



PATHOGENS CAUSING NEONATAL SEPSIS AT MCH HOSPITAL NAWABSHAH.

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ABSTRACT

BACKGROUND : A particular kind of neonatal illness known as "neonatal sepsis" occurs when a newborn infant has a bacterial blood stream infection (BSI) accompanied by a fever, such as meningitis, pneumonia, pyelonephritis, or gastroenteritis. Neonatal sepsis is often referred to as "sepsis neonatorum" in older texts. Clinically, criteria concerning hemodynamic compromise or respiratory failure are useless since these symptoms often do not appear in newborns until death is certain and cannot be avoided. Early-onset sepsis (EOS) and late-onset sepsis (LOS) are the two subtypes of neonatal sepsis. Sepsis that manifests during the first 72 hours of life is referred to as LOS, while sepsis that manifests after 7 days (or 72 hours, depending on the system employed) is referred to as EOS. In underdeveloped nations, neonatal sepsis is the leading cause of infant mortality in both hospitals and communities. **OBJECTIVES:** To identify the causative organism among neonatal sepsis maternal MCH Hospital Nawabshah. **MATERIAL METHODS: STUDY SETTINGS:** The study was conducted at Paeds Ward of MCH Nawabshah, SBA. **Study Population:** Data was collected from patients at MCH Nawabshah, SBA. **STUDY DESIGN:** Cross-Sectional Study. **Duration of study:** June 2023-December 2023. **SAMPLE SIZE: 285** **RESULTS:** E Coli was found in 90(31.5%), Klebsiella in 37 in 13%, S.Aureus in 18(6.3%), H.influenza in 15(5%), Pseudomonas Aueroginosa in 4 (1.4%), Group B Streptococcus in 30(10.5%) and V. Streptococcus in 6(2.3%). Total patients in which blood culture was positive were 200(70%) and 85(30%) had no growth. **CONCLUSION:** It is concluded that neonatal sepsis is more common in low birth weight and most of neonates were premature (before 37 weeks of gestation). E. coli and Staph Aureus were the most common organism involved in developing neonatal sepsis.

KEY WORDS; Neonates, Sepsis, Premature, E.Coli, Staphylococcus Aureus.

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INTRODUCTION

After prematurity, neonatal sepsis (NS) is the second most prevalent cause of infant fatalities in underdeveloped nations.^{1,2} According to the World Health Organization, four million newborns pass away each year. Pakistan currently has a newborn death rate of 44 per 1000 live births. Neonatal sepsis-related mortality is three times greater in underdeveloped nations like Pakistan than in

the industrialized world.³ NS is a systemic infection that affects newborns under 28 days of age, and a positive blood culture indicates bacterial growth. NS sepsis is categorized as either late onset (age >72 hours) or early onset (age of presentation <72 hours)⁴ In industrialized nations, there are around 34 cases of neonatal mortality (NM) for every 1000 live births. Between 30% and 50% of newborn fatalities are caused by infections and

