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Quitasol, AG, Gozar, JD, Calitis, MSFP. Comparison of Antibiotic Recommendation between Early Onset Neonatal Sepsis Calculator and American Academy of Pediatrics 2018 Guidelines in a Tertiary Hospital
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ORIGINAL ARTICLE

COMPARISON OF ANTIBIOTIC RECOMMENDATION BETWEEN EARLY ONSET NEONATAL SEPSIS CALCULATOR AND AMERICAN ACADEMY OF PEDIATRICS 2018 GUIDELINES IN A TERTIARY HOSPITAL

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ABSTRACT

Background*:* Many neonates are started on antibiotics even if they are well-appearing due to presence of risk factors. The Early Onset Sepsis (EOS) calculator is a web-based tool that calculates for composite risk scores for sepsis and limits empiric antibiotic therapy only as necessary.

Objective: This study aims to determine if there is a significant difference between the proportion of neonates recommended for antibiotics using the EOS calculator and AAP guidelines for neonatal sepsis.

Methods: This is a retrospective hospital-based cohort study where review of charts of neonates ≥34 weeks age of gestation (AOG) who were started on intravenous antibiotics within 72 hours of life for the period of 2019 to 2023 was done. Peripartum risk factors were used to calculate for EOS risk score and categorize those to be recommended for treatment using the score as well as the AAP guidelines. Newborns with growth on blood culture were identified. McNemar's test was used to determine if there is a significant difference between the two proportions. Sensitivity and specificity of both tools were calculated.

Results: Out of 916 neonates, 345 (38%) and 469 newborns (51%) were advised empiric antibiotic therapy by the EOS calculator and AAP 2018 guidelines respectively. A McNemar Test revealed a significantly lower proportion of neonates recommended for antibiotic treatment using the EOS calculator ($p < 0.001$). Blood culture was taken from 208 newborns and six had positive isolates. Both the EOS calculator and AAP guidelines had 100% sensitivity and recommended antibiotics for these culture-proven sepsis cases. EOS calculator had a higher specificity (45% vs 32%).

Conclusion: The EOS calculator as a risk assessment tool could significantly reduce use of antibiotics. The proportion of those who were recommended for antibiotics using the EOS calculator was significantly lower by 13% (p value = <0.001) compared to those who were recommended for antibiotics using the AAP 2018 guidelines. This proves to be a considerable reduction in the use of antibiotics through the EOS calculator. The EOS calculator also had higher specificity in recommending initiation of empiric antibiotic therapy compared to the AAP 2018 guidelines. Prospective use of the EOS calculator and experimental studies are needed to investigate safety in its use.

KEYWORDS: sepsis, newborn, calculator

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INTRODUCTION

Neonatal sepsis, a leading cause of infant morbidity and mortality in the Philippines with an incidence of 4-9 cases per 1,000 livebirths, is classified into early onset and late onset sepsis.[1] Early onset neonatal sepsis is an infection occurring before seventy-two hours of life where the cause of infection is likely through vertical transmission from maternal infection.[2.] Due to the high burden of neonatal sepsis in the Philippines, there is rampant use of antibiotics even in asymptomatic well-appearing babies. A large variation has also been noted in the current practice and management of neonatal sepsis.[2]

Local recommendations in the management of early onset sepsis are in line with the American Academy of Pediatrics (AAP) 2018 guidelines which considers giving antibiotics to the following: 1) any newborn infant who is ill appearing 2) a mother with a clinical diagnosis of chorioamnionitis 3) a mother who is colonized with Group B Streptococcus (GBS) and who received inadequate intrapartum antibiotic prophylaxis, with a duration of rupture of membranes (ROM) being >18 hours or birth before 37 weeks' gestation or 4) a mother who is colonized with GBS who received inadequate intrapartum antibiotic prophylaxis but with no additional risk factors. These, however, received comments for vagueness of criteria as categorizing an ill-appearing newborn is subjective to the clinician.[3]

