EUROX 19 (2023) 100221

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology: X

journal homepage: www.journals.elsevier.com/european-journal-of-obstetrics-and-gynecology-and-reproductive-biology

# Procalcitonin levels in maternal serum and cord blood as marker for diagnosis of early onset neonatal sepsis

Puja Yadav [a], Kavita Agarwal [a,*], Anita Rani [b], Rupali Dewan [a], Harish Chellani [c]

[a] Deptt. Of Obs. & Gynae, VMMC & Safdarjung Hospital, Delhi, India
[b] Deptt. of Biochemistry, VMMC & Safdarjung Hospital, Delhi, India
[c] Deptt. Of Paediatrics, VMMC & Safdarjung Hospital, Delhi, India

ARTICLE INFO

*Keywords:*
Procalcitonin
Neonatal sepsis
C-Reactive Protein

ABSTRACT

*Objectives:* To assess the diagnostic accuracy of Procalcitonin in maternal serum and umbilical cord blood samples to predict Early onset neonatal sepsis (EONS).

*Study Design:* It was a Prospective analytical cohort study. Pregnant women ≥ 34 weeks gestation in active labour, with risk factors for EONS were included in the study. Maternal blood samples at recruitment and umbilical cord blood samples after delivery were taken for Total leucocyte count (TLC), high sensitivity C-Reactive Protein (hs-CRP) and Procalcitonin. Newborns were classified into non-infected, suspected and proven infection. Sensitivity, specificity and diagnostic accuracy of maternal and cord blood procalcitonin, TLC and hs-CRP were calculated.

*Results:* A total of 200 women were recruited. Maternal procalcitonin had a superior diagnostic accuracy of 99% compared to maternal TLC and maternal hs-CRP. Also, cord blood procalcitonin had a diagnostic accuracy of 95%.

*Conclusion:* Procalcitonin in both maternal as well as cord blood is a promising biomarker to detect EONS with high diagnostic accuracy.

## Introduction

The incidence of clinical sepsis in neonates in India is 17,000 per one lakh live births [1]. Neonatal sepsis encompasses infections like pneumonia, septicemia, meningitis, arthritis, osteomyelitis and urinary tract infections. Early onset neonatal sepsis (EONS) is a clinical syndrome presenting within first 72 h of life. It usually presents with respiratory distress and pneumonia. Maternal genital tract is the most common source of infection. EONS is the major cause of neonatal morbidity and mortality and hence require early diagnosis and treatment. Therefore, antibiotics are often started in suspected cases of EONS without waiting for bacteriological culture reports and results of inflammatory markers [2]. Such therapeutic approach alter microbiota of newborn, lead to resistant bacteria, necrotizing enterocolitis and make them prone to nosocomial infections, metabolic, autoimmune, allergic pathologies [3]. In this era of multi-drug resistance, antibiotics should be used to treat neonates only after identification of babies at risk [4].

Various hematological indices like white blood cell (WBC) count, absolute neutrophil count, immature/total neutrophil ratio and serological markers like high sensitivity C-reactive protein (hs-CRP) have been used for identification of at risk babies but have low sensitivity [4]. The Gold standard, blood cultures have risk of low yield / false negative results after antenatal antibiotic exposure. Also, sample drawn are mostly low volumes and report takes at least 48 h [5]. Additionally, in India, blood culture testing facility is not available in most of the district hospitals [1].

Procalcitonin (PCT) level has been reported to increase in bacterial infections in newborns. However, there is physiological rise in PCT level in newborns during first 48–72 hrs of life [2]. Studies have found that PCT value in maternal serum or umbilical cord blood sample can help distinguish infected from healthy newborns [5]. Also, it is superior to WBC count and CRP values [6]. However, the diagnostic accuracy of PCT in maternal serum and cord blood in predicting EONS remains to be validated. The present study was planned to assess the diagnostic accuracy of PCT in maternal serum and umbilical cord blood samples to predict EONS.

