ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Bacterial pathogens and treatment outcomes in neonatal sepsis: A comparative observational study across various hospital settings

Radhika B[1], Vijayasri BSS[2], Vidyasagar V[3], Jyothi Prakash Raju S[4]

[1,2]Assistant Professor, [3]Postgraduate Resident, Department of Microbiology, Government Medical College, [4]Professor, Department of Paediatrics, GEMS Medical College, Srikakulam, Andhra Pradesh, India

Submission: 16-02-2024 Revision: 15-04-2024 Publication: 01-06-2024

ABSTRACT

Background: Neonatal sepsis is a leading cause of neonatal morbidity and mortality globally, with variations in causative bacteria and treatment efficacy across health-care facilities. **Aims and Objectives:** The aims and objectives of the study are to analyze the bacterial pathogens causing neonatal sepsis and the effectiveness of their treatment in diverse hospital environments. By highlighting the differences in treatment success rates, antibiotic resistance profiles, and the pathogens involved, this study demonstrate the impact of health-care practices and infrastructure on the management of neonatal sepsis. **Materials and Methods:** The study encompassed 100 neonates with sepsis, evenly distributed across the three hospital types. It involved identifying bacterial pathogens through blood cultures, assessing antibiotic sensitivity, and examining treatment outcomes such as success rate, mortality, hospital stay duration, and complication rates. Statistical methods were employed to evaluate differences in outcomes among the settings. **Results:** Seventy percent of neonates tested positive for bacterial pathogens, with a 60% predominance of Gram-positive over Gram-negative bacteria (40%). *Staphylococcus aureus* (22%) and *Streptococcus agalactiae* (18%) were the leading pathogens. Notably, resistance was high against ampicillin (65%) and gentamicin (40%) but lower for cephalosporins and vancomycin. The overall success rate of treatments was 80%, with the tertiary care hospital achieving an 88% success rate, significantly outperforming the private hospitals (72%). The mortality rate was 10%, and 30% of the cases developed complications, predominantly respiratory distress syndrome. **Conclusion:** Hospital setting significantly influences the management and outcomes of neonatal sepsis, with tertiary care centers showing better results. These findings highlight the need for focused antimicrobial stewardship and the adoption of sophisticated care protocols in less advanced settings to improve neonatal sepsis outcomes.

Key words: Neonatal sepsis; Bacterial pathogens; Antibiotic resistance; Treatment outcomes

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v15i6.62811

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Newborns with a systemic infection that frequently results in considerable morbidity and mortality are at risk for neonatal sepsis, a serious global health issue.[1] Numerous factors, including the type of pathogenic bacterial infections that vary among health-care settings, affect the incidence and outcomes of newborn sepsis.[2] This variety emphasizes how crucial it is to comprehend these diseases' epidemiology and resistance patterns to enhance newborn outcomes and optimize treatment approaches.[3]

The growing problem of antibiotic resistance, which reduces the efficacy of traditional treatments and calls for a more focused approach to antibiotic management, adds to the burden of newborn sepsis.[4] This problem is

Address for Correspondence:
Dr. Jyothi Prakash Raju S, Professor, Department of Paediatrics, GEMS Medical College, Srikakulam, Andhra Pradesh, India.
Mobile: +91-9246635157. **E-mail:** drjprsklmped@yahool.com

especially severe in resource-constrained environments,[5] where the choice of empirical antibiotics could not be in line with local patterns of resistance, which could result in less-than-ideal results.

Aims and objectives

The aim of this study is to compare the bacterial pathogens responsible for neonatal sepsis and the outcomes of their treatments across three distinct hospital settings: A government teaching tertiary care hospital, a private teaching hospital (Gems Hospital Ragolu), and a private hospital (Dwaraka Sai Children Hospital).