A recently adapted risk assessment tool that has been used by some western countries is the early-onset sepsis (EOS) calculator. It is an online website created by Kaiser Permanente in December 2012 where variables are entered into a calculating matrix prior to starting empiric antibiotics. It aims to promote judicious use and prevent adverse effects from inappropriate use of antibiotics.[4] Several studies recommend the EOS calculator as a reliable risk assessment tool that could lessen antibiotic use. In a meta-analysis of 13 studies with 175,752 newborns, all reveal a lower relative risk for antibiotic therapy. Across these studies, there was no readmission and no mortality among those not recommended for antibiotics by the EOS calculator.[5,6,7,8] In contrast, in another meta-analysis involving 11 studies and 75 sepsis cases, they found that 14-22 cases would have resulted in delayed or missed treatment compared to if the National Institute for Health and Care Excellence (NICE) guidelines have been followed. This study recommended further evaluation of the calculator before its introduction into Clinical practice particularly in the United Kingdom.[9]

This research explored on the antibiotic recommendation of the EOS calculator and AAP 2018 guidelines among neonates started on intravenous antibiotics before 72 hours of life due to risk factors for sepsis and investigated if there is a significant difference between the two proportions. It identified newborns recommended for antibiotic therapy according to the EOS calculator versus newborns recommended for antibiotic therapy according to the AAP 2018 guidelines. It also determined who among those recommended for antibiotic therapy by EOS calculator and AAP guidelines are culture-proven sepsis. Sensitivity and specificity of the EOS calculator and AAP guidelines were calculated based on culture-proven sepsis cases. The study also looked into the profile of newborns as to APGAR score, age of gestation, birth weight mode of delivery, maternal history and determined the risk factors for starting antibiotics.

MATERIALS AND METHODS

This was a retrospective cohort study in a private tertiary hospital involving neonates ≥34 weeks AOG and started on IV antibiotics within 72 hours of admission from 2019-2023. Newborns delivered outside the hospital under study and those with congenital anomalies were excluded as such malformations may result to clinical manifestations that may affect the risk score for sepsis.

The researcher manually checked on the list of eligible newborns from the monthly census and all charts who fulfilled the inclusion criteria were retrieved and reviewed. Patient profile and risk

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factors for sepsis were noted and listed by the investigator using an excel data sheet.

To determine who among the newborns are recommended for antibiotic treatment by the EOS calculator, risk factors were encoded using a web-based tool as shown below to derive the intrapartum risk score.

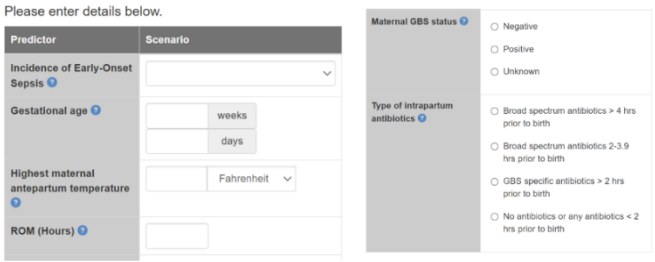

Fig 1. Sample EOS Calculator

Newborns were also categorized as *well, equivocal* or *with clinical illness* based on the EOS calculator classification as shown below.

Table 1. Kaiser Permanente EOS Calculator Clinical Classification for Neonates

Clinical exam	Description
Clinical illness	1. Persistent need for nasal cannula positive airway pressure / high flow nasal cannula / mechanical ventilation (outside of the delivery room) 2. Hemodynamic instability requiring vasoactive drugs 3. Neonatal encephalopathy / perinatal depression ▪ Seizure ▪ APGAR score at 5 minutes <5 4. Need for supplemental oxygen ≥ 2 hours to maintain oxygen saturations > 90% (outside the delivery room)
Equivocal	1. Persistent physiologic abnormality ≥ 4 hours ▪ Tachycardia (HR ≥ 160) ▪ Tachypnea (RR ≥ 60) ▪ Temperature instability (≥ 100.4 F or < 97.5 F) ▪ Respiratory distress (grunting, flaring or retracting) not requiring supplemental oxygen 2. Two or more physiologic abnormalities lasting for ≥ 2 hours ▪ Tachycardia (HR ≥ 160) ▪ Tachypnea (RR ≥ 60) ▪ Temperature instability (≥ 100.4 F or < 97.5 F) ▪ Respiratory distress (grunting, flaring or retracting) not requiring supplemental oxygen Note: abnormality can be intermittent.
Well appearing	No persistent physiologic abnormalities

