The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 3, Issue 6, 2025

"IMPLEMENTATION OF NEONATAL SEPSIS CALCULATOR IN A TERTIARY CARE HOSPITAL IN PAKISTAN "

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DOI: https://doi.org/10.5281/zenodo.18092765

Keywords
Neonatal Sepsis Calculator, implementation, hospitals

Article History
Received: 08 June 2025
Accepted: 28 June 2025
Published: 30 June 2025

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Abstract

Objective: *The purpose of the research is to find out Implementation of Neonatal Sepsis Calculator in a Tertiary care Hospital in Pakistan*

Study Design: *prospective observational study*

Study Duration: *06 months from December 24-May 25*

Study Place: *Department of Paediatrics, CMH Lahore*

Methods: *This observational study was to done in the NICU of a tertiary care hospital in Lahore, Pakistan. 110 neonates with gestation period of 34 weeks or more and PROM of 18 hours or more were sampled consecutively. Demographic and maternal baseline factors were filled in and inputted into the Neonatal EOS Calculator. Clinical examination, CBC, CRP at 36 hours, and blood culture at birth were done on neonates. Management was based on calculator recommendations. Data was analyzed using SPSS 25 and p-value less than 0.05 was considered significant.*

Results: *One hundred and ten (110) newborns with a gestational age 34 weeks and above and whose membranes were ruptured were used. The median EOS risk in births was 3.97 per 1000 live births which rose to 5.24 per 1000 live births after clinical examination. 57.3 percent of the neonates were to be put on empiric antibiotics with full compliance to the management prescribed by the calculators. The EOS calculator had great sensitivity (85.7%) as well as negative predictive value (97.9%) but low specificity (44.7%). High CRP and low leukocyte counts had significant relation with culture-confirmed EOS.*

Conclusion: *The Neonatal EOS Calculator was practical and non-harmful to use in a tertiary care Pakistani setting. It was found to be highly sensitive and negative predictively values to eliminate early-onset sepsis, rational use of antibiotics, and had possibilities to enhance antimicrobial stewardship in neonates with delayed rupture of membranes.*

INTRODUCTION

Neonatal sepsis is a leading contributor to morbidity and mortality of any baby born all over the world, and it presents a great clinical and social health problem especially in low- and middle-income countries (LMICs) like Pakistan. Sepsis during neonatal period - particularly the early-onset sepsis (EOS) that happens within the first 72 hours of life is a life-threatening disorder which is systemically infected and inflamed as a result of bacterial assault. Clinical manifestations of EOS are usually mild and unspecific, which makes it difficult to diagnose them at a young age and necessitates extensive empiric antibiotic treatment and extensive laboratory analysis to reduce the risk of not treated infection. The conventional methods of risk assessment emphasize maternally determined risk factors and general clinical eligibility, which might not be specific, increasing interventions, antibiotic use, and spending health care which do not always enhance outcomes.[1]

The neonatal sepsis burden in Pakistan is specifically hefty because of a high neonatal mortality and low resources in tertiary care facilities. Research involving tertiary hospitals in Pakistan suggests that clinically suspected neonatal sepsis is very high and the cases that are culture proven are significant, which are mostly caused by Gram-negative organisms with high antimicrobial resistance profiles, complicating the management and necessitating better diagnostic and treatment interventions. Moreover, lack of diagnostic precision of traditional laboratory biomarkers also poses a challenge in the decision-making process of the clinicians, where there is a prolongation of empiric antibiotic administration with its related risks, including antimicrobial resistance and interference with the developing neonatal microbiome.[2]

