of neonatal mortality and morbidity worldwide. The bacteriological profile of neonatal sepsis is under constant change. Blood culture is still the mainstay of investigation of sepsis. The objective is to study bacteriological profile in the neonates with neonatal sepsis and to determine the antibiotic sensitivity pattern of the bacteria **Materials And Methods:** After obtaining ethical committee clearance and informed consent from the parents of subjects. Prospective study of all blood culture positive sepsis cases among neonates admitted to neonatal intensive care unit with sample size of 150. Blood samples were collected with aseptic precaution prior to initiation of antibiotic therapy and BACT/Alert and VITEK blood culture isolation methods were used and antibiotic sensitivity pattern was evaluated. Data was entered into Microsoft excel sheet and analysed using IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp. Qualitative and quantitative analysis was done. P value <0.05 was considered significant. **Results:** Among 150 neonates with blood culture proven sepsis most common organisms isolated were S.haemolyticus (25%), Burkolderia cepacia (16.5%), Klebsiella (15%) Gram positive isolates were sensitive to vancomycin (80%), linezolid (75%), gentamicin (60%). Gram negative isolates were sensitive to meropenem (56%), cefipime and gentamicin (30%) respectively. Gram positive isolates were resistant to piperacillin + tazobactam (46%), ciprofloxacin (46%), amoxycillin + clavulunate (35%). Gram negative isolates were resistant to piperacillin +tazobactam (60%), amikacin (50%), colistin (40%), gentamicin (40%) **Conclusion:** There is increasing trend of antibiotic resistance to commonly used antibiotics and even to higher antibiotics also use of broad spectrum antibiotics as empirical therapy should be modified to narrow spectrum as guided by the culture sensitivity report to prevent emergence of drug resistance hence there is need for continuous surveillance for antibiotic susceptibility to look for resistance pattern and practice antibiotic stewardship.

INTRODUCTION

Sepsis is a one of the most common causes of neonatal mortality globally[1]. Neonatal infections currently cause about 1.6 million deaths annually in developing countries. It is the leading cause of neonatal mortality and morbidity in India [2]

Nearly one third of neonatal mortality in India is due to neonatal sepsis and death occurs in 30%of culture positive neonates[3]

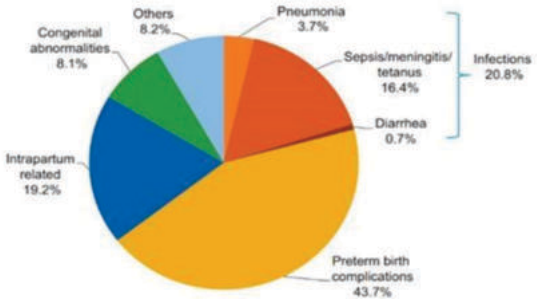

Chart 1: Causes Of Neonatal Deaths In India:[4]

Definition

Neonatal sepsis is clinical syndrome characterised by signs and symptoms of infection with or without accompanying bacteremia in the first month of life. It encompasses various systemic infections of the newborn such as septicemia, meningitis, pneumonia, arthritis, osteomyelitis, and urinary tract infections

Neonatal sepsis may be classified according to time of onset of disease as early onset sepsis and late onset sepsis[2]

Early Onset Sepsis (EOS)

It presents at or before 72 hours of life. In severe cases, the neonate may be symptomatic at birth. Infants with EOS usually presents respiratory distress and pneumonia. The source of infection is generally the maternal genital tract. maternal/ perinatal conditions have been associated with an increased risk of EOS.

Based on the studies from India, the following risk factors seem to be associated with an increased risk of early onset sepsis

1. spontaneous prematurity, Low birth weight(<2500gm)
2. Foul smelling and/or meconiumstained liquor.
3. Rupture of membranes >24 hours.
4. Single unclean or > 3 sterile vaginal examination(s) during labor.
5. Prolonged labor (sum of 1st and 2nd stage of labor>18 hrs).
6. Perinatal asphyxia (Apgar score <4 in 1 minute.)[5]

Late Onset Sepsis (LOS)

It usually presents after 72 hours of age. LOS can be either healthcare associated infectionor community-acquired. The neonate usually presents with sepsis, pneumonia or meningitis.[6]

Various factors that predispose to an increased risk of nosocomial sepsis include, prematurity, admissions in intensive care unit, mechanical ventilations, invasive

procedures, administration of parenteral fluids, and use of stock solutions.