* Correspondence to: Department Obs. And Gynae, VMMC & Safdarjung Hospital, New Delhi 110029, India.
*E-mail address:* drku93@gmail.com (K. Agarwal).

https://doi.org/10.1016/j.eurox.2023.100221
Received 22 March 2023; Received in revised form 9 July 2023; Accepted 29 July 2023
Available online 30 July 2023

## Materials and methods

The study was conducted in the Department of Obstetrics and Gynaecology in collaboration with Department of Paediatrics and Biochemistry after getting ethical clearance from the institute. It was a Prospective analytical cohort study conducted over a period of 18 months from November 2020–22.

Sample size was calculated from study of Oria O. which found sensitivity and specificity of cord blood PCT was 100% and 95.2% respectively [7] and the study of Cetin O. that observed sensitivity and specificity of maternal blood PCT was 85.2% and 86.7% respectively [6]. Taking these values as reference, the minimum required sample size with desired precision of 10%, 95% power of study and 5% level of significance was found to be 184 patients. To reduce margin of error, total sample size was taken as 200.

Pregnant women $\geq$ 34 weeks gestation in active labour, with no contraindication for vaginal delivery and with risk factors for EONS were included in the study. The risk factors included were foul smelling liqour, meconium stained liquor (MSL), leaking per vaginum (LPV) > 18 h [8], single unclean or > 4 sterile per vaginum (PV) examination during labour, intrapartum fever, febrile illness with evidence of bacterial infection within 2 weeks prior to delivery. Exclusion criteria were women with medical disorder, renal, cardiac disease, diabetes mellitus, women receiving intrapartum antibiotic > 4 h prior to delivery (study has found intrapartum antibiotic given >4 h before delivery was associated with decreased risk) [9], multiple gestation, fetal growth restriction, gross congenital anomaly and neonate requiring admission to NICU for reasons other than sepsis.

Informed consent was taken from all the recruited patients. Detailed medical history, obstetric history, general physical examination and obstetric examination findings were noted in a proforma. At the time of recruitment, maternal blood samples were taken for Complete blood count (CBC) with total leucocyte count (TLC), hs-CRP and PCT. Progress of labour was plotted on partogram. Labour duration, intrapartum events, mode of delivery were noted. Within 5 min of birth of the baby but before the delivery of placenta, umbilical cord blood sample was taken after clamping the cord from placental end on two sides, wiping in between cord with spirit and blood was drawn using a 22-gauge needle. Samples were taken for CBC with TLC, hs-CRP and PCT. Baby details like sex, birthweight, apgar score, need for NICU admission were noted in the proforma. Procalcitonin was done by Diazyme Pro-Calcitonin assay based on the latex enhanced immune turbidimetric assay. Hs-CRP was done by the Beckman Coulter AU Analyzer. Immune complexes are formed during the immunological reaction between the CRP of the patient serum and rabbit anti-CRP antibodies coated on latex particles.

All mothers were monitored in postpartum period for any signs of infection, fever, foul smelling lochia, abdominal tenderness. Management of newborns was done as per the hospital protocol. Asymptomatic newborn received essential newborn care and were monitored for next 48 h for clinical signs and symptoms of early neonatal sepsis. In symptomatic newborns with 2 antenatal risk factors, sepsis screen (CBC with TLC, hs-CRP, PCT, blood culture) was done. If negative, then repeated after 12 h and if positive, then antibiotic therapy was initiated. In case of foul smelling liquor or presence of $\geq$ 3 antenatal risk factors, blood culture and lumbar puncture was done and antibiotic therapy was initiated.

Newborns were classified (CDC criteria) into non-infected, proven infection or probable infection. Non -infected were defined as having no clinical (Fever> 37.8 °C, hypothermia < 35 °C, tachycardia, bradycardia, poor perfusion, hypotension, respiratory distress, seizures, lethargy) or biological signs of sepsis (WBC count > 25.109/L or < 4.109/L, platelet count< 150.109/L, immature neutrophil proportion> 5% and CRP level $\geq$ 20 mg/L). Probable/ suspected infection i.e. by the association of clinical and biological signs of infection. Infected newborns were defined by the positive microbiological blood or cerebrospinal fluid culture (proven infection).

The primary outcome measures were number of newborns with proven infection, probable infection and non-infected. Diagnostic accuracy, sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) of Procalcitonin, TLC and hs-CRP in maternal serum and umbilical cord blood for diagnosis of EONS. The secondary outcomes were maternal and neonatal morbidity and mortality.

