e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(10); 280-288

Original Research Article

Evaluation of Maternal and Neonatal Risk Factors and Outcomes of EOS

Saurabh Kumar Singh[1], Mala Kumar[2]

[1]Assistant Professor, Department of Pediatrics, Hind Institute of Medical Sciences, Ataria, Sitapur, Lucknow

[2]Profeesor (HOD), Department of Pediatrics, K.G.M.U, Lucknow

Received: 25-07-2023 / Revised: 28-08-2023 / Accepted: 30-09-2023

Corresponding author: Dr. Saurabh Kumar Singh

Conflict of interest: Nil

Abstract:

Introduction: Maternal and neonatal risk factors affect the development of "early-onset sepsis (EOS)" in infants. Group B Streptococcus infection and preterm membrane rupture are two examples of maternal causes. Prematurity, low birth weight, and mother colonization are all factors that pose a danger to newborns. Preventing EOS and its severe repercussions, like septic shock and long-term developmental difficulties, requires prompt diagnosis and treatment.

Aim and Objectives: This study aims to evaluate the impact of various maternal and neonatal variables on the outcomes of early-onset sepsis.

Method: From September 2014 to August 2015, K.G. Medical University's Lucknow NICU observed term and preterm infants at risk of Early-Onset Sepsis. Babies who left the NICU within 24 hours or died were eliminated. Antenatal, peripartum, maternal, and neonatal EOS risk factors and pre-admission antibiotic exposure were examined. For a better understanding of NICU EOS, neonates were divided into "High Suspicion of EOS (HS-EOS)" and Low Suspicion groups.

Result: Figure 1 and Table 1 shows culture-positive "Early-Onset Sepsis (EOS)" and neonatal EOS isolates. Table 2 shows antibiotic susceptibility for treatment decisions. Table 3 shows baseline commonalities in culture-proven and most probable EOS newborns. Table 4 lists frequent EOS symptoms. Figure 2 stresses TLC's role in culture-proven sepsis detection. Figure 3 shows neonatal pneumonia risk factors. Table 5 and 6 shows maternal neonatal meningitis risk factors and early diagnosis and treatment enhance newborn outcomes for culture-positive EOS.

Conclusion: Escherichia coli and Staphylococcus aureus cause most NICU early-onset sepsis; ampicillin, cephalosporin, and amoxicillin resistance is widespread; piperacillin and amikacin are first-line treatments.

Keywords: Maternal and neonatal risk factors, "early-onset sepsis (EOS)", premature rupture of membranes (PROM)", " maternal neonatal meningitis risk factors".

Introduction

"Early-onset sepsis(EOS)" is an intense and potentially life-threatening situation that mainly impacts neonates within the first few days of newborns. In order to effectively fight this danger, it is crucial to consider both maternal and neonatal risk factors and comprehend the consequences associated with EOS [1]. The maternal risk factors for EOS encompass a span of critical considerations. Principal among these is maternal illnesses, with "Group B Streptococcus (GBS)" being a main issue. Maternal GBS disease can be communicated to the neonate during the newborn, making it critical for healthcare providers to perform timely screening and administer proper treatment to mitigate the threat of EOS [2]. Furthermore, the "premature rupture of membranes (PROM)" poses an important risk, as it compromises the protecting barrier, improving the exposure of neonates to infection. Intrapartum fever, frequently expressive of maternal infection, and chorioamnionitis, which pertains to inflammation of the fetal membranes and amniotic fluid, are also important factors that boost the probability of EOS. Vigilant monitoring and surveillance of these maternal risk factors are urgent to prevent EOS in neonates [3]. Neonatal risk aspects play an equally key role in specifying the probability of EOS. The gestational age of the neonate is a paramount aspect, with premature infants being at an enormously higher risk due to their underdeveloped immune systems. The immature gestational age, and the incredible susceptibility to disease, create rapid intervention and careful monitoring necessary for these vulnerable infants [4]. Besides, low birth weight is a significant risk factor, as it frequently accompanies prematurity and further weakens the neonate's