To overcome these obstacles, the neonatal early-onset sepsis calculator (commonly known as the sepsis calculator) has been developed as a quantitative, risk-based decision aid, which can be used to guide initial newborn care, and incorporate maternal risk factors, obstetric variables, and the clinical status of the infant to come up with an individualized estimate of likelihood of EOS. The calculator groups the neonates based on risk and offers evidence-based advice on whether to observe or administer antibiotics and thus enhances prudent use of antibiotics and reduces unnecessary invasive procedures. In high-income implementation studies, adoption of the sepsis calculator was also found to be linked with large reductions in the use of empiric antibiotics, laboratory tests, and NICU hospitalizations with no higher rates of missed EOS or adverse events. According to meta-analyses of observational studies, moderate quality of evidence exists in support of the claim that the implementation of sepsis calculator decreases the use of antibiotics and healthcare facilities and safety is not at risk with no significant difference in mortality or readmission rates compared with traditional management strategies.[3,4]

Although international data suggests high usefulness of the sepsis calculator, LMICs evidence, and more precisely tertiary care hospitals in Pakistan has scarce evidence. Pakistan neonatal units have a special epidemiological profile, resource-related limitations, and microbial environment, which can affect the efficacy and usability of sepsis risk stratification tools. Thus, the possible use of the neonatal sepsis calculator in this area of interest is important to determine how it can be utilized to enhance antimicrobial stewardship, clinical care optimization, and unnecessary healthcare burden.[5]

This paper discusses adopting the neonatal sepsis calculator in a tertiary care hospital in Pakistan, its effects on clinical decision-making, antibiotics use, and early neonatal outcomes, and puts results into perspective over the larger context of neonatal sepsis management in resource-constrained environments.

Methodology

It is a prospective observational study that aims at evaluating the effectiveness of the Neonatal Sepsis Calculator as a predictor of Early Onset Neonatal Sepsis (EONS) in preterm neonates with Premature Rupture of Membranes (PROM). The research was carried out by tracking the neonates within a specific time and comparing the risk evaluations of the calculator with the actual clinical results. The research was carried out within a tertiary care hospital in Pakistan, namely, in the neonatal intensive care unit (NICU), where suspected neonatal sepsis cases are treated and observed. It

took place in a 6-month duration; between December 24-May 25, in a tertiary care hospital in Lahore. This time was selected to have enough time and collect and analyze the data. The sample size was calculated using Cochran's formula[6] for an unknown population proportion:

$$n = \frac{Z^2 \times p(1-p)}{E^2}$$

- (Z) is the Z-value for 95% confidence (1.96),
- (p) is the estimated proportion of neonates at risk of EONS (0.04 or 4%),
- (E) is the margin of error (0.05 or 5%). Thus, the calculated sample size is approximately 110 neonates.

The sampling technique used was non-probability consecutive sampling. Neonates born with PROM of 18 hours or more and a gestational age of 34 weeks or more during the study period were included in the sample until the desired sample size of 110 neonates was reached.

Inclusion Criteria:

1. Neonates with a gestational age of 34 weeks or more.
2. Neonates born with Premature Rupture of Membranes (PROM) for 18 hours or more.
3. Neonates whose maternal Group B Streptococcus (GBS) status is either unknown or not available.
4. Neonates whose type of intrapartum antibiotics used is documented.
5. Parental consent for participation in the study.

Exclusion Criteria:

1. Neonates born before 34 weeks gestational age.
2. Neonates whose PROM duration is less than 18 hours.
3. Neonates with known maternal GBS colonization and the status is known.
4. Neonates whose complete data regarding intrapartum antibiotics is unavailable.
5. Neonates with congenital anomalies or diagnosed with sepsis prior to admission.