For statistical analysis, categorical variables were presented in number and percentage and continuous variables were presented as mean ± standard deviation. Diagnostic tests were used to calculate sensitivity, specificity, NPV and PPV. DeLong et al. test was used to compare area under the curve of maternal serum markers with cord blood markers for predicting early neonatal sepsis. A p value of $< 0.05$ was considered significant. Analysis was done using SPSS version 21.0.

## Results

A total of 200 pregnant women were recruited in the study. The mean age (years) was 25 ± 3.34 and most of the women (n = 59) were primipara. Out of 200 women recruited, 40% had LPV > 18 h, 27.5% had MSL, 4.0% had foul smelling liquor, 20.5% had more than 4 PV examinations, 15% had intrapartum fever and 19% had urinary tract infection. Most of the women (62%) had preterm vaginal delivery. In the postpartum period, 79% women had no morbidity, 13% had fever, 6.5% had UTI and 1.5% had PPH. The mean birth weight (Kg) of newborns was 2.32 ± 0.53. The mean APGAR at 1 min was 7.57 ± 0.53 and the mean APGAR (5 min) was 8.69 ± 0.95. The mean maternal procalcitonin level (ng/ml) was 0.043 ± 0.14. The mean TLC (/$mm^3$) was 10863.37 ± 4986.49. The mean hs-CRP (mg/L) was 6.98 ± 3.48. The mean umbilical cord blood procalcitonin (ng/ml) was 0.13 ± 0.24. The mean cord blood TLC (/$mm^3$) was 9140.63 ± 3040.02. The mean cord blood hs-CRP (mg/L) was 0.37 ± 0.59.

Out of 200 neonates, 169 (84.5%) had no sepsis, 24 (11.5%) cases were suspected and 7 (4%) cases were of proven sepsis [Fig. 1]. In 7 cases of proven sepsis by culture, Klebsiella Pneumoniae was the most

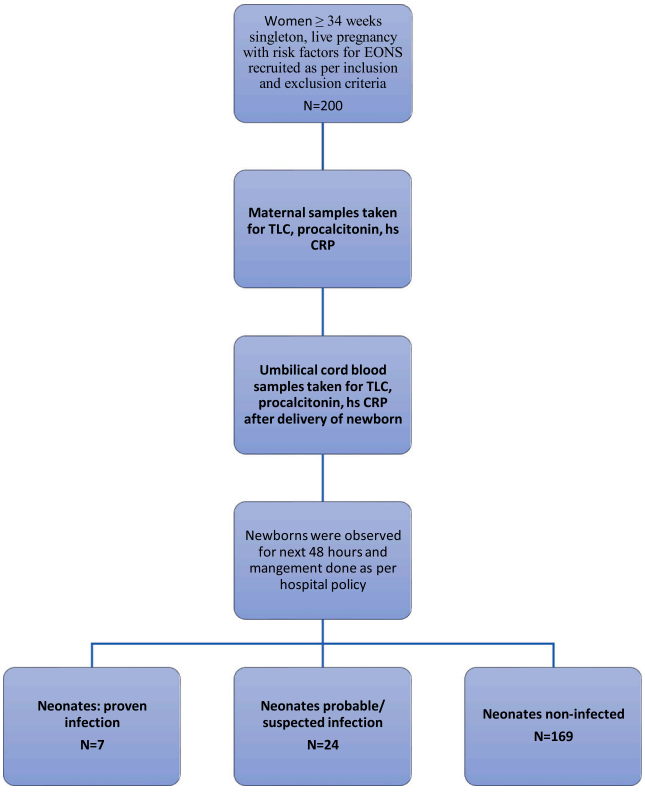


**Fig. 1.** Flowchart.

common organism isolated followed by E. Coli, Staphylococcus aureus and coagulase negative Staphylococcus. Penicillin and cephalosporin resistance was seen in all the cases. Organisms were found to be sensitive to Piperacillin-Tazobactum, fluoroquinolones and aminoglycosides. All the neonates with suspected/ proven sepsis were transferred to NICU for observation. No neonatal mortality occurred and all were discharged from the hospital with no complaints. Maternal age and parity were not found to have statistically significant association with EONS. The maternal risk factors found to have statistically significant association with EONS were foul smelling liquor, leaking PV > 18 h, MSL, > 4 PV examinations and intrapartum fever. Prematurity and low birth weight were found to have statistically significant association with EONS [Table 1].