immune defence. Invasive methods, a common need in neonatal care, can inadvertently introduce bacteria into the bloodstream, thereby improving the risk of EOS. Estimates to reduce infection risk during these methods, such as rigorous aseptic techniques, are important. Maternal colonization with GBS or other pathogenic bacteria is however another substantial neonatal risk factor, emphasizing the significance of specifying and addressing maternal colonization during prenatal care [5]. The newborn risk factors discussed collectively underscore the importance of implementing rigorous care practices and infection prevention measures within the neonatal critical care unit. In comparison to "early cord clamping (ECC)", which was frequently performed within 10-15 seconds after delivery, "delayed cord clamping (DCC)" for a minimum duration of 30 seconds immediately after birth was found to be crucial in facilitating the transfer of blood from the placenta to the newborn. The practice of "early cord clamping (ECC)" was commonly implemented within a timeframe of 10 to 15 seconds following the delivery process. There is a growing body of evidence that demonstrates the advantages of "delayed cord clamping (DCC)" in both term and preterm newborns. The advantages encompass elevated hemoglobin levels and iron status, enhanced neurodevelopment in newborns and children, reduced prevalence of anemia, elevated blood pressure, decreased need for transfusions, and decreased incidence of "intraventricular hemorrhage (IVH)", chronic lung disease, necrotizing enterocolitis, and late-onset sepsis [6]. In addition, DCC has been shown to increase the amount of iron in the blood. Polycythemia, jaundice, and a greater need for phototherapy are potential risks associated with DCC. "Maternal postpartum hemorrhage" or the demand for a "maternal blood transfusion" are other possible adverse effects of DCC. A committee decision that approved DCC in preterm newborns was published not too long ago by the "American College of Obstetricians and Gynecologists (ACOG)". DCC has been shown to enhance hemodynamic outcomes and reduce hospital mortality in a number of systematic reviews and meta-analyses, which provided support for the guidelines now in place that encourage using DCC in preterm newborns [7]. Moreover, DCC was typically carried out for 30 seconds to 5 minutes, or until the cord stopped pulsating, whichever came first. It was still debatable as to when, exactly, doctors should clip the umbilical cord of newborns, both full-term and premature. In light of the controversy surrounding the effects of early versus delayed umbilical cord clamping on mother and newborn outcomes, the goal of this paper was to give a complete and up-to-date summary of the relevant literature on the topic [8-11]. In evaluating the consequences of EOS, it is apparent that convenient recognition and surveillance of risk factors are key in reducing the morbidity and mortality related to this condition. Neonates who formulate EOS may encounter a range of negative consequences, such as septic shock, organ dysfunction, and long-term developmental issues [12,13]. Premature diagnosis and prompt initiation of antibiotics can substantially enhance the prognosis for affected newborns. Nevertheless, delays in diagnosis and therapy can lead to devastating outcomes. Similarly, the overuse of antibiotics in neonates without EOS can contribute to the growth of antibiotic resistance, highlighting the necessity for valid usage of antimicrobial agents. Moreover, comprehending the maternal and neonatal risk factors linked with EOS [14,15]. Their potential consequences are crucial for healthcare providers to formulate helpful prevention and management methods, eventually protecting the health and well-being of neonates during the essential early days of life.

Method

Research Design

This prospective observational cohort study was conducted in the NICU at K.G. Medical University, Lucknow, from September 2014 to August 2015. Term and preterm neonates with "Early-Onset Sepsis (EOS)" or "at risk" for EOS were studied. EOS-suspected newborns with clinical signs were included, while those who left the NICU before the EOS examination or died within 24 hours were excluded. Antenatal and peripartum events, maternal and neonatal EOS risk factors, and antibiotic exposure before admission were assessed in the study. Later, clinical profiles and maternal risk factors divided neonates into two groups: 1) High Suspicion of EOS (HS-EOS) and 2) Low Suspicion. To understand NICU EOS, this study compared outcomes and features between different groups.

Inclusion and exclusion criteria

Inclusion

- Neonates (term as well as preterm) admitted in NICU with clinical.
- features suggestive of EOS or "at risk" for EOS.

Exclusion criteria:

- Birth weight less than 1200g.
- Newborn with major congenital anomaly
- Consent not obtained.
- Neonates with severe asphyxia (Apgar <4 at 5 minutes or HIE stage 3).
- Neonates with HMD.