After encoding both maternal risk factors and clinical status of the newborn, a risk score was derived from the EOS calculator based on this formula from the Bayem's theorem.

$$\frac{(Prior\ Probability\ of\ EOS)}{(1 - Prior\ Probability\ of\ EOS)} \times Likelihood\ ratio\ of\ Clinical\ Presentation = Posterior\ Odds\ of\ EOS$$

$$\frac{Posterior\ Odds\ of\ EOS}{(1 + Posterior\ Odds\ of\ EOS)} = Posterior\ Probaility\ of\ EOS$$

From the composite risk score, a clinical recommendation was reached whether to start antibiotics or not based on the stratification shown below.

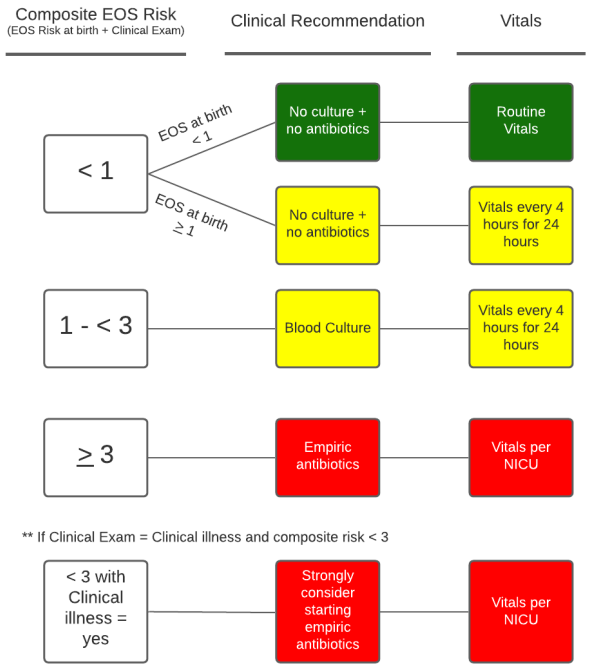

Fig 2. Clinical recommendation for initiation of antibiotics by the EOS calculator based on EOS risk score

The same set of maternal intrapartum risk factors and newborn profile were used to identify newborns recommended for antibiotic treatment using the AAP 2018 guidelines.

Newborns warranting antibiotics based on the EOS Calculator

Newborns with an EOS risk score of more than or equal to three as derived from the EOS calculator warranted use of antibiotics.

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Newborns warranting antibiotics based on the AAP 2018 Guidelines

Newborns who fell under any of the following criteria warranted use of antibiotics:

1. is ill appearing;
2. born to a mother with a clinical diagnosis of chorioamnionitis;
3. born to a mother who is colonized with Group B Streptococcus (GBS) and who received inadequate intrapartum antibiotic prophylaxis, with a duration of rupture of membranes (ROM) lasting >18 hours or birth before 37 weeks gestation; or
4. born to a mother who is colonized with GBS who received inadequate intrapartum antibiotic prophylaxis but with no additional risk factors.

Newborns with a blood culture taken prior to antibiotic therapy were identified and data on these were used to calculate for the sensitivity and specificity of the EOS calculator and AAP 2018 guidelines respectively.

Data Analysis and Statistical tools

Descriptive statistics were used in profiling the newborns. Mean birth weight and percentages for intrapartum risk factors were derived to determine the most common reasons for starting antibiotics.

To compare those recommended for antibiotic therapy based on the EOS risk score and AAP guidelines, the researcher utilized a 2x2 table.