The data collection of this study was conducted in a prospective manner among the neonates that fulfilled the inclusion criteria when they were admitted to the neonatal intensive care unit (NICU) at the tertiary care hospital. At the moment of enrollment, precise demographic and clinical information (such as the gestational age, the duration of premature rupture of membranes (PROM), maternal GBS (Group B Streptococcus) status (which was regarded as unknown with all participants), and the information on the type of intrapartum antibiotics) was collected. The information was then entered into the Neonatal Sepsis Calculator, which provided an evaluation of the risk score that showed the possibility of Early Onset Neonatal Sepsis (EONS). The neonates were also subjected to standard clinical examination and laboratory tests, such as complete blood count (CBC), C-reactive protein (CRP) test at 36 hours old, and blood cultures at birth in addition to the use of the calculator. These lab tests, and the results of the clinical examination, were necessary to track the condition of the neonates and define whether some of the recommendations provided by the Neonatal Sepsis Calculator (e.g., the need to initiate antibiotics) should be taken. The calculator predictions were followed to the letter and the neonates were administered according to their clinical status that was closely monitored within the initial 36 hours of life. Besides, clinical results, such as the presence or absence of sepsis and the general reaction of the neonate on the treatment, were also reported. The results of the blood cultures, CBC data, CRP data and clinical outcomes were subsequently compared against the recommendations provided by the Neonatal Sepsis Calculator to determine its effectiveness in making clinical decisions and forecasting the development of EONS. The collected data were well systemized to be analyzed and the correlation of the risk scores assigned to the calculator with the actual clinical outcomes were analyzed in an all inclusive manner.

The data gathered was also analyzed using SPSS. The descriptive statistics were used to summarize the demographic information, clinical variable and laboratory results of the neonates. Categorical variables like gender, gestational age and type of intrapartum antibiotics were calculated using

percentages and frequencies and continuous ones including age at birth, length of PROM and laboratory investigations such as CBC and CRP calculated mean and standard deviations. To determine the diagnostic accuracy of the Neonatal Sepsis Calculator, the sensitivity and specificity, positive predictive value (PPV) and the negative predictive value (NPV) were estimated in terms of comparing the calculator output with the real clinical outcomes, including the occurrence of Early Onset Neonatal Sepsis (EONS). To assess how the recommendations given by the Neonatal Sepsis Calculator match the clinical data, the relationship between the risk scores and the laboratory results (CBC, CRP, blood culture results) was cross tabulated as such. Secondly, the calculator predicted that the chi-square tests and t-tests could be applied to investigate statistically significant variations between the groups with and without sepsis. The distributions of the neonates by their risk scores and clinical outcomes were presented in tables and the sensitivity, specificity and predictive values were summarised. This discussion aided in measuring the effectiveness of the Neonatal Sepsis Calculator in the detection of the highest risk neonates with EONS and the provision of clinical care. The ultimate data analysis offered information about the usefulness of the tool at a tertiary care hospital and about the possible implications of the tool on the detection of sepsis and management of antibiotics in the first place.

Results:

This section provides the findings of the research concerning the implementation of the Neonatal Early-Onset Sepsis (EOS) Calculator at a Pakistani tertiary care hospital in the cohort of neonates delivered with gestational age of 34 weeks or more and after the prolonged rupture of membranes (PROM 18 hours and more). The main aim of this chapter is to specify the study cohort as well as to assess the performance of the Neonatal Sepsis Calculators in the given clinical setting by comparing the recommendations of the calculator and laboratory investigation and outcomes.

Namely, the calculator was used on the predetermined baseline of incidence of early-onset neonatal sepsis (4 per 1000 live births), gestational age at birth, length of PROM, maternal Group B Streptococcus (GBS) status (Unknown), and the nature of intrapartum antibiotic exposure. The risk management course of action was then suggested by calculating the risk of EOS and integrating into it the clinical examination category of each neonate. These prescriptions including regular observation up to blood culture and/or the start of empiric antibiotics were adopted during patient management.

The findings are structured in such a way that they give a clear description of baseline maternal/neonatal parameters, EOS calculator risk estimates and recommendations distribution, compliance with recommended antibiotic initiation, and frequency/pattern of laboratory findings (CBC, CRP at 36 hours and blood culture sent at birth). The chapter also compares the diagnostic performance of the calculator recommendations with culture-confirmed EOS and also finds out the relationships among the calculator output, laboratory results and the clinical status of the patient in order to determine the clinical utility of the calculator in this PROM-based cohort.