Factors that might increase the risk of community-acquired LOS include poor hygiene, poor cord care, bottle-feeding and pre-lacteal feeds.

Investigations

Since treatment should be initiated in a neonate suspected to have sepsis without any delay, only minimal and rapid investigations should be undertaken.[7]

Laboratory evaluation of a neonate with symptoms include complete blood counts with differential counts, immature to total neutrophil ratio [I:T ratio], absolute neutrophil count, peripheral smear and blood culture.

Owing to this delay in definitive diagnosis some other tests have been evaluated like C-reactive proteins and Procalcitonin

Blood Culture

It is the gold standard for diagnosis of septicemia and should be performed in all cases of suspected sepsis prior to starting antibiotics. A positive blood culture with sensitivity of the isolated organism is the best guide to antimicrobial therapy.

Since samples collected from indwelling lines and catheters are likely to be contaminated, cultures should be collected only from a fresh veni-puncture site. All blood cultures should be observed for at least 72 hours before they are reported as sterile.[8]

The use of BACTEC BD blood culture system is better for rapid identification of blood borne pathogens followed by determining actual antimicrobial treatment in the scenario of multi drug resistance[9]

MATERIALS AND METHODS

- **Study Design:** Prospective observational study.
- **Study Setting:** Department of Pediatrics, MRMC, Kalaburagi.
- **Study Sample:** 150 cases
- **Sampling Procedure:** Purposive Sampling.
- **Study Duration:** 18 months (1st MARCH 2021- 31st AUGUST 2022)

Source Of Data

The data will be collected from babies with neonatal sepsis admitted to tertiary care hospital attached to Mahadevappa Rampure Medical College, Kalaburagi, Karnataka

Consent: Informed consent is taken in patients own vernacular language.

Methods Of Collection Of Data

Sampling Procedure

The resident doctor/staff should wear sterile gloves prior to the procedure and prepare a patch of skin approx. 5-cm in diameter over the proposed veni-puncture site.

This area should be cleansed thoroughly with alcohol, followed by povidone iodine, and followed again by isopropyl-alcohol. Povidone-iodine should be applied in concentric circles moving outward from the centre.

The skin should be allowed to dry for at least 1 minute before the sample is collected. One-mL sample of blood should be adequate for a blood culture bottle containing 5-10 mL of culture media

Inclusion Criteria

1. All neonates with clinical history, signs and symptoms of sepsis with
2. Positive blood culure , admitted in nicu of tertiary care hospital

Exclusion Criteria

1. Neonates who received antibiotics before and got admitted to hospital
2. Neonates with more than 7 days of home stay or previous hospitalization

Data Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp. Results on continuous measurement are presented as Mean ± SD and categorical as frequency, percentage. Inferential statistics like Chi-square test/Fisher Exact test and independent t-test were used to compare the two groups. P value <0.05 was considered statistically significant.

RESULTS

Among 150 neonates with culture positive sepsis, EOS accounted for 50.7% and LOS accounted for 49.3%. About 51.3% were term and 48.7% were pre term. 52.7 % were born via normal vaginal delivery (NVD) and 47.3% were born via LSCS, EOS was more commonly seen with normal vaginal delivery. There was significant association between mode of delivery and onset of sepsis. 60% were male and 40% female. There was no significant association between gender and onset of sepsis. 25.3% had presence of PROM (prolonged rupture of membrane) and there is significant association between presence of PROM >18 hrs and early onset sepsis, with p-value of 0.001.

Among 150 neonates with blood culture proven sepsis most common organisms isolated were staphylococcus haemolyticus (25%), Burkolderiacepacia (16.5%), Klebsiella (15%). Gram positive isolates were sensitive to vancomycin (80%), linezolid (75%), gentamicin (60%). Gram negative isolates were sensitive to meropenem (56%), cefipime and gentamicin (30%) respectively. Gram positive isolates were resistant to piperacillin + tazobactam (46%), ciprofloxacin (46%), amoxycillin +clavulunate (35%). Gram negative isolates were resistant to piperacillin +tazobactam (60%), amikacin (50%),colistin (40%), gentamicin (40%).