		Antibiotics recommended by the **EOS calculator?** Yes	No
Antibiotics recommended by the **AAP guidelines?**	Yes		
	No		

Significant difference between the two proportions was identified through Mcnemar's test using the SPSS software.

Neonates with a blood culture sample taken prior to antibiotic therapy were identified. The sensitivity and specificity of the EOS calculator and AAP 2018 guidelines were calculated using the following 2x2 table:

	Start antibiotics	Culture-proven sepsis cases	Clinical Sepsis
EOS/AAP 2018 recommendation	YES	(a)	(b)
	NO	(c)	(d)

Sensitivity is the proportion of individuals classified as positive by the gold standard who are correctly identified by the study test. From the table, it was calculated as:

$$\text{Sensitivity} = \frac{a}{a + c}$$

Specificity is the proportion of individuals classified as negative by the gold standard who are correctly identified by the study test. From the table, it was calculated as:

$$\text{Specificity} = \frac{d}{b + d}$$

Ethical considerations

The study underwent review and obtained the approval of the Ethics and Research committee before study initiation. As this was a retrospective study, a waiver of documentation of informed consent was obtained. Confidentiality of information was ensured with the use of a unique alphanumeric code for all newborns included in the study.

RESULTS

A total of 1,147 neonates from January 1, 2019 to September 30, 2023 were identified to have been started on antibiotics within the first 72 hours of life. Excluded however were 231 newborns as they were less than 34 weeks age of gestation (214), had congenital anomaly (12) or were outborn deliveries (5).

Of the 916 neonates included in the study, 17 had an APGAR score of less than 5 on the first minute of life requiring resuscitation.

Eighty percent were classified as full term babies while twenty percent were late preterms. Mean birth weight was 2871 grams. Sixty five

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percent of newborns were delivered via cesarean section. Table 2 shows the profile of the neonates included in the study.

Table 2. Neonatal profile and characteristics

Profile of neonates	n (%)
APGAR score	
APGAR score of <5 in the first minute	17 (1.8)
APGAR score of <9,9	87 (9)
APGAR Score of 9,9	829 (91)
Mean score at 1st minute ± SD	8.7 ± 1.1
Mean score at 5th minute ± SD	8.9± 0.7
Age of gestation	
34 weeks to 36 6/7 weeks	182 (19.9)
37 weeks to 42 weeks	734 (80.1)
Birth weight	
1000-1999 grams	43 (4.7)
2000-2499 grams	155 (16.9)
2500-2999 grams	327 (35.7)
3000-3499 grams	318 (34.7)
3500-3999 grams	67 (7.3)
>4000 grams	6 (0.7)
Mean birth weight in grams ± SD	2871.3 ± 483.3
Mode of delivery	
Normal spontaneous vaginal delivery	272 (29.7)
Vacuum assisted vaginal delivery	49 (5.3)
Cesarean section	595 (65.0)

Eighteen percent of newborns were started on empiric antibiotic therapy due to poor suck and premature rupture of membranes, respectively. Fifteen percent presented with signs and symptoms of respiratory distress such as tachypnea, alar flaring and retractions requiring oxygen support. Another fifteen percent had two or more intrapartum risk factors or had a risk factor with poor neonatal outcome. Fourteen percent were given IV antibiotics due to maternal history of infection.

Ten percent of newborns were well-appearing but had deranged laboratory parameters such as elevated white blood cell count or C-reactive protein. Another nine percent were also well-appearing but meconium stained. The table below shows the reasons for starting antibiotics based on intrapartum risk factors and neonatal outcome.