4.1 Study population and baseline characteristics

A total of **110** neonates met the inclusion criteria. Mean gestational age was **36.55 ± 1.42 weeks** and PROM duration was **46.42 ± 39.41 hours** (median **35.5 hours**). Maternal fever was present in **9 (8.2%)** cases. Maternal **GBS status was unknown in all cases** as per protocol.

Table 4.1 Baseline maternal and neonatal characteristics (n = 110)

Characteristic	Value
Sample size (n)	110
Baseline EOS incidence used in calculator (per 1000)	4
Gestational age (weeks), mean ± SD	36.55 ± 1.42

Gestational age (weeks), median (IQR)	36.57 (35.46–37.57)
Gestational age (weeks), range	34.00–40.86
PROM duration (hours), mean ± SD	46.42 ± 39.41
PROM duration (hours), median (IQR)	35.5 (22.3–51.0)
PROM duration (hours), range	18.0–226.0
Maternal fever present, n (%)	9 (8.2%)
GBS status	Unknown (100%)
Clinical examination category, n (%)	
• Well appearing	58 (52.7%)
• Equivocal	24 (21.8%)
• Clinical illness	28 (25.5%)
Intrapartum antibiotic exposure, n (%)	
• Ampicillin	39 (35.5%)
• None	21 (19.1%)
• Penicillin	15 (13.6%)
• Clindamycin	14 (12.7%)
• Cefazolin	10 (9.1%)
• Vancomycin	9 (8.2%)
• Broad-spectrum (Amp+Gent)	2 (1.8%)

4.2 Neonatal Sepsis Calculator risk estimates and recommendations

The EOS risk at birth was low overall (median **3.97 per 1000**). Risk after clinical examination showed marked right-skew due to higher risks assigned to equivocal/ill-appearing neonates (median **5.24 per 1000**, maximum **236.91 per 1000**).

Table 4.2 EOS risk estimates (per 1000 live births)

Risk estimate	Value
EOS risk at birth (per 1000), median (IQR)	3.97 (2.85–6.76)
EOS risk at birth (per 1000), mean ± SD	5.07 ± 3.10
EOS risk after clinical exam (per 1000), median (IQR)	5.24 (1.66–39.02)
EOS risk after clinical exam (per 1000), mean ± SD	32.77 ± 52.45

The calculator recommendations were:

- **Empiric antibiotics:** 63 (57.3%)
- **Blood culture only:** 38 (34.5%)
- **No culture, no antibiotics:** 9 (8.2%)

Table 4.3 Calculator recommendation distribution (n = 110)

Calculator recommendation	n (%)
Empiric antibiotics	63 (57.3%)
Blood culture	38 (34.5%)
No culture, no antibiotics	9 (8.2%)

Recommendations varied strongly by initial clinical examination category in this dataset.

Table 4.4 Clinical examination category vs calculator recommendation

Clinical_exam	Blood culture	Empiric antibiotics	No culture, no antibiotics	Total
Clinical illness	0	28	0	28
Equivocal	0	24	0	24
Well appearing	38	11	9	58
Total	38	63	9	110

4.3 Implementation adherence (antibiotic initiation)

The implemented management followed the calculator's antibiotic recommendations exactly in this dataset.

Table 4.5 Antibiotic initiation by calculator recommendation

Calculator recommendation	Antibiotics started (n/total, %)
Empiric antibiotics	63 / 63 (100.0%)
Blood culture	0 / 38 (0.0%)
No culture, no antibiotics	0 / 9 (0.0%)

4.4 Laboratory investigations (CBC and CRP at 36 hours)

CBC parameters and CRP at 36 hours were available for all neonates. Overall, CRP values were low with a right-skewed distribution (median **1.30 mg/L**, range up to **26.00 mg/L**).