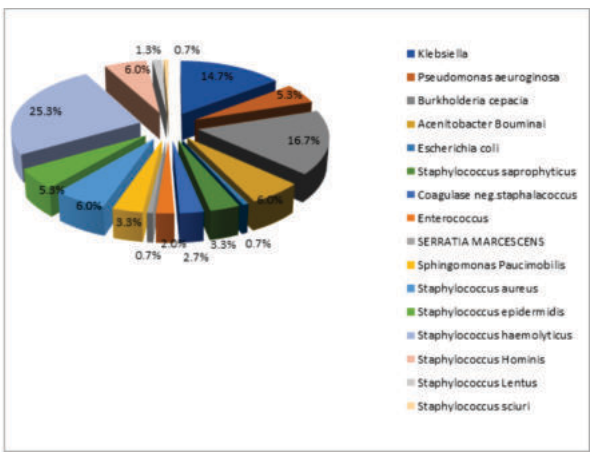

Chart 2: Distribution of gram positive and gram negative organisms.

DISCUSSION

Blood culture remains to be the gold standard investigation for diagnosis of neonatal sepsis, to know the bacteriological profile and antibiogram, present study was conducted. In this prospective study, we examined blood culture of 150 neonates

In our study, among the 150 neonates with blood culture positive sepsis 51.5% had EOS and 49.5% had LOS. Similar incidence was found in the Thakur et al[10], Rath et al[11], Kurma et al[12]

H Apabi et al[13], P Jyothi et al[14], kumar et al, Vaniya et al[15], Gandhi S et al[16],

However increased LOS when compared to EOS has been reported in the studies done by Kayange N et al [17](2010), Kishore et al (2020) [18], Karambin MM et al (2011)[19] and Shrestha NJ et al (2011)[20]

Among the admitted neonates with blood culture positive sepsis 51% term 49% were pre term. This incidence was similar in Thakur et al[10], Vaniya et al[15], Rath et al[11].

In our study, among study population with blood culture positive sepsis, 52.7% were LBW babies .this incidence was similar in the Thakur et al[10], Rath et al[11], Kurmar et al[12] Aggarwal et al[21], Jyothi et al[14], Kishore et al[18].

A very strong association of culture proven sepsis (94%) with prematurity was reported by Chauhan Setal B et al (2012).[22]

In our study, among the admitted neonates with blood culture positive sepsis, Gram positive were 52% and gram negative were 48% similar incidence was seen in the Thakur et al, Rath et al, Kurma et al[12], Mohakud et al[23]. In our study, among the admitted neonates with blood culture positive sepsis, antibiotics which were most commonly sensitive to Gram Positive isolates were vancomycin, linezolid similar was seen in Rath et al[11], Jyothi et al[14] And antibiotics which were most commonly sensitive to Gram Negative isolates were Meropenem, cefepime

In our study, among the admitted neonates with blood culture positive sepsis, antibiotics which were most commonly Resistant to Gram Positive isolates were ciprofloxacin, meropenem, piperacillin + tazobactam similar to Kurma et al[12] and Antibiotics which were most commonly Resistant to Gram Negative isolates were, piperacillin + tazobactam, Amikacin, gentamicin similar to Kurma et al[12], Vaniya et al[15].

In our study, among the admitted neonates with blood culture positive sepsis, most common organism isolated in neonates born via NVD was klebsiella this incidence was similar in kumar et al[12] and most common organism isolated in neonates born via LSCS was staph. Haemolyticus.

In our study, among the admitted neonates with blood culture positive sepsis, most common organism isolated in EOS was klebsiella was similar to Jyothi et al and most common organism isolates in LOS was staph. Haemolyticus

Among the admitted neonates with blood culture positive sepsis, most common gram positive isolate Staph. haemolyticus and most common gram negative isolate was Burkholderia cepacian

Table No. 1: Comparing Most Sensitive Antibiotic For Gram Positive And Gram Negative Isolates Of Our Study With Other Studies

Author, State,/Institute	Duration / Year Type,	Most sensitive antibiotics for Gram Positive isolates	Most sensitive Antibiotics for Gram Negative isolates
Rath et al KIMS Odisha	2019 (retro-spective)	Linezolid 92% Vancomycin 85 % Teicoplanin 85 %	Colistin 76% Ciprofloxacin 64% Meropenam 50%
Vaniya et al MP shah govt medical college Jamnagar Gujarat	2015 (pros-pective)	Ampicillin +salbactum 71% Gentamicin 63% Co trimoxazole (55.8%)	Gatifloxacin 75% Ofloxacin 60%
Jyothi et al B M Patil medical college Vijayapura, Karnataka	2013 (pros-pective)	Linezolid 91% Tetracycline 68%	Imipenam 93% Amikacin 52% Gentamicin 51%
In our study , M.R Medical college Tertiary care teaching hospital,Kalaburagi	2021 (retrospecti ve)	Vancomycin 80% Linezolid 75% Gentamicin 58%	Meropenam 56% Cefipime 30%