MATERIALS AND METHODS

Study design and setting

This research is structured as a comparative observational study; the study is conducted at Government Medical College Srikakulam, incorporating cases from its associated tertiary care hospital, alongside comparisons with a private teaching hospital (Gems Hospital Ragolu) and a private hospital (Dwaraka Sai Children Hospital).

Study period

The study spans a full year, from January 2023 to December 2023, making it possible to evaluate patterns of antibiotic resistance and seasonal fluctuations in sepsis cases.

Population

The study population consists of 100 neonates diagnosed with sepsis, with participants equally distributed among the three hospital settings (approximately 33 neonates per setting).

Inclusion criteria

Neonates diagnosed with sepsis within the first 28 days of life.

Neonates admitted to one of the three study hospitals during the study period.

Exclusion criteria

Neonates with congenital infections.

Neonates transferred from other hospitals where antibiotic treatment was initiated.

Sample size calculation

The sample size for this comparative observational study was determined based on preliminary estimates of the treatment success rate variance among the different hospital settings. Assuming an 80% overall treatment success rate from prior literature, with an expected 15% difference in success rates between any two hospital types, and aiming for a power of 80% to detect this difference at a significance level of 0.05, the sample size was calculated using a two-sided Chi-square test for equality of proportions. Considering potential loss to follow-up and incomplete data, we estimated a 10% increase in the required sample size, resulting in approximately 33 neonates per hospital setting (100 neonates in total). This calculation ensures sufficient statistical power to discern clinically relevant differences in treatment outcomes, antibiotic resistance profiles, and pathogen prevalence among the study hospitals.

Data collection

Identification of bacterial pathogens

Blood cultures are conducted on neonates suspected of sepsis to identify bacterial pathogens.

Antibiotic sensitivity testing

Antibiotic sensitivity profiles of the isolated pathogens are determined to guide treatment decisions and analyze resistance patterns.

Treatment outcome measures

Data on treatment success rates, mortality, length of hospital stay, and incidence of complications are collected and analyzed.

Statistical analysis

Data will be analyzed using statistical software. Descriptive statistics will summarize demographic and clinical characteristics. Comparative analyses, such as Chi-square tests for categorical variables and ANOVA for continuous variables, will be used to compare outcomes across hospital settings. A $P<0.05$ will be considered statistically significant.

Ethical considerations

The study protocol was approved by the Institutional Ethics Committee, GEMS Medical College, Srikakulam Andhra Pradesh, India (IEC/GEMS/2023/16). The study was conducted in accordance with ethical guidelines and standards. Informed consent was obtained from all participants.

RESULTS

Study population and demographics

One hundred newborns from three different hospital settings in Srikakulam were included in this study: Gems Hospital Ragolu, a private teaching hospital, Government General Hospital, a government teaching tertiary care hospital, and Dwaraka Sai Children Hospital, a private hospital. The gestational age of the neonates ranged from 28 to 42 weeks, with a mean of 37.5 weeks. With 51 men and 49 women taking part in the study, the gender distribution was almost equal (Table 1).

Incidence of bacterial pathogens

In 70% of the newborn cases, bacterial infections were found. The detected pathogens were categorized as follows:

Sixty percent of the cases contained Gram-positive bacteria, with the most common species being *Staphylococcus aureus* (22%) and *Streptococcus agalactiae* (Group B *Streptococcus*, 18%).

Forty percent of the illnesses were caused by Gram-negative bacteria, of which the most common were *Escherichia coli* (15%) and *Klebsiella pneumoniae* (12%).

There was no significant difference in the incidence rate of bacterial pathogens between the various hospital settings (P>0.05) (Table 2).

Antibiotic sensitivity patterns

Among the bacterial isolates, resistance to gentamicin (40%) and ampicillin (65%) was especially high.

Vancomycin and cephalosporins (cefotaxime and ceftazidime), which had resistance rates of 15% and 25%, respectively, were shown to have a higher susceptibility.

Twenty percent of the isolates had multidrug-resistant organisms detected in them; the prevalence of these organisms was the same in both types of hospitals (P>0.05) (Table 3).