septicemia.⁵ Although bacterial culture is the gold standard for diagnosis, C Reactive Protein (CRP) is often regarded as an early diagnostic sign because of the slow turnaround time of bacterial culture.⁶ In contrast, CRP has a poor sensitivity even if it is highly specific for neonatal sepsis. The hunt for the perfect diagnostic marker, or battery of indicators, for the identification of newborn sepsis is still ongoing since most of them fall short of the standards needed for clinical practice, despite their positive promises.⁷ Prematurity or low birth weight is the most significant neonatal risk susceptible to infection that might cause sepsis.⁸ Compared to full-term normal birth weight newborns, preterm low birth weight infants have an infection rate that is three to ten times greater.⁹ Neonatal sepsis, which is more prevalent in underdeveloped nations than in industrialized ones, is characterized as a disseminated illness with a positive blood culture within the first month of life.¹⁰ Different types of organisms may cause different mortality rates in cases of newborn sepsis.¹¹ *Neisseria gonorrhoeae*, *Streptococcus pyogenes*, *Enterococcus faecalis*, and *Streptococcus pneumoniae* in newborns in the community are the causes of both early and late sepsis. Gram negative bacteria and enterococci have the greatest fatality rate in neonatal sepsis. Moreover, *Neisseria meningitidis*, meningitis, pneumonia, osteomyelitis, brain abscesses, and early-onset sepsis have all been linked to *Ureaplasma* species and *Mycoplasma hominis*.^{12, 13} The incidence of pathogens varies greatly depending on the international context, with Gram-negative organisms accounting for a significant portion of the burden in regions with little resources.¹⁴ The range of microorganisms responsible for newborn sepsis differs among nations and sometimes shifts across centers within a single nation.¹⁵ Neonatal sepsis is most often caused by group B streptococci (GBS). The most often found microorganisms linked to newborn sepsis with an early start are *Escherichia coli* and *Streptococcus agalactiae* (GBS). Around 400,000 livebirths occurred in academically based neonatal centers in the USA between 2006 and 2009. Of them, 389 newborn children had early-onset illness, with 29% having *E. coli* and 43% having GBS.^{16, 17} The absolute neutrophil count, platelet count, immature/total leukocytes ratio (I:T), and C-reactive protein are hematologic indicators that

are used to test for neonatal sepsis. The sole gold standard test for NS diagnostic confirmation is blood culture.^{18,19}

RATIONALE OF STUDY:

Neonatal sepsis is one of the leading causes of mortality and morbidity throughout the world, and mostly affects developing countries. Pakistan is one of the under-developing countries. The aim of this study to identify causative organisms among neonatal sepsis, furthermore the result of this study helped to make strategies to decrease the frequency and also early management of neonatal sepsis.

MATERIAL & METHODS

Study setting: This study was conducted at the Pediatrics Department of MCH, Nawabshah Shaheed Benazir Abad. **Study design:** Cross sectional study. **Sampling technique:** Non-probability convenience sampling technique. **Duration of study:** Six months after approval of synopsis. **Sample size: 285** **Sample size calculation formula** Sample size is calculated by Rao soft sample size calculator using $P = \text{Prevalence}$ 25 Confidence level = 95% Margin of Error = 60% Population size = 200000 $n = 285$ Sample size will be 285

Inclusion criteria

1. Age < 28 days.
2. Both Gender.
4. Parents / Guardian Willing for participation for study.

Exclusion criteria

1. Age >28 days.
3. Not willing for participation in body.

Data collection Procedure: The research was carried out with permission from the Medical Superintendent of MCH Hospital, Nawabshah, and the approval of the summary from the Ethical Review Committee (ERC) of Peoples University of Medical & Health Sciences for women Nawabshah (SBA). Moreover, each parent provided explicit written approval or agreement. Guardian in the study. The data was collected on pre-designed structured questionnaire. All the data was kept confidential, and no any information was conveyed to anyone.

Results: 40(14%) aged between 1-10 days, 60(21%) age was between 11-20 days, 185(65%) age was between 21-28 days. 40(14%) patients weight was <1500gms, 110 (39%) patients' weight was 1500-2500gms and weight of 135(47%) patients was >2500 grams.

80(28%) patients gestational age was <34 weeks and 90(32%) patients gestational age was 34-37 weeks and 115(40%) patients' gestational age was >37 weeks. 90(32%) mode of delivery was spontaneous vaginal delivery and 195(68%) delivered by Caesarean section. 153(53%) were male and 135(47%) were female. 75(26%) patients' TLC was 3000-4000, 67(23.5%) patients' TLC was 5000-7000, 98(34.5%) patients TLC was 6000-8000 and TLC of 45(16%) patients were >10000. Platelets of 90(31.5%) patients were 20000-50000, 51000-90000 of 90(31.5%) patients, 80(28%) patients' platelets were 91000-130000 and of 25(9%) patients' were 400000-550000. C - reactive protein was positive in 150(52.6%) and negative in 135(47.4%). Blood Culture was positive in 200(70%) and negative in 85(30%) patients. E Coli was found in 90(31.5%), Klebsiella in 37 in 13%, S.Aureus in 18(6.3%), H.influenza in 15(5%), Pseudomonas Aueruginosa in 4 (1.4%), Group B Streptococcus in 30(10.5%) and V. Streptococcus in 6(2.3%). Total patients in which blood culture was positive were 200(70%) and 85(30%) had no growth.