Table 4.6 Summary of CBC and CRP results (n = 110)

Parameter	Mean ± SD	Median (IQR)	Range
CRP at 36 hours (mg/L)	2.82 ± 3.76	1.30 (0.83–2.80)	0.50–26.00
Total leukocyte count ($\times 10^9$/L)	12.56 ± 4.82	12.45 (9.62–16.50)	3.00–24.10
Hemoglobin (g/dL)	17.07 ± 1.83	16.90 (15.80–18.10)	13.60–21.90
Platelets ($\times 10^9$/L)	254.3 ± 76.5	254.0 (197.8–300.0)	64.0–450.0
Neutrophils (%)	48.10 ± 15.85	46.5 (37.2–58.8)	12.0–86.0
Lymphocytes (%)	41.10 ± 15.63	40.5 (30.2–50.8)	10.0–80.0

4.5 Blood culture findings (sent at birth) and early outcomes

Blood cultures were obtained at birth for all neonates. Culture positivity (confirmed EOS) was **7/110 (6.4%)**. One neonatal death occurred.

Table 4.7 Blood culture results and isolated organisms

Blood culture finding	Value
Blood culture sent at birth	110 (100%)
No growth	103 (93.6%)
Culture positive (confirmed EOS)	7 (6.4%)
• Staphylococcus aureus	2 (28.6%)
• Enterococcus faecium	2 (28.6%)
• Citrobacter freundii	2 (28.6%)

• Group B Streptococcus	1 (14.3%)

Outcome: 109 (99.1%) were discharged and 1 (0.9%) expired.

4.6 Efficacy of the calculator using culture-confirmed EOS as reference

To assess diagnostic performance, a **positive calculator test** was operationally defined as **"Empiric antibiotics"** recommendation, and the reference standard was **culture-confirmed EOS** (blood culture positive).

Table 4.8 2×2 table: empiric antibiotics recommendation vs culture-confirmed EOS

	Confirmed EOS (culture +)	No EOS (culture -)	Total
Empiric antibiotics (Yes)	6	57	63
Empiric antibiotics (No)	1	46	47
Total	7	103	110

Table 4.9 Diagnostic performance indices

Performance measure	Value
Sensitivity	85.7%
Specificity	44.7%
Positive predictive value (PPV)	9.5%
Negative predictive value (NPV)	97.9%
Accuracy	47.3%

4.7 Correlation of calculator recommendations with investigations (culture-positive vs culture-negative)

Culture-positive neonates showed **significantly higher CRP** and **significantly lower TLC** compared with culture-negative neonates. Other CBC indices, gestational age, and PROM duration did not differ significantly.

Table 4.10 Comparison of culture-positive vs culture-negative neonates (Welch t-test)

Variable	Culture-positive (n=7) mean ± SD	Culture-negative (n=103) mean ± SD	p-value*
Gestational age (weeks)	36.39 ± 1.44	36.56 ± 1.43	0.767
PROM duration (hours)	45.19 ± 25.61	46.50 ± 40.26	0.903
EOS risk at birth (per 1000)	5.37 ± 2.80	5.05 ± 3.13	0.779
EOS risk after exam (per 1000)	24.30 ± 34.89	33.35 ± 53.51	0.542
CRP at 36h (mg/L)	**12.69 ± 6.97**	**2.15 ± 2.26**	**0.007**
Total leukocyte count ($\times 10^9$/L)	**6.89 ± 4.11**	**12.95 ± 4.64**	**0.007**
Hemoglobin (g/dL)	17.41 ± 2.11	17.04 ± 1.82	0.612
Platelets ($\times 10^9$/L)	225.86 ± 88.29	256.25 ± 75.68	0.405
Neutrophils (%)	55.14 ± 16.53	47.62 ± 15.77	0.259
Lymphocytes (%)	33.14 ± 15.53	41.64 ± 15.61	0.207

*p-values from Welch's independent samples t-test; significance threshold set at $p < 0.05$.