Table 3. Reasons for starting antibiotics

Reason for starting antibiotics	n (%)
Intrapartum risk factors	
History of maternal infection within two weeks prior delivery	129 (14)
Maternal fever hours prior or upon delivery	15 (1.6)
Premature rupture of membranes (PROM)	161 (17.6)
Meconium stained	79 (8.6)
Neonatal outcome	
Respiratory distress requiring oxygen	137 (15)
Poor suck	167(18.2)
Derangement of laboratory parameters	95 (10.4)
Multiple combined factors	**133 (14.5)**

Table 4 shows the newborns started on antibiotics due to multiple risk factors (having both an intrapartum risk factor and with clinical manifestations) as follows:

Table 4. Multiple combined factors specified with intrapartum risk factor and outcome

Multiple combined factors	133 (14.5)
Respiratory distress + intrapartum risk factor	70 (7.6)
poor suck + intrapartum risk factor	35 (3.8)
PROM + other factors	68 (7.4)
maternal UTI + other factors	35 (3.8)

There were 345 newborns (38%) for whom antibiotics were recommended based on the EOS calculator and 469 newborns (51%) for whom antibiotics were recommended based on the AAP 2018 guidelines.

Table 5. Recommended for antibiotics based on EOS calculator and AAP guidelines

		AAP 2018		
		No	Yes	Total
EOS	No	422 (46.1)	149 (16.3)	571 (62.3)
	Yes	25 (2.7)	320 (34.9)	**345 (37.7)**
Total		447 (48.8)	**469 (51.2)**	916 (100.0)

A McNemar Test reveals that the proportion of those who were recommended for antibiotics using the EOS calculator were significantly lower ($p < 0.001$) than those who were recommended for antibiotics using the AAP guidelines.

Out of 916 newborns, only 208 had a blood culture done with available results. Two hundred two (202) of these had no growth while six (2.9%) had

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culture positive results. Both the EOS calculator and the AAP 2018 antibiotic guidelines recommended antibiotic treatment based on the matrix and criteria in all the six newborns with positive growths.

Table 6. Neonates with growth on blood culture and recommendation for antibiotic based on EOS calculator and AAP 2018 guidelines

Newborn ID no.	Organism identified from blood culture	EOS calculator antibiotic recommendation	AAP 2018 guidelines antibiotic recommendation
Newborn #570	Staphylococcus haemolyticus	YES	YES
Newborn #578	Streptococcus agalactiae	YES	YES
Newborn #595	Pantoaea spp.	YES	YES
Newborn #636	Staphylococcus warnerii	YES	YES
Newborn #669	Sphingomonas paucimobilis	YES	YES
Newborn #731	Enterobacter cloacae complex	YES	YES

Based on the identified culture-proven sepsis cases, the sensitivity and specificity of the EOS calculator and AAP guidelines were calculated. Both the EOS calculator and AAP 2018 guidelines had 100% sensitivity. The EOS calculator had a specificity of 45% compared to the AAP 2018 guidelines of 32%.

EOS Sensitivity and Specificity			
	Start antibiotics	Culture-proven sepsis cases	Sepsis not proven by culture
EOS calculator recommendation	YES	6 (a)	112 (b)
	NO	0 (c)	90 (d)

Sensitivity: $\frac{a}{a+c}$ = **100%**

Specificity: $\frac{b}{b+d}$ = **44.6%**

AAP 2018 Guidelines Sensitivity and Specificity			
	Start antibiotics	Culture-proven sepsis cases	Sepsis not proven by culture
AAP guideline recommendation	YES	6 (a)	138 (b)
	NO	0 (c)	64 (d)

Sensitivity: $\frac{a}{a+c}$ = **100%**

Specificity: $\frac{b}{b+d}$ = **31.7%**

DISCUSSION

Neonatal sepsis is a major cause of morbidity and mortality in the Philippines.[1] Due to the high incidence of sepsis, there is a tendency to start empiric antibiotic treatment to neonates with risk factors, even in well-appearing babies. [2]

A study from a tertiary hospital in the Philippines investigated the clinical and bacteriologic profile of neonatal sepsis and found that the most common maternal risk factor was history of urinary tract infection, followed by premature rupture of membranes > 18 hours.[10] In our study, the most common intrapartum risk factor for starting antibiotics is prolonged premature rupture of membranes followed by maternal history of urinary tract infection. Both the EOS calculator and AAP 2018 guidelines suggest that antibiotic treatment for maternal history of infection and premature rupture of membranes be weighed with other factors, especially when the mother has had intrapartum antibiotic prophylaxis prior to delivery. [3,4] In the Philippines, screening for Group B streptococcus (GBS) is not routinely done thus all newborns were classified as having unknown status for maternal GBS in the EOS calculator. This is one limitation in the application of the EOS calculator in the local setting.