Table No. 2 Comparing Most Resistant Antibiotic For Gram Positive And Gram Negative Isolates Of Our Study With Other Studies

Author, State,/ Institute	Duration / Year Type,	Most Resistant antibiotics for Gram Positive isolates	Most Resistant antibiotics for Gram Negative isolates
Thakur et al Rural tertiary hospital North India	2020 (cross sectional)	Penicillin 87%	Cephalosporins 89% Aminoglycoside 67% Amoxy +clav 66%
Kumar et al Rural hospital, Tamilnadu	2017 (Retrosp ective)	Penicillin 71% Ciprofloxacin 54%	Ampicillin 96% Piperacillin +Tazobactem 72% Cephalosporins 56%
Vaniya et al MP shah govt medical college Jamnagar Gujarat	2015 (pros-pective)	Cloxacillin 57% Cefotaxime 56%	Cefotaxime (91%) Piperacillin +Tazobactem (91%)
Jyothi et al B M Patil medical college Vijayapura, Karnataka	2013 (pros-pective)	Penicillin 90% Cloxacillin 84%	Ampicillin 97% Amoxy +clav 93%
In our study , MR Medical college BTGH & STGH ,Kalaburagi	2021 (Pros-pective)	Ciprofloxacin (52%) Meropenam (51%) Piperacillin + tazobactam (50%)	Piperacillin + tazobactam (60%) Amikacin (50%),Genta-micin(40%) Colistin (40%)

CONCLUSION

In our study, we observed higher incidence of Culture proven sepsis was found in neonates born via Vaginal Delivery (52.7%) than LSCS, LBW babies were more commonly seen with culture positive sepsis Significant co relation with history of PROM >18 Hrs

Predominant gram positive isolates were Staph. haemolyticus (25%), Staph. aureus (6%), staph. hominis (6%). Predominant gram negative isolates were Burkholderia cepacia (16.5%), Klebsiella (15%), Acinetobacter baumanii(6%). Gram positive isolates were sensitive to vancomycin (80%), linezolid (75%), gentamicin (60%). Gram negative isolates were sensitive to meropenem (56%), cefipime and gentamicin (30%) respectively. Gram positive isolates were resistant to piperacillin + tazobactam (46%), ciprofloxacin (46%), amoxycillin + clavulunate (35%). Gram negative isolates were resistant to piperacillin +tazobactam (60%), amikacin (50%),colistin (40%), gentamicin (40%).

There is increasing trend of antibiotic resistance to commonly used antibiotics and even to higher antibiotics thus early

change to vancomycin or linezolid in case of no improvement or deterioration, also use of broad spectrum antibiotics as empirical therapy should be modified to narrow spectrum as guided by the culture sensitivity report to prevent emergence of drug resistance hence there is need for continuous surveillance for antibiotic susceptibility to look for resistance pattern and practice antibiotic stewardship.

Limitation Of The Study

- Fungal isolates and sensitivity was not considered
- contamination spores were seen with few culture reports