Treatment outcomes and hospital stay

Treatment for neonatal sepsis had an overall success rate of 80%. Notably, treatment success was 72% in the combined secondary care settings of Gems Hospital and Dwaraka Sai Children Hospital, while it was 88% in the tertiary care setting of Government General Hospital (P<0.05). Septic shock and multiorgan failure were the main reasons for the 10% fatality rate.

Compared to secondary care settings, where hospital stays lasted an average of 19 days, tertiary care settings had hospital stays that lasted 14 days on average (P<0.01) (Table 4).

Complications

Thirty percent of the cases had complications documented, with the most prevalent being respiratory distress syndrome at 8% and necrotizing enterocolitis at 4%.

In secondary care settings, there was a higher prevalence of problems, although the difference was not statistically significant (P>0.05) (Table 5).

DISCUSSION

The results of our investigation illuminated important facets of the management of newborn sepsis, demonstrating that 70% of the cases had bacterial infections identified. Significantly, the prevalence of Gram-positive bacteria increased, with the most prevalent species being *S. agalactiae* and *S. aureus*. This observation aligns with the global trend of Gram-positive bacteria becoming the primary cause of newborn sepsis, a noteworthy development that warrants consideration in the clinical management of this illness.[6-8] The observed resistance to widely prescribed antibiotics, such as gentamicin and ampicillin, highlights an increasing worry regarding antibiotic resistance, which presents a significant obstacle in the selection of appropriate empirical antibiotic regimens in newborn care settings.[9,10]

Our data also showed that treatment success rates varied throughout hospital contexts, with tertiary care hospitals

Table 1: Study population and demographics

Characteristic	Total (n=100)	Government general hospital	Gems hospital Ragolu	Dwaraka sai children hospital
Number of neonates	100	34	33	33
Mean gestational age (weeks)	37.5	37.4	37.6	37.5
Gender				
Male	51	17	17	17
Female	49	17	16	16

Table 2: Incidence of bacterial pathogens

Pathogen type	Overall (n=70) (%)	Government general hospital (%)	Gems hospital Ragolu (%)	Dwaraka sai children hospital (%)
Gram-positive bacteria	60	58	62	60
Staphylococcus aureus	22	23	21	22
Streptococcus agalactiae	18	18	18	18
Gram-negative bacteria	40	42	38	40
Escherichia coli	15	15	16	14
Klebsiella pneumoniae	12	13	11	12

Table 3: Antibiotic sensitivity patterns

Antibiotic	Resistance rate (%)	Government general hospital (%)	Gems hospital Ragolu (%)	Dwaraka sai children hospital (%)
Ampicillin	65	66	64	65
Gentamicin	40	42	38	40
Cefotaxime	25	24	26	25
Ceftazidime	25	23	27	25
Vancomycin	15	14	16	15
Multidrug-resistant organisms	20	20	20	20

Table 4: Treatment outcomes and hospital stay

Outcome	Overall (n=100) (%)	Government general hospital (%)	Gems hospital Ragolu (%)	Dwaraka sai children hospital (%)
Treatment success rate	80	88	72	80
Mortality rate	10	8	12	10
Average hospital stay (days)	16.5	14	19	16

Table 5: Complications

Complication	Incidence rate (%)	Government general hospital (%)	Gems hospital Ragolu (%)	Dwaraka sai children hospital (%)
Respiratory Distress Syndrome	18	16	20	18
Meningitis	8	7	9	8
Necrotizing enterocolitis	4	3	5	4

showing noticeably superior results. This contrast emphasizes how important it is to have a strong health-care infrastructure and access to cutting-edge diagnostic and therapeutic options to improve sepsis outcomes.[11] It also emphasizes how crucial it is to put in place thorough antimicrobial stewardship programs to direct the prudent use of antibiotics.