Selected categorical associations (culture-confirmed EOS)

Comparison	Culture-positive proportion	p-value
Maternal fever (Yes vs No)	Yes: 1/9 culture+; No: 6/101 culture+	0.460 (Fisher)
Clinical exam category (3 groups)	Well: 3/58 culture+; Equivocal: 1/24; Ill: 3/28	0.543 (χ^2)
Calculator recommendation (3 categories)	Empiric: 6/63 culture+; Culture only: 1/38; No action: 0/9	0.279 (χ^2)

Discussion:

This paper assessed the Neonatal Early-Onset Sepsis (EOS) Calculator implementation and diagnostic accuracy in a Pakistani tertiary care hospital in neonates with a gestational age at birth of 34 weeks or more (PROM ≥18 hours) and rupture of membranes. The results indicate that the calculator was practical to apply, with full compliance with recommendations and high sensitivity and negative predictive values with culture-confirmed EOS and some significant limitations to specificity and positive predictive value in this high-risk group.

Neonatal sepsis is one of the primary causes of low- and middle-income countries (LMIC) neonatal morbidity and mortality, as impediments to clinical decision-making in Pakistan include the lack of access to high-quality biomarkers, elevated background infection and antimicrobial resistance. PROM is a known risk factor of EOS and the management policies have been used to support liberal use of antibiotics, which often ends in over treatment of culture-negative neonates. To overcome this problem, the EOS calculator was created to offer personalized risk estimates using both maternal risk factors and neonatal clinical status as means of supporting antibiotic stewardship without jeopardizing patient safety.[7]

In the current research, the total EOS risk at birth was low, although the PROM was prolonged, and the median of the estimated risk was 3.97 per 1000 live births. This observation demonstrates the importance of multivariable risk stratification because PROM is not invariably accompanied by high EOS in cases where other maternal and intrapartum conditions are ideal. Nevertheless, addition of neonatal clinical examination with large significance on post-exam risk estimates that were more influential in equivocal and clinically ill neonates produced a skewed right distribution of EOS risk. It is observed that this fact agrees with the prior research that has shown that neonatal clinical condition is a significant contributor to EOS risk and management choices in the framework of the calculator.[8,9]

Over 57.3% of the neonates were advised empiric antibiotics, and it is significant compared to the proportions reported in most studies of high-income countries with the implementation of the EOS calculator. The difference is probably due to the fact that the PROM-based cohort selection, lack of reported maternal GBS screening, and the range of 4 per 1000 which the calculator uses as an epidemiological background were selected to indicate local epidemiology. The significance of these contextual factors is to ensure a calculation of baseline incidence and risk levels is calibrated to local conditions to apply the calculator to LMICs.[10]

One of the strengths of this paper was that all the recommendations of the calculators were followed. Neonates, to which the empiric antibiotics were recommended, were treated, and none of those to which observation or blood culture was suggested was unduly exposed to antibiotics. This can be used to indicate how operationally feasible the EOS calculator is to implement in a busy tertiary care unit, and indicates that clinicians will be willing to use the tool successfully when incorporated into the standard care pathways.[11]

The proportion of culture-confirmed EOS within this cohort was 6.4 and this is greater than culture-confirmed EO rates in many high-income contexts but the same as those found in South Asian neonatal units. The range of isolated was not typically described in Western literature and consisted mostly of Staphylococcus aureus, Enterococcus faecium, and Citrobacter freundii and only one case of Group B Streptococcus. This microbiological trend supports the epidemiology of this region and strengthens the

low applicability of GBS-centric prevention tools in the environment where GBS screening is not a routine practice and Gram-negative organisms are still the leading causes of neonatal sepsis.[12]

The EOS calculator was very sensitive (85.7%), and had a very good negative predictive value (97.9%), when culture-confirmed EOS was used as the reference standard. Clinical implications of these results are that neonates who were in the low-risk category according to the calculator were highly unlikely to suffer EOS and this showed that the neonates in this category were safe to be without antibiotics. The same high negative predictive values have been found in international validation studies and meta-analyses supporting the use of the calculator as a safe rule-out tool of EOS.[13]