Statistical analysis

This study's data was entered into Excel and analyzed using SPSS 15.0 and Epi-info. Expectations were used to determine the sample size. It was expected that 50% of newborns with

"high suspicion of EOS" and 20% of those with "low suspicion of EOS" would have positive sepsis screens. Based on these assumptions, sample size calculations were made to ensure the study had enough statistical power to detect significant changes between groups.

Result

Figure 1 shows the number of culture-positive "Early-Onset Sepsis (EOS)" and the most probable EOS cases per thousand newborns. The graph shows two lines: culture-positive EOS and most probable EOS, plotted against incidence per thousand neonates. As the incidence per thousand neonates climbs from 0 to 250, culture-positive EOS cases rise correspondingly, suggesting a linear connection. Most probable EOS follows a similar trend but is consistently lower than culture-positive EOS. This visualisation shows that culture-positive EOS is more common than most probable EOS across different population sizes.

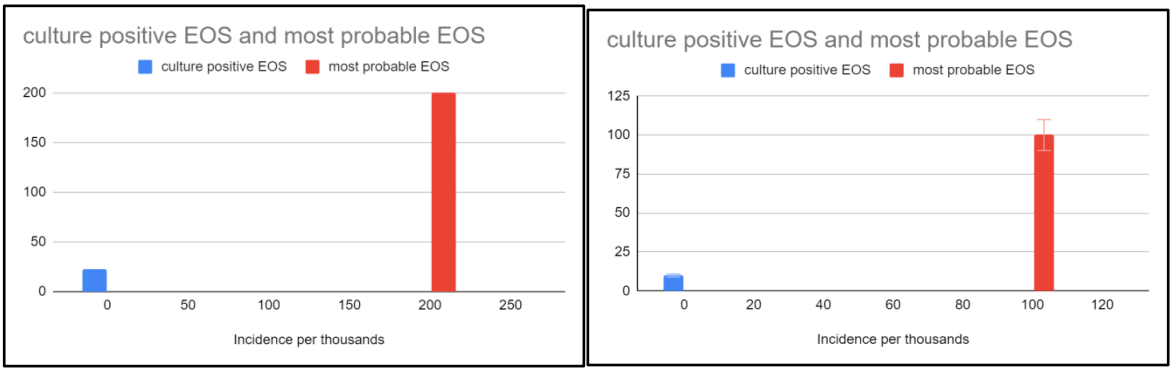

Figure 1: Incidence of culture-positive EOS and most probable EOS

Table 1 shows isolates from newborns with "Early-Onset Sepsis". Each specimen type and isolate count are listed in the table. E. coli (6 isolates) and Staphylococcus aureus (4 isolates) predominated in the blood samples. Acinetobacter, Pseudomonas, and Enterococcus faecalis were also isolated in two cases. CSF samples contained Enterococcus faecalis and Staph aureus isolates. One E. coli and one Citrobacter isolate were detected in CSF. Pathogens were found in blood and CSF samples from neonatal EOS cases in this investigation.

Table 1: Profile of isolates in neonates with EOS

Specimen	Number Of Isolates	Names Of Isolates
Blood	6	E. coli
	6	Staph. Aureus
	4	Enterococcus faecalis
	2	Pseudomans
	2	Acinetobacter
CSF	2	Enterococcus faecalis
	1	Staph aureus
	1	E coli
	1	Citrobacter

Table 2 shows the antibiotic susceptibility of "Early-Onset Sepsis (EOS)" neonate isolates. The table shows what antibiotics Escherichia, Acinetobacter, Pseudomonas, Citrobacter, Staph aureus, and Enterococcus are susceptible (S) or resistant (R) to. Most Escherichia (n=6) were responsive to ampicillin (A), cefotaxime (C), ceftriaxone (CTR), and gentamicin (GEN), but resistant to P/T and imipenem. Acinetobacter (n=2) was resistant to most antibiotics but susceptible to amikacin and levofloxacin. Amikacin (AK) worked on Pseudomonas, although most other antibiotics did not. A few antibiotics worked on Citrobacter. Only vancomycin (VA) and linezolid (LZ) were effective against Staph aureus (n=6). Erythromycin (ERY) and clindamycin (CD) resistant, Enterococcus (n=4) was ampicillin-sensitive. This data helps determine neonatal EOS treatment by revealing organisms' antibiotic susceptibility patterns.