Table No I showing frequency of patients according to age

Age in days	Frequency	Percentage %
1-10	40	14
11-20	60	21
21-28	185	65
Total	n=285	n=100

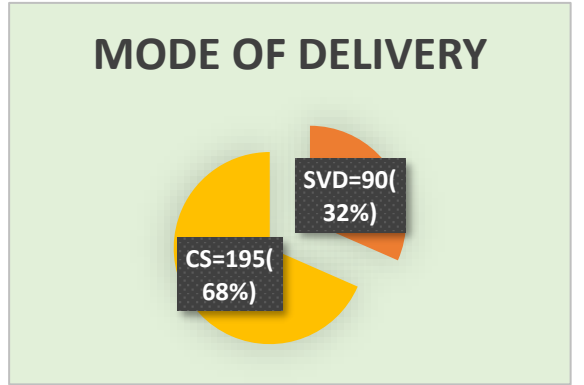
Table No II showing frequency of patients according to weight.

Weight in grams	Frequency	Percentage %
<1500	40	14
1500-2500	110	39
>2500	135	47
Total	n=285	n=100

Table No III showing frequency according to gestational age of patients.

Gestational Age in weeks	Frequency	Percentage %
<34	80	28
34-37	90	32
>37	115	40
Total	n=285	n=100

PIE CHART I SHOWING MODE OF DELIVERY



PIE CHART II GENDER RATIO OF NEONATES

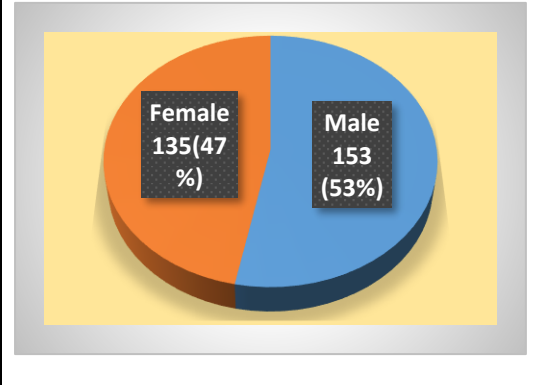


Table No IV showing Hematological variables

TLC	Frequency	%
3000-4000	75	26
5000-7000	67	23.5
6000-8000	98	34.5
>10000	45	16
Total	n=285	n=100%

Platelets (cells/mm ³)	No of patients	%
20000-50000	90	31.5
51000-90000	90	31.5
91000-130000	80	28
400000-550000	25	9
Total	n=285	n=100%

Table No V showing Hematological variables and their frequencies.

Hematological variable	Result	No of patients	%
CRP	Positive	150	52.6
	Negative	135	47.4
Blood Culture	Positive	200	70
	Negative	85	30

Table No VI showing the prevalence of Bacteria

Bacteria	Frequency	Numerical %
E. Coli	90	31.5%
Klebshiella	37	13%
Staphylococcus Aureus	18	6.3%
Hemophilus Influenza	15	5%
Pseudomonas Aeruginosa	4	1.4%
Group B streptococcus	30	10.5%
Viridians Streptococcus	6	2.3%
Total	n=200	n=70%

Table No VII Antibiotic sensitive/resistance patterns for gram negative bacterial isolates