Nevertheless, the specificity was small (44.7%), and the positive predictive value was low (9.5%), which means that a significant percentage of neonates treated with empiric antibiotics were eventually culture-negative. This is the expected limitation of EOS risk stratification especially with high-risk cohorts and low prevalence of disease, and is is as expected and reported in the literature. Notably, the clinical objective of EOS management is to reduce the number of missed cases rather than the problem of false positives, as false positive may be disastrous in terms of the outcomes of untreated sepsis.[14]

Laboratory results also gave extra knowledge. CRP levels of culture-positive neonates were significantly greater at 36 hours and significantly less overall leukocyte counts were observed in comparison to culture-negative neonates, which confirms the diagnostic value of CRP as an adjunctive tool when used in conjunction with a clinical evaluation and risk-stratification. Nevertheless, no remarkable variation was found in gestational age and the duration of PROM or in the risk estimates of EOS, indicating that laboratory markers might provide incremental data compared to the calculation results in some specific situations.[15]

A major implication of this study concerns the antimicrobial stewardship in the neonatal units in resource constrained environments. Unexpectedly, excessive and prolonged exposure to antibiotics in neonates has been linked to negative effects, such as gut microbiome disturbance, a rise in the risk of necrotizing enterocolitis, invasive fungal infections, and the rise of multidrug-resistant organisms. The EOS calculator could be very important in Pakistan where antimicrobial resistance is a growing issue in the public health and where the rationalization of antibiotic usage is necessary to guarantee patient safety. The negative predictive value is very high in this study, which supports the fact that the calculator can safely identify the neonates who are under the extreme risk of EOS and thus provide an evidence-based option to the use of the blanket antibiotic in infants who have been exposed to PROMs.[16]

Moreover, the high adherence rate and successful execution that was seen in this cohort indicate that even in the high-volume tertiary care hospitals, EOS calculator can be successfully integrated into the routine clinical practices. This is especially applicable in the environment where the decisions of the clinicians are usually biased by the fear of failing to detect sepsis instead of estimating risks quantitatively. Universalization of care based on calculator-directed processes can decrease inter-clinician variation, enhance uniformity in care of the neonate, and maximize the use of laboratory resources. Nevertheless, local adaptation is also required, especially when it comes to baseline EOS incidence and existing patterns of microbes. The implementation plans of the future need to include periodic local epidemiological monitoring and the ongoing audit in order to maintain the effectiveness and safety of EOS calculator in various neonatal care settings.

Limitations:

This research has a number of limitations. To begin with, its single-centre nature and the small sample size, including the small amount of culture-confirmed EOS cases, could limit the generalizability of the results. Second, the maternal Group B Streptococcus status was not known in each of them, which could have affected the estimation of EOS risks and restricted the analysis of the calculator performance in GBS-positive environments. Hence generalization of results cannot be done.

Conclusion:

This study showed that the Neonatal Early-Onset Sepsis Calculator can be safely and effectively implemented in a tertiary care hospital in Pakistan in

the neonatal population The calculator facilitated the stratification of risks in a methodical way by combining maternal risk and neonatal clinical conditions, resulting in the standardization of treatment decisions and full compliance with the recommended use of antibiotics. The EOS calculator was found to have a high level of sensitivity and good negative predictive value of culture-confirmed EOS and this demonstrates that the calculator is very reliable and it has a good negative predictive value in identifying low-risk neonates who will be able to avoid antibiotics without risking their lives. The strong compliance with calculator-directed recommendations also points to its acceptability in clinician circles and to its possible ability to decrease variability in practices of high-risk neonatal groups. In general, the results justify the implementation of the Neonatal EOS Calculator into the routine neonatal practice of the resource-limited environment as the method to improve antimicrobial stewardship, resource usage, and patient safety.

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