REFERENCES

1. Liu L, Oza S, Hogan D, et al. Global, regional, and national causes of child mortality in 2000-13, with projections to inform post-2015 priorities: an updated systematic analysis. Lancet 2015;385:430-40
2. Vergnano S, Sharland M, Kazembe P, et al Neonatal sepsis: an international perspective Archives of Disease in Childhood - Fetal and Neonatal Edition 2005;90:F220-FF224
3. Chaurasia S, Sivanandan S, Agarwal R, Ellis S, Sharland M, Sankar MJ: Neonatal sepsis in South Asia: huge burden and spiralling antimicrobial resistance. BMJ. 2019, 364:k5314. 10.1136/bmj.k5314
4. Sankar MJ, Neogi SB, Sharma J, Chauhan M, Srivastava R, Prabhakar PK, et al. State of newborn health in India. J Perinatol. 2016;36(s3):S3.
5. Tripathi, Shalini. (2010). Neonatal Sepsis: Past, present and future; a review article. Internet Journal of Medical Update. 5. 10.4314/ijmu.v5i2.56163.
6. Baltimore RS. Neonatal nosocomial infections. Semin Perinatol 1998;25-32
7. Gerdes JS, Polin R. Early diagnosis and treatment of neonatal sepsis. Indian J Pediatr1998;65:63-78.
8. Kirn, T. J., and Weinstein, M. P. Update on blood cultures: how to obtain, process, report, and interpret. Clin. Microbiol. Infect 2013. 19,513-520.
9. Singhal, Esha & Goyal, Rahul &Behara, R.. (2016). comparative evaluation of blood culture by conventional method and bactec using blood samples of icu patients and antibiogram of isolated pathogens. srms Journal of Medical Science. 1. 10.21761/jms.v1i2.7450.
10. Thakur S, Thakur K, Sood A, Chaudhary S. Bacteriological profile and antibiotic sensitivity pattern of neonatal septicaemia in a rural tertiary care hospital in North India. Indian J Med Microbiol. 2016 Jan-Mar;34(1):67-71. doi: 10.4103/0255-0857.174108. PMID: 26776121.
11. Soumini Rath, Santosh Kumar Panda*, Manas Kumar Nayak, Deepti Damayanty Pradhan, Rath S et al. Int J Contemp Pediatr. 2019 Mar;6(2):487-490
12. Veereswara Rao Kurma, MS Raju, Triveni Manchu, Kalyani Manchu. Neonatal sepsis: clinical spectrum, bacteriological profile and antibiotic sensitivity patterns in neonatal intensive care unit in a tertiary care Hospital. International Journal of Contemporary Medical Research 2019;6(6):F1-F4
13. Apabi H, Paikhomba KH, Touthang J, Arun P, Mohon LB. Bacteriological Profile and Antibiotic Susceptibility Pattern of the Isolates in the Neonatal Septicemia in Northeast India. Int J Sci Stud 2019;6(11):59-65.
14. Jyothi P, Basavaraj MC, Basavaraj PV. Bacteriological profile of neonatal septicemia and antibiotic susceptibility pattern of the isolates. J Nat Sci Biol Med. 2013 Jul;4(2):306-9. doi: 10.4103/0976-9668.116981. PMID: 24082722; PMCID: PMC3783770
15. Vaniya HV, Patel NM, Agrawal JM, Trivedi HR, Dhanani JV, Balat JD. Antimicrobial culture sensitivity pattern in neonatal sepsis in a tertiary-care hospital. Int J Med Sci Public Health 2016;5:661-665
16. Gandhi S, Ranjan KP, Ranjan N, Sapre N,Masani M. Incidence of neonatal sepsis in tertiary care hospital: an overview. Int J Med Sci Public Health 2013;2:548-552
17. Kayange N, Kamugish E, Mwizamhoyla DM. Predictors of Positive blood culture and deaths among neonates with suspected sepsis in a tertiary care hospital. Mwanza-Tanzania. BMC Pediatr 2010; 10(39):1-9.
18. Kishore S, Ahmar R, Kumar A, Kumar M, Gupta R, Gupta AK, Kumar R, Sharan S, Prakash J Bacteriological profile and antibiotic susceptibility of neonatal sepsis in neonatal intensive care unit of a tertiary care medical institute of Eastern India: A retrospective cross-sectional study. Panacea J Med Sci 2021;11(1):99-105.
19. Karambin MM and Zarkesh M. Enterobacter the most common pathogen of neonatal septicemia in Rasht, Iran. Iran J Pediatr 2011; 21(1):83-87.
20. Shrestha P, Das BK, Bhatta NK, Jha DK, Das B, Setia A, et al. Clinical and bacteriological profiles of blood culture positive sepsis in newborns. J Nepal Paediatr Soc 2008;27:64-7
21. Agrawal A, Awasthi S, Ghanghoriya P, Singh S. Study of current status of bacteriological prevalence and profile in an inborn unit of SNCU in central India. Int J ContempPediatr2018;5:764-9
22. Chauhan S, Viren V, Bimal C. C-reactive protein in early diagnosis of neonatal septicemia. Natl J Med Res; 2012; 2:276-8.
23. Mohakud N K, Mishra J P, Nayak M K, et al. (May 31, 2022) Bacteriological Profile and Outcome of Culture-Positive Neonatal Sepsis in a Special Newborn Care Unit Setting, Odisha. Cureus 14(5): e25539. DOI 10.7759/cureus.25539