Table 2: Antibiotic Susceptibility Pattern

ORGANISM		A/C	P/T	CTR	CPM	IMI	GEN	AK	LE	
Escherichia (n=6)	S	2(33.3)	3(50)	2(33.3)	3(50)	5(83)	2(33.3)	2(33.3)	4(66.7)	
	R	4(66.7)	(3)50	4(66.7)	3(50)	1(16.6)	4(66.7)	4(66.7)	2(33.3)	
Acinetobacter N=2	S	-	1(50	0	1(50	1(50	1(50	1(50	2(100)	
	R		1	2(100)	2(100)	1(50)	1(50)	1(50)	0	
Pseudomonas	S	-	1(50)	-	1(50)	1(50)	1(50)	1(50)	2(100)	
	R	-	1(50)	-	1(50)	1(50)	1(50)	1(50)	0	
Citrobacter	S	0	1	1	1	1	0	0	0	
	R	0	0	0	0	0	1	1	1	
ORGANISM		Amp	A/C	CX	GEN	LE	ERY	CD	VA	LZ
Staph aureus (n=6)	S	-	2(33.3)	3(50)	4(66.7)	4(66.7)	3(50)	2(33.3)	5(83.3)	6(100)
	R	-	6(66.7)	4(50)	2(33.3)	2(33.3)	3(50)	4(66.7)	1(16.7)	0
Enterococcus (n=4)	S	4 (100)	-	-	-	3 (75%)	3(75%)	-	4(100)	4(100)
	R	0	-	-	-	1 (25%)	1(25%)	-	0	0

Table 3 compares baseline features of neonates with "Early-Onset Sepsis (EOS)" with culture-proven EOS (n=21) and most probable EOS (n=263). The table shows factors and their p-values, demonstrating the significance of differences between groups. It demonstrates that gender distribution was similar between groups (p=0.6949). The two groups did not vary in delivery weight below 1500 grams, birth asphyxia, meconium-stained fluid, PROM greater than 24 hours, maternal fever, or other variables. The two groups had similar mean birth weights and gestations (p=0.9765 and p=0.8765). These results indicate that neonates with culture-proven EOS and those with the most probable EOS have similar baseline features.

Table 3: Profile of neonates with EOS

Base Line Characteristics	No. of Neonates		p value
	Culture Proven (n=21)	Most Probable (n=263)	
Male	15 (71.4%)	198 (76.1%)	0.6949
Birth Weight < 1500 gm	2 (9.5%)	26 (10.3%)	0.9595
Birth asphyxia	2 (9.5%)	58 (18.7%)	0.1922
Meconium stained liquor	1 (4.3%)	17 (6.4%)	0.759
PROM> 24 hrs	12 (57.1%)	160 (60.6%)	0.7391
Maternal Fever	7 (13.3%)	36 (13.5%)	0.2563
Foul Smelling Liquor	4 (19%)	20 (6.7%)	0.0812
Prolonged Labour	2 (9.5%)	20 (6.7%)	0.7131
Unclean Pv Examination	12 (57.1%)	156 (59.6%)	0.8465
Mean weight in gm (SD)	2417.14(718.75)	2389(602.67)	0.9765
Mean gestation in weeks (SD)	36.4 wks(1.8)	37.6 (2.3)	0.8765

Table 4 shows the clinical symptoms of newborns with "Early-Onset Sepsis (EOS)", including culture-proven and most probable sepsis. The table shows the frequency and proportion of neonates experiencing EOS symptoms. The most common symptom was refusal to feed (52.4%), followed by lethargy (49.1%) and hypothermia (39.3%). Although less common, respiratory distress (34.4%), abdominal distension (22.2%), and convulsions (11.1%) were reported. Fewer infants had jaundice (9.8%), apnea (3.2%), and sclerema (1.9%). These clinical features help diagnose EOS and show the variety of symptoms newborns with suspected sepsis might have, underlining the significance of early detection and management in this vulnerable population.