Many babies were started on antibiotics due to meconium staining. From the recently published local clinical guidelines on neonatal sepsis, presence of meconium stain is not an indication for antibiotic therapy unless the baby manifests with symptoms. [2]

For neonatal outcome, the most common presenting sign of a newborn with suspected sepsis in this study is respiratory distress, followed by poor feeding. This is consistent with another local study on neonatal sepsis in the country.[10] The AAP guidelines recommend treatment of ill-appearing newborns who present with any non-specific sign or symptom attributed to sepsis, subject to the clinical judgment of the medical staff.[3] The EOS calculator on the other hand, puts more weight on the clinical outcome of the neonate in recommending antibiotic treatment. It does not however include poor suck in the calculation, unless the baby manifests with physiologic abnormalities.[4]

Ten percent of newborns in this study were started on antibiotics due to increased white blood cell count and elevated C-reactive protein despite having no clinical signs and symptoms of sepsis. The Clinical Practice Guidelines for Neonatal Sepsis in the Philippines strongly recommend that a single abnormal parameter in a CBC done within the 6th - 24th hour of life not be used alone to diagnose sepsis.[2]

It is observed that in comparison to the EOS calculator and AAP recommendations, there is note of antibiotic overuse in actual practice. Only 345 newborns (38%) and 469 neonates (51%) were recommended for treatment by the EOS calculator and AAP guidelines respectively. In a similar study in a private tertiary hospital in the Philippines, out of 330 patients who received therapy, only 14% were recommended for antibiotics by the EOS calculator and 39% by the AAP guidelines.[11]

In this study, a significant proportion of neonates who were recommended to start antibiotics by the AAP guidelines and not by the EOS calculator were due to problems in feeding. This may be a limitation of the EOS calculator as it does not include poor suck in its calculation matrix.[4]

Data analysis using the Mcnemar test revealed that the EOS calculator could significantly decrease antibiotic use (p value of <0.001). However, assessing the safety of implementing the EOS calculator in the local setting is beyond the scope of this retrospective chart review.

In a meta-analysis of 11 studies that investigated 75 early onset sepsis cases, the probability of a missed case by the EOS calculator was 0.19-0.31.[9] In a local study, out of 11 culture-proven sepsis cases, only six were recommended to be started on antibiotics by both the EOS calculator and the AAP guidelines.[11]

In this study, all cases with growth on blood culture were recommended for antibiotics by the EOS calculator and AAP guidelines. Another study that utilized the EOS calculator prospectively also reported no missed cases nor readmissions for sepsis.[8] It recommended the EOS calculator to be a useful and reliable tool for risk assessment of sepsis which could significantly reduce antibiotic utilization.[8]

This study recommends conducting future researches on the prospective application and implementation of use of the EOS calculator prior to starting empiric antibiotic therapy. Further investigation on the safety of its use in clinical practice is also warranted. A modified EOS calculator is recommended in the local setting to include feeding difficulty or poor suck as one of the factors for calculating the risk score for sepsis.

CONCLUSION

This study determined if there is a significant difference between the proportion of neonates recommended for antibiotics using the EOS calculator and AAP guidelines for neonatal sepsis.

The proportion of those who were recommended for antibiotics using the EOS calculator was significantly lower by 13% than those who were recommended for antibiotics using the AAP 2018 guidelines. This proves to be a significant reduction in the use of antbiotics with the use of the EOS calculator. The EOS calculator also had a higher specificity compared to the AAP guidelines.

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CONFLICT OF INTEREST

None declared.