Our research confirms the body of literature by showing that the care setting has a major influence on newborn sepsis outcomes. The clear advantage of tertiary settings over secondary ones in terms of results can be ascribed to a number of things, such as easier access to specialist care, more sophisticated diagnostic equipment, and a wider array of treatment alternatives.[12,13] These variations highlight the critical need for region-specific recommendations that allow for more individualized and successful treatment plans by accounting for local pathogen profiles and resistance patterns.[14,15]

Clinical implications

The study emphasizes how important targeted antibiotic management is to achieving the best possible outcomes for newborn sepsis. To counter the growing wave of antibiotic resistance, hospitals – especially those in secondary care settings – must give top priority to implementing advanced care protocols, which include quick diagnostic methods and evidence-based antibiotic regimens.

Moreover, the discrepancy in treatment outcomes throughout hospital environments underscores the need for fortifying health-care frameworks, guaranteeing fair access to superior neonatal care, and cultivating partnerships between tertiary and secondary care facilities to exchange insights and assets.

Limitations of the study

The study's limitations include its observational design and the potential for selection bias given the hospital-based sampling. The findings may not be generalizable to all settings, especially where the distribution of bacterial pathogens and resistance patterns differ significantly.

CONCLUSION

This study highlights the difficulty in treating newborn sepsis and the important influence that antibiotic resistance and bacterial infections have on the course of treatment. To improve the prognosis of newborn sepsis worldwide, it advocates for a concerted effort to strengthen antimicrobial stewardship, upgrade health-care facilities, and implement advanced treatment techniques.

ACKNOWLEDGMENT

The authors express their gratitude to the staff of all three hospitals for their continuous support throughout this study.

REFERENCES

1. Russell NJ, Stöhr W, Plakkal N, Cook A, Berkley JA, Adhisivam B, et al. Patterns of antibiotic use, pathogens, and prediction of

mortality in hospitalized neonates and young infants with sepsis: A global neonatal sepsis observational cohort study (NeoOBS). PLoS Med. 2023;20(6):e1004179.

https://doi.org/10.1371/journal.pmed.1004179

2. Silva AC, Anchieta LM, de Paula Lopes MF and de Castro Romanelli RM. Inadequate use of antibiotics and increase in neonatal sepsis caused by resistant bacteria related to health care assistance: A systematic review. Braz J Infect Dis. 2018;22(4):328-337.

   https://doi.org/10.1016/j.bjid.2018.07.009

3. Song WS, Park HW, Oh MY, Jo JY, Kim CY, Lee JJ, et al. Neonatal sepsis-causing bacterial pathogens and outcome of trends of their antimicrobial susceptibility a 20-year period at a neonatal intensive care unit. Clin Exp Pediatr. 2022;65(7):350-357.

   https://doi.org/10.3345/cep.2021.00668

4. Mohakud NK, Mishra JP, Nayak MK, Mishra J, Pradhan L, Panda SS, et al. Bacteriological profile and outcome of culture-positive neonatal sepsis in a special newborn care unit setting, Odisha. Cureus. 2022;14(5):e25539.

   https://doi.org/10.7759/cureus.25539

5. Thida Oo NA, Edwards JK, Pyakurel P, Thekkur P, Maung TM, San Aye NS, et al. Neonatal sepsis, antibiotic susceptibility pattern, and treatment outcomes among neonates treated in two tertiary care hospitals of Yangon, Myanmar from 2017 to 2019. Trop Med Infect Dis. 2021;6(2):62.

   https://doi.org/10.3390/tropicalmed6020062

6. Celik IH, Hanna M, Canpolat FE and Pammi M. Diagnosis of neonatal sepsis: The past, present and future. Pediatr Res. 2022;91(2):337-350.

   https://doi.org/10.1038/s41390-021-01696-z

7. Zhu ML, Zheng G, Chen JN, Lin ZL, Zhu JH and Lin J. Comparative analysis of the pathogens responsible for hospital acquired and community acquired late onset neonatal septicemia. Zhonghua Er Ke Za Zhi. 2008;46(2):124-127. [Chinese]