Table 4: Clinical Features in EOS (Culture proven and most probable sepsis)

Sign/Symptoms	Numbers (%)
Refusal to Feed	160 (52.4%)
Lethargy	156 (49.1%)
Hypothermia	120 (39.3%)
Respiratory Distress	105 (34.4%)
Abdominal distension	68 (22.2%)
Convulsions	34 (11.1%)
Jaundice	30 (9.8%)

Apnea	10 (3.2%)
Sclerema	6 (1.9%)

Figure 2 combines culture-proven sepsis to "TLC (Total Leukocyte Count)" below 5000 cells per cubic millimetre and clinical profile. Culture-proven sepsis neonates' sepsis screen results, CRP levels greater than 10 mg/l, MicroESR, TLC, and ANC are shown in the table. Each parameter's results are categorized as positive or negative and given as percentages. All patients with positive TLC results below 5000 cells per cubic millimetre were associated with a high suspicion of sepsis, while none were observed in the low suspicion group. This image highlights the ability of TLC levels to detect culture-proven sepsis in newborns, especially those with high clinical suspicion.

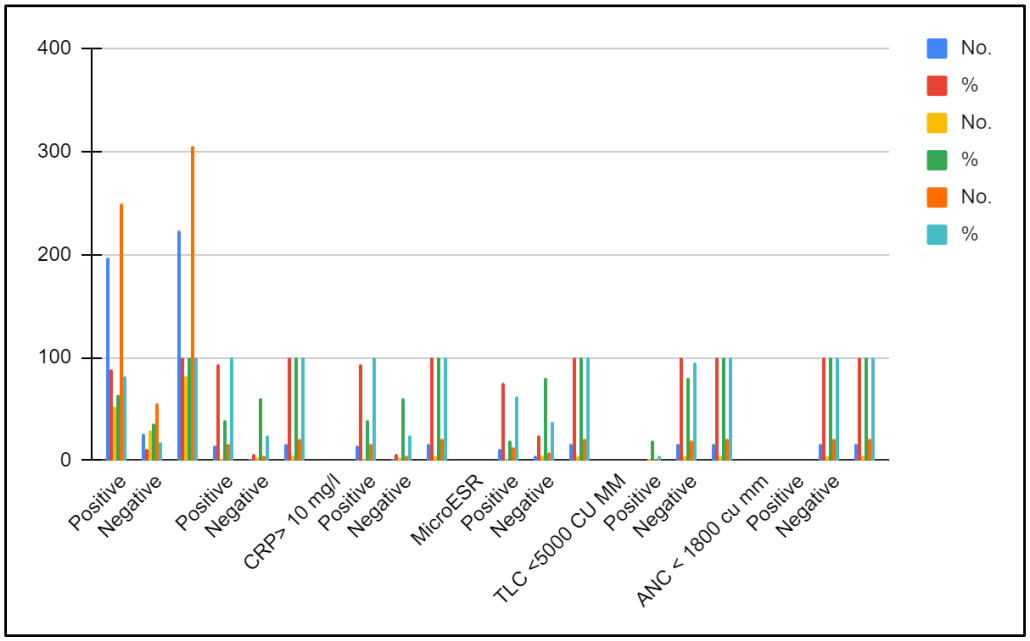

Figure 2: Association of TLC < 5000 cumm with the clinical profile in Culture-proven sepsis

Figure 3 shows newborn risk variables for culture-proven "Early-Onset Sepsis (EOS)" and pneumonia. Patients with pneumonia (n=5) and those without pneumonia (n=16) are listed. In these groups, birth weight less than 1500 grams, meconium-stained liquid, and Apgar scores between 4-6 at 5 minutes after birth are examined. All pneumonia cases had birth weights over 1500 grams, and neither group had meconium-stained liquor. In pneumoniac newborns, 4-6 Apgar scores at 5 minutes after birth were more common. Clinical assessments should consider newborn risk factors for pneumonia in culture-proven EOS, as this data shows.