Antibiotic	E Coli	Klebsh iella	Pseudo monas	Group B Streptococcus	Staph Aureus
Amikacin	89 S 16 R	23 S 34 R	1 S 3 R	50 S 20 R	22 S 6 R
Ceftriaxone	92 S 13 R	33 S 24 R	3 S 1 R	54 S 16 R	20 S 8 R
Cefotaxime	90 S 15 R	21 S 36 R	2 S 2 R	60 S 10 R	20 S 8 R
Ampicillin	70 S 35 R	20 S 37 R	1 S 3 R	12 S 58 R	21 S 7 R
Cefixime	60 S 45 R	34 S 23 R	1 S 3 R	22 S 48 R	13 S 15 R

DISCUSSION

A clinical illness known as neonatal sepsis is defined by infection-related signs and symptoms that are often linked to bacteremia. This condition may further worsen multiorgan

failure by triggering a systemic inflammatory response syndrome. Gram-positive bacteria such as Streptococcus pneumoniae, Enterococcus, Staphylococcus aureus, and Escherichia coli are among the bacteria that cause early-onset newborn sepsis. Acinetobacter baumannii, coagulase-negative staphylococci (CONS), gram-negative bacteria, and viral infections such as echovirus, enterovirus, parechovirus, coxsackie virus, adenovirus, parainfluenza virus, rhinovirus, and coronavirus are among the agents that cause late-onset newborn sepsis. Although fungal causes are rare, Candida is the most prevalent kind.²⁰

269 (36.3%), 140 (18.9%), 129 (17.4%), and 203 babies (27.4%) of the 741 instances of bacteremia in the research had birth weights of less than 1,000 g (very low birth weight), 1,000–1,499 g (low birth weight), and $\geq 2,500$ g (normal birth weight). Regarding the GA, sepsis was noted in 136 babies (18.4%) whose GA was $\leq 26+0$ weeks, 319 babies (43.1%) whose GA was between 26 and 34 weeks, 100 babies (13.5%) whose GA was between 34 and 37 weeks, and 186 babies (25.1%) whose GA was more than 37 weeks. 40 patients (14%) in my research weighed less than 1500 grams, 110 patients (39%) weighed between 1500 and 2500 grams, and 135 patients (47%) weighed more than 2500 grams. The gestational age of 80 (28%) patients was less than 34 weeks, 90 (32%) patients was between 34 and 37 weeks, and 115 (40%) patients was more than 37 weeks.²¹

A peripheral blood smear (which searches for toxic granulation, vacuolization, and Dohle bodies) and a leukocytic count are often used to detect neonatal sepsis. Neutropenia, defined as an absolute neutrophil count at 4 hours of less than 1,000/mm³, is considered to be a reliable indicator of infant sepsis with an early start. Even though the WBC count has limitations since its values change within the first 12 hours of life, many measurements made throughout the day might provide more information than a single test. A study by found that leucopenia (WBC count $< 5,000/\text{mm}^3$) had a high specificity (91%) but a weak sensitivity (29%) for identifying infant sepsis. Other studies have shown that leukopenia is a more reliable predictor after more than four hours than leukocytosis (WBCs $> 20,000/\text{mm}^3$). At a 200 pg/mL cutoff level, the granulocyte monocyte

colony-stimulating factor had a substantial negative predictive value in one study. Even though the most sensitive biomarker is the immature-to-total neutrophil (I: T) ratio, there is still variation dependent on gestational age and postnatal age. Full-term babies with an I:T ratio > 0.27 and preterm neonates with a ratio > 0.22 have a higher likelihood of being diagnosed with neonatal sepsis.²² Platelets may also reveal sepsis. Sepsis causes a reduction in platelet synthesis and an increase in mean platelet volume (MPV) due to the formation of younger and bigger platelets. Since MPV indicates a rise in the diameter of produced platelets, it clinically predicts platelet production rate and activation. Another study compared to healthy people, newborns with sepsis had an overall higher MPV. Additionally, there is an increase in platelet distribution width (PDW), which suggests platelet size heterogeneity. PDW rises when platelet anisocytosis occurs. PDW and MPV are correlated physiologically, and their changes often follow one another. Platelet indices may be used to evaluate the response to therapy and are helpful in diagnosis and follow-up. 75 patients (26%) in my research had a TLC of 3000–4000, 67 patients (23.5%) had a TLC of 5000–7000, 98 patients (34.5%) had a TLC of 6000–8000, and 45 patients (16%) had a TLC of >10000. 90 (31.5%) patients had platelets between 20000 and 50000, 90 (31.5%) patients had platelets between 51000 and 90000, 80 (28%), and 25 (9%), had platelets between 400000 and 550000.²³