REFERENCES

1. Capili, C. Association of Clinical and Laboratory Parameters of Patients with Neonatal Sepsis. Pediatric Infectious Disease Journal [Internet]. 2016; 17(1):28-34. Available from: https://www.pidsphil.org/home/wp-content/uploads/2017/08/jo50_ja03.pdf
2. Clinical Practice Guidelines on Neonatal Sepsis Task Force. Clinical Practice Guidelines for the Screening, Diagnosis, Treatment and Prevention of Neonatal Sepsis. 2019. Available from: https://drive.google.com/file/d/1op2N265RLJbTizyECWmKLaUL6KKcekCa/view
3. Puopolo K, Benitz W, Zaoutis T. Management of Neonates Born at ≥35 0/7 Weeks' Gestation With Suspected or Proven Early-Onset Bacterial Sepsis. American Academy of Pediatrics. 2018 December [cited 2023 Oct]; 142 (6): e2018-2894. Available from: https://doi.org/10.1542/peds.2018-2894
4. Neonatal Sepsis Calculator [Internet]. 2021 [cited 2023 Oct]. Available from: https://neonatalsepsiscalculator.kaiserpermanente.org/GenFAQ.aspx
5. Laccetta G, Ciantelli M, Tuoni C, Sigali E, Miccoli M, Cuttano A. Early-onset sepsis risk calculator: a review of its effectiveness and comparative study with our evidence-based local guidelines. Italian Journal of Pediatrics [internet]. 2021 March [cited 2023 Oct]; 47(1): 73. Available from: https://doi.org/10.1186/s13052-021-01028-1
6. Huseynova R, Mahmoud L, Aljobair F, Huseynov O, Career H, Jaganathan P, et al. Use of Early-Onset Sepsis Risk Calculator for Neonates ≥ 34 Weeks in a Large Tertiary Neonatal Centre, Saudi Arabia. Cureus [Internet]. 2021 April [cited 2023 Oct]; 13(4): e14620. Available from: https://doi.org/10.7759/cureus.14620
7. Achten N, Klingenberg C, Benitz W, Stocker M, Schlapbach L, Giannoni E, et al. Association of Use of the Neonatal Early-Onset Sepsis Calculator With Reduction in Antibiotic Therapy and Safety. JAMA Pediatrics [Internet]. 2019 Sept [cited 2023 Oct]; 173(11), 1032-1040. Available from: https://doi.org/10.1001/jamapediatrics.2019.2825
8. Leonardi B, Binder M, Griswold K, Yalcinkaya G, Walsh M. Utilization of a Neonatal Early-Onset Sepsis Calculator to Guide Initial Newborn Management. Pediatric Quality and Safety [Internet]. 2019 Oct [cited 2023 Oct]; *4(5), e214.* Available from: https://doi.org/10.1097/pq9.0000000000000214
9. Pettinger K, Mayers K, McKechnie L, Phillips, R. Sensitivity of the Kaiser Permanente early-onset sepsis calculator: A systematic review and meta-analysis. EClinicalMedicine [Internet]. 2019 Dec [cited 2023 Oct] 19, 100227. Available from: https://doi.org/10.1016/j.eclinm.2019.11.020
10. Azurin E, Marasigan A, Ang J. Clinical and Bacteriologic Profile of Neonatal Sepsis in a Tertiary Care Hospital: A 5-Year Review. Pediatric Infectious Disease Society of the Philippines Journal [Internet]. 2020;21(2):39–47. Available from: http://www.pidsphil.org/home/wp-content/uploads/2020/10/005_Vol-21-No-2_Azurin_Neonatal_Sepsis_formattedv3.pdf
11. Beannda, A., Doctor, K., Bernabe, J. The comparison between management recommendations of the Neonatal Early Onset Sepsis Calculator and CDC/AAP Guidelines among culture-proven early onset sepsis admitted at University of East Ramon Magsaysay Memorial Medical Center from January 2013 to December 2017. HERDIN Health Sciences Journal [Internet], 2019 Jun [cited 2023 Oct]; 8(1):20-28. Available from: https://www.herdin.ph/index.php/partner/journal?view=research&cid=70965