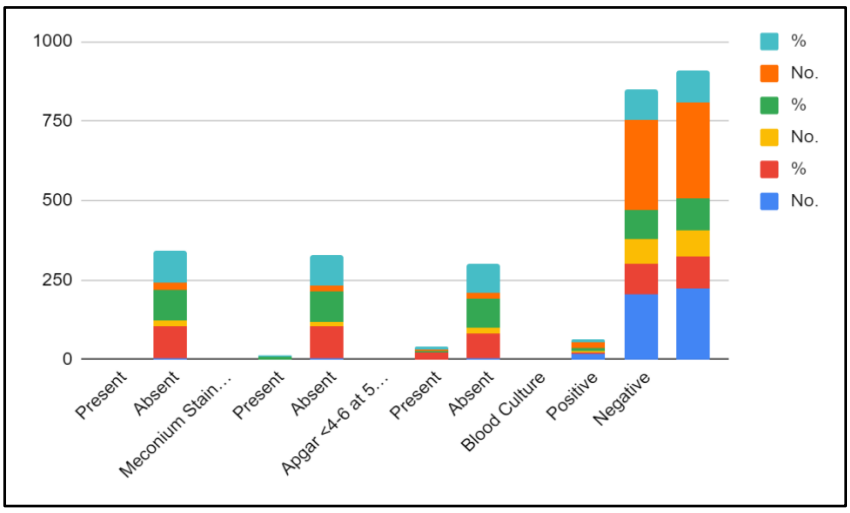

Figure 3: Association of Neonatal risk factors in culture-proven EOS with pneumonia

Table 5 presents maternal risk variables for culture-proven "Early-Onset Sepsis (EOS)" and neonatal meningitis. Neonatals with and without meningitis are separated in the table. It assesses maternal risk factors in these individuals, including fever, LPV, protracted labor, foul-smelling liquor, and filthy PV (Per Vaginal) inspection. Mothers with fever, LPV, foul-smelling beverages, and dirty PV exams were more common in infants with meningitis. These maternal risk variables may be linked to newborn meningitis in culture-proven EOS, stressing the importance of maternal factors in sepsis clinical assessment.

Table 5: Association of Maternal risk factors in Culture proven EOS with meningitis

Risk factor	Meningitis		No Meningitis		Total	
	No.	%	No.	%	No.	%
Maternal Fever						
Present	1	6.7	2	33.3	3	14.3
Absent	14	93.3	4	66.7	18	85.7
LPV						
Present	11	73.3	1	16.7	12	57.1
Absent	4	26.7	5	83.3	9	42.9
Prolonged Labour						
Present	2	13.3	0	0	2	9.5
Absent	13	86.7	6	100	19	90.5
Foul smelling liquor						
Present	4	26.7	0	0	4	19
Absent	11	73.3	6	100	17	81
Unclean PV						
Present	11	73.3	1	16.7	12	57.1
Absent	4	26.7	5	83.3	9	42.9

Table 6 shows the study's Early-Onset Sepsis (EOS) neonates' outcomes. LAMA (Leave Against Medical Advice), Expiry (dead), and Discharge are its neonatal outcome categories. None of 21 culture-positive EOS cases departed without medical advice, one died, and 20 were discharged. Of the 308 neonates with the most probable sepsis, 13 left against medical advice, 4 died, and 291 were released. In newborns with culture-positive EOS vs most probable sepsis, early diagnosis and adequate medical therapy improve outcomes, especially in culture-proven sepsis.

Table 6: Outcome of neonates with EOS

	LAMA	Expiry	Discharge
Culture Positive EOS (21)	0	1	20
Most probable sepsis (308)	13	4	291

Discussion

With the widespread consumption of intrapartum antibiotic medications, the prevalence of neonatal symptoms that appear as sepsis has decreased; nonetheless, early-onset sepsis continues to be a potentially lethal illness, especially in extremely low-birth-weight newborns [16]. The initial postnatal period may not show any clinical indications of neonatal infection since they are non-specific. Baby test results and maternal and baby clinical traits have been used to determine whether newborns are at risk to start giving them antibiotics right away to halt the course of more serious disease [17]. On the other hand, our study found that the percentage of infants with "Early-Onset Sepsis (EOS)" and the most likely EOS cases per thousand are shown in Figure 1. Two lines can be seen on the graph: Plotting EOS with a culture-positive result and the most likely EOS against incidence per 1,000 neonates. With such methods, practically all preterm newborns and 15% of symptomatic term & late preterm infants are evaluated. Similarly, our study shows that culture-positive EOS cases increase proportionally as the incidence per thousand newborns increases from 0 to 250, showing a linear relationship. Though it has a comparable pattern, most likely EOS continuously registers lower than culture-positive EOS. By using multivariate prediction models, it may be feasible to more precisely identify newborns who have the greatest risk and to restrict their exposure to antibiotics [18].