In a study, of the 895 strains that were cultured from the newborns, 475 (53.0%) and 112 (12.5%) were found to have CoNS and Staph aureus, respectively. Sixty-seven (45.3%) of these microorganisms were gram-positive. *Klebsiella pneumoniae* accounted for 64 cases, or 7.1% of all gram-negative bacteria. This pathogen was the most common. The next most common pathogens were *Burkholderia cepacia*, *E. coli*, *Pseudomonas aeruginosa*, and *Enterobacter cloacae*. Among the 475 CoNS patients, *Staphylococcus epidermis* and *Staphylococcus capitis* were found in 347 and 91 cases, respectively. *S. capitis* was discovered in 34 instances (7.1%) of newborns with GA < 26 weeks, 43 cases (9.0%) between 26 weeks and 34 weeks, and 14 cases (2.9%) above 34 weeks. *S. capitis* was the most common species among babies with GA between 26 and 34

weeks of age. Among the 475 instances of CoNS in babies with GA < 26 weeks, *S. epidermis* was also found in 138 cases (29.0%) above 34 weeks, 153 cases (32.2%) between 26 weeks and 34 weeks, and 56 cases (11.7%) overall.²⁴

In my study, *E. coli* was found in 90(31.5%), *Klebsiella* in 37 in 13%, *S. aureus* in 18(6.3%), *H. influenza* in 15(5%), *Pseudomonas aeruginosa* in 4 (1.4%), Group B *Streptococcus* in 30(10.5%) and *V. Streptococcus* in 6(2.3%). Total patients in which blood culture was positive were 200(70%) and 85(30%) had no growth.

CONCLUSION

It is concluded that neonatal sepsis is more common in low birth weight and most of neonates were premature (before 37 weeks of gestation). *E. coli* and *Staph aureus* were the most common organism involved in developing neonatal sepsis.

ETHICS APPROVAL: The ERC gave ethical review approval.

CONSENT TO PARTICIPATE: written and verbal consent was taken from subjects and next of kin.

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AUTHORS' CONTRIBUTIONS:

All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated in the work to take public responsibility of this manuscript. All authors read and approved the final manuscript.

CONFLICT OF INTEREST: No competing interest declared

REFERENCES:

1. Popescu CR, Cavanagh MMM, Tembo B, Chieme M, Lufesi N, Goldfarb DM, et al. Neonatal sepsis in low-income countries: epidemiology, diagnosis and prevention. Vol. 18, Expert Review of Anti-Infective Therapy. Taylor and Francis Ltd; 2020.37 (1):443-52.
2. Charles MVP, Kalaivani R, Venkatesh S, Kali A, Seetha KS. Evaluation of procalcitonin as a diagnostic marker in neonatal sepsis. *Indian J Pathol Microbiol.* 2018;61(1):81–4.