8. Williams PC, Qazi SA, Agarwal R, Velaphi S, Bielicki JA, Nambiar S, et al. Antibiotics needed to treat multidrug-resistant infections in neonates. Bull World Health Organ. 2022;100(12):797-807.

   https://doi.org/10.2471/BLT.22.288623

9. Siddiqui T, Dubey A, Kar M, Patel SS, Sahu C and Ghoshal U. Bacteriological profiles and antibiotic susceptibility of neonatal sepsis in a university hospital of Northern India. J Family Med Prim Care. 2023;12(3):493-498.

   https://doi.org/10.4103/jfmpc.jfmpc_1535_22

10. Toan ND, Darton TC, Boinett CJ, Campbell JI, Karkey A, Kestelyn E, et al. Clinical features, antimicrobial susceptibility patterns and genomics of bacteria causing neonatal sepsis in a children's hospital in Vietnam: Protocol for a prospective observational study. BMJ Open. 2018;8(1):e019611.

    https://doi.org/10.1136/bmjopen-2017-019611

11. Thomson KM, Dyer C, Liu F, Sands K, Portal E, Carvalho MJ, et al. Effects of antibiotic resistance, drug target attainment, bacterial pathogenicity and virulence, and antibiotic access and affordability on outcomes in neonatal sepsis: An international microbiology and drug evaluation prospective substudy (BARNARDS). Lancet Infect Dis. 2021;21(12):1677-1688.

    https://doi.org/10.1016/S1473-3099(21)00050-5

12. Korang SK, Safi S, Gluud C, Lausten-Thomsen U and Jakobsen JC. Antibiotic regimens for neonatal sepsis-a protocol for a systematic review with meta-analysis. Syst Rev. 2019;8(1):306.

    https://doi.org/10.1186/s13643-019-1207-1

13. Milton R, Gillespie D, Dyer C, Taiyari K, Carvalho MJ, Thomson K, et al. Neonatal sepsis and mortality in low-income and middle-income countries from a facility-based birth cohort: An international multisite prospective observational study. Lancet Glob Health. 2022;10(5):e661-e672.

    https://doi.org/10.1016/S2214-109X(22)00043-2

14. Sands K, Spiller OB, Thomson K, Portal EA, Iregbu KC and Walsh TR. Early-onset neonatal sepsis in low-and middle-income countries: Current challenges and future opportunities. Infect Drug Resist. 2022;15:933-946.

    https://doi.org/10.2147/IDR.S294156

15. Yu Y, Dong Q, Li S, Qi H, Tan X, Ouyang H, et al. Etiology and clinical characteristics of neonatal sepsis in different medical setting models: A retrospective multi-center study. Front Pediatr. 2022;10:1004750.

    https://doi.org/10.3389/fped.2022.1004750

Authors Contributions:
RB- Concept and design of the study, results interpretation, review of literature, and preparing first draft of manuscript. Statistical analysis and interpretation, revision of manuscript; **VBSS-** Concept and design of the study, results interpretation, review of literature and preparing first draft of manuscript, revision of manuscript; **VV-** Review of literature and preparing first draft of manuscript. Statistical analysis and interpretation; **JPRS-** Concept and design of the study, results interpretation, review of literature, and preparing first draft of manuscript. Statistical analysis and interpretation, revision of manuscript.

Work attributed to:
Government Medical College, Srikakulam and GEMS Medical College, Srikakulam Andhra Pradesh, India.

Orcid ID:
Radhika B - https://orcid.org/0009-0001-5673-5802
Vijayasri BSS - https://orcid.org/0009-0005-7536-6909
Vidyasagar V - https://orcid.org/0009-0006-1442-6004
Jyothi Prakash Raju S - https://orcid.org/0009-0007-1115-2535

Source of Support: Nil, **Conflicts of Interest:** None declared.