Another well-known risk factor that contributes to poor perinatal outcomes is intrapartum fever. In this study, we examined the causes of intrapartum maternal fever related to infant early-onset sepsis (EOS) & assessed the clinical characteristics of intrapartum maternal fever [19]. Furthermore, our study presents newborn risk variables for culture-proven "Early-Onset Sepsis (EOS)" and pneumonia. It also evaluates maternal risk factors in these

people, such as fever, LPV, protracted labor, foul-smelling liquor, and filthy PV (Per Vaginal) inspection. Between January 1 and December 31, 2019, 568 neonates who were delivered to moms who had intrapartum paternal fever (temperature peak 38 degrees Celsius) were included in this investigation of a retrospective cohort [20]. Newborns were split into groups of EOS and non-sepsis babies in line with the diagnostic standards for early-onset neonatal sepsis (EOS). To determine the risk variables for EOS, laboratory test results, clinical information, and demographic data were analysed. In contrast, our study found that among 21 culture-positive EOS cases passed away without medical advice, 1 died, and 20 were released. Of the 308 neonates with the most probable sepsis, 13 left against medical advice, 4 died, and 291 were discharged. EOS is independently linked to both elevated maternal WBC counts & maternal HCA diagnoses. WBC levels in pregnant women can serve as a sensitive sign to detect EOS early [21].

Create a mathematical model based on maternal intrapartum risk variables to calculate the likelihood of newborn early-onset bacterial infection. The performance of algorithms determined by risk-factor threshold values is inferior to that of prediction models based on data accessible in the immediate postpartum period [22]. Maternal risk variables would be related to infant meningitis in culture-proven EOS, stressing the significance of maternal factors in sepsis clinical tests, it has been found by our study. With the use of the neonatal physical examination & laboratory results, this model may create a posterior probability for infant sepsis, which can be used to inform treatment choices [23].

Neonatal early-onset sepsis (EOS) risk factors may be controllable, despite mounting evidence to the contrary. Based on a literature analysis and professional perspectives, Its goal was to identify possible clinical risk factors for EOS. Prematurity, one-min Apgar score, & birth weight were neonatal-related risks for EOS. Maternal risk factors were gestational age and urinary tract infection. Risk factors during delivery included premature membrane split, chorioamnionitis, and intrapartum fever [24].

Neonatal early-onset sepsis (EOS), which affects term and late-preterm infants, is an extremely rare but potentially lethal disease. Large numbers of uninfected neonates are evaluated by EOS algorithms according to risk-factor threshold values, which leads to needless antibiotic doses and the division of mother and child [25]. In a perfect world, risk classification would be quantifiable, use ways to preserve information, and be easily ported to current, full electronic medical records. If EOS risk assessment was conducted using simply objective data, as opposed to the currently advised methods, fewer newborns might need to be assessed and experimentally treated for the condition. Our Prospective study is necessary to ensure the accuracy and security of using the sepsis risks framework to guide clinical decision-making [26].

to specify a quantitative classification strategy for neonates under Those who are 34 weeks pregnant and in danger of early-onset sepsis (EOS). It was split validation. employed in a retrospective stacked case-control research that we carried out. According to Each baby's sepsis risk at delivery was documented using objective maternal factors, demographics, specific clinical milestones, and crucial symptoms observed within the initial 24 hours of birth [27]. On the derivation dataset, we created a risk categorization system for EOS combining recursive partitioning with logistic regressionc regression. The validation dataset was then subjected to this technique. It is feasible to establish more effectiveness By integrating objective maternal data with shifting objective neonatal clinical findings, techniques are being developed for the assessment and management of EOS in terms of late preterm babies. Careful implementation of our plan might lead to a reduction in the annual need for antibiotic treatment for 80,000 to 240,000 babies in the US [28].

Conclusion

This study concluded that Early-Onset Sepsis (EOS) accounts for about a fourth of the patient load in our Neonatal Intensive Care Unit (NICU). Gram-positive and gram-negative sepsis were comparable, with Escherichia coli and Staphylococcus aureus being the most prevalent pathogens. The audit showed that these microorganisms are resistant to Ampicillin, third-generation cephalosporins, and amoxicillin clavulanic acid. The data suggest using Piperacillin and amikacin as first-line antibiotics in our facility. Due to the high occurrence of MRSA and VRSA, vancomycin should be avoided and imipenem, levofloxacin, and linezolid should be used as second-line treatments. This audit helps our NICU choose empirical medications to address neonatal sepsis.

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