3. Gandhi P, Kondekar S. A Review of the Different Haematological Parameters and Biomarkers Used for Diagnosis of Neonatal Sepsis. *EMJ Hematol.* 2019;7(1):85–92.
4. Balayan S, Chauhan N, Chandra R, Jain U. Molecular imprinting based electrochemical biosensor for identification of serum amyloid A (SAA), a neonatal sepsis biomarker. *Int J Biol Macromol.* 2022;195:589–97.
5. E DSS. Clinical and Epidemiological Profile of Neonatal Sepsis in Referral Care NICU in South Kerala. *J Med Sci Clin Res.* 2017;05(03):327–33.
6. Kumar R, Kumari A, Kumari A, Verma N. Evaluation of perinatal factors in neonatal sepsis at tertiary centre. *Int J Reprod Contraception, Obstet Gynecol.* 2017;6(11):4981.
7. 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 Heal.* 2022;10(5):e661–72.
8. Iroh Tam PY, Bendel CM. Diagnostics for neonatal sepsis: Current approaches and future directions. 2017. 82. 574–83.
9. Popescu CR, Cavanagh MMM, Tembo B, Chiume M, Lufesi N, Goldfarb DM, et al. Neonatal sepsis in low-income countries: epidemiology, diagnosis and prevention. Vol. 18, *Expert Review of Anti-Infective Therapy.* 2020. 443–52.
10. Fleischmann-Struzek C, Goldfarb DM, Schlattmann P, Schlapbach LJ, Reinhart K, Kissoon N. The global burden of paediatric and neonatal sepsis: a systematic review. Vol. 6, *The Lancet Respiratory Medicine.* 2018 Mar;6(3):223-230.
11. Murthy S, Godinho MA, Guddattu V, Lewis LES, Sreekumaran Nair N. Risk factors of neonatal sepsis in India: A systematic review and meta-analysis. *PLoS One.* 2019, 25;14(4):2156-83.
12. Ng S, Strunk T, Jiang P, Muk T, Sangild PT, Currie A. Precision Medicine for Neonatal Sepsis. *Front Mol Biosci.* 2018;26;(5):70-77.
13. Balayan S, Chauhan N, Chandra R, Kuchhal NK, Jain U. Recent advances in developing biosensing based platforms for neonatal sepsis. *Biosensors and Bioelectronics,* PMID: 2020;292-97;
14. Fell DB, Hawken S, Wong CA, Wilson LA, Murphy MSQ, Chakraborty P, Lacaze-Masmonteil T, Potter BK, Wilson K. Using newborn screening analytes to identify cases of neonatal sepsis. *Sci Rep.* 2017; 21;7(1):180-88.
15. Wynn JL, Polin RA. Progress in the management of neonatal sepsis: the importance of a consensus definition. *Pediatr Res.* 2022;83(1-1):13-15.
16. Memar MY, Alizadeh N, Varshochi M, Kafil HS. Immunologic biomarkers for diagnostic of early-onset neonatal sepsis. *J Matern Fetal Neonatal Med.* 2019 ;32(1):143-153.
17. Kim F, Polin RA, Hooven TA. Neonatal sepsis. *BMJ.* 2020;371:367-72.
18. Celik IH, Hanna M, Canpolat FE, Pammi M. Sepsis and infection: two words that should not be confused. *Vincent JL. Front Med (Lausanne)* 2023;10:1156-73.
19. Diagnosis of neonatal sepsis: the past, present and future. *Pediatr Res.* 2022;91:337–350.
20. Jui J, et al. (American College of Emergency Physicians) . "Ch. 146: Septic Shock". In Tintinalli JE, Stapczynski JS, Ma OJ, Cline DM, Cydulka RK, Meckler GD (eds.). *Tintinalli's Emergency Medicine: A Comprehensive Study Guide (7th ed.)*. New York: McGraw-Hill. 2021;. 1003–14.
21. Deutschman CS, Tracey KJ . "Sepsis: current dogma and new perspectives". *Immunity.*2014; 40 (4): 463–475.
22. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. "The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)". *JAMA.*2016; 315 (8): 801–810.
23. Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al.. "Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016". *Intensive Care Medicine.*2020; 43 (3): 304–377.
24. Jawad I, Lukšić I, Rafnsson SB. "Assessing available information on the burden of sepsis: global estimates of incidence, prevalence and mortality". *Journal of Global Health.*2022; 2 (1): 010404.