The maternal TLC at a cut off value ≥ 15,000/mm$^3$ was able to detect 26 cases of EONS and falsely picked up 17 cases. Receiver operating characteristic curve (ROC curve) analysis found the cut-off of cord blood TLC was ≥ 12,000/mm$^3$. At this cut-off, it predicted 30 cases of sepsis and falsely predicted 1 case. The cut-off of maternal procalcitonin was ≥ 0.078 ng/ ml which predicted all cases of sepsis and falsely predicted 2 cases. The cut-off of cord blood procalcitonin was ≥ 0.35 ng/ ml. It predicted all cases of sepsis and falsely predicted 10 cases. The maximum diagnostic value of maternal hs-CRP (mg/l) was at ≥ 10. It predicted only 19 cases and falsely predicted 34 cases. The umbilical cord hs-CRP (mg/l) at cut-off ≥ 0.30 predicted only 16 cases and falsely predicted 53 cases. [Table 2; Fig. 2].

Maternal procalcitonin had a superior diagnostic accuracy of 99% compared to maternal TLC and maternal hs-CRP. Also, cord blood procalcitonin had a diagnostic accuracy of 95% compared to cord blood TLC and cord blood hs-CRP diagnostic accuracy of 99% and 66.2%. Both maternal and cord blood procalcitonin had sensitivity of 100%. The specificity of cord blood procalcitonin was slightly less in comparison to maternal blood procalcitonin (94.1% versus 98.8%) [Table 3]. There was no statistically significant difference in the diagnostic performance of maternal and cord blood PCT (p = 0.163).

**Table 1**
Association of obstetric and neonatal parameters with EONS.

| Obstetric and neonatal parameters | No. of participants N = 200 | Sepsis present (proven and clinical suspicion) N = 31 | P value |
|---|---|---|---|
| Age (years) | 114 | 15 | 0.563 |
| 18–25 | 74 | 14 | |
| 26–30 | 12 | 2 | |
| 31–35 | | | |
| Parity | 48 | 13 | 0.081 |
| Para 0 | 59 | 8 | |
| Para 1 | 50 | 5 | |
| Para 2 | 43 | 5 | |
| ≥ Para 3 | | | |
| Maternal risk factors | 80 | 31 | < |
| LPV> 18 h | 55 | 21 | 0.001 |
| MSL | 8 | 7 | < |
| Foul smelling liquor | 41 | 29 | 0.001 |
| > 4 PV | 30 | 23 | < |
| Intrapartum fever | 38 | 8 | 0.001 |
| H/O UTI | | | < |
| | | | 0.001 |
| | | | < |
| | | | 0.001 |
| | | | 0.293 |
| Neonatal Parameters | 124 | 25 | 0.046 |
| Fetal maturity | 63 | 6 | < |
| Preterm | 13 | 0 | 0.001 |
| Term | 15 | 10 | |
| Post term | 40 | 18 | |
| Birth weight (Kg) | 44 | 3 | |
| < 1.5 | 101 | 0 | |
| 1.5–2.0 | | | |
| 2.0–2.5 | | | |
| ≥ 2.5 | | | |

**Table 2**
Diagnostic efficacy of laboratory parameters in predicting sepsis.

| Lab parameters | Sepsis proven N = 7 | Sepsis suspicion N = 24 | Sepsis absent N = 169 |
|---|---|---|---|
| Maternal TLC ≥ 15,000 cells/ mm$^3$ | 4 | 22 | 17 |
| Cord blood TLC ≥ 12,000 cells/ mm$^3$ | 7 | 23 | 1 |
| Maternal procalcitonin ≥ 0.078 ng/ml | 7 | 24 | 2 |
| Cord blood procalcitonin ≥ 0.35 ng/ml | 7 | 24 | 10 |
| Maternal hs-CRP ≥ 10 mg/l | 6 | 13 | 34 |
| Cord blood hs-CRP ≥ 0.30 mg/l | 4 | 12 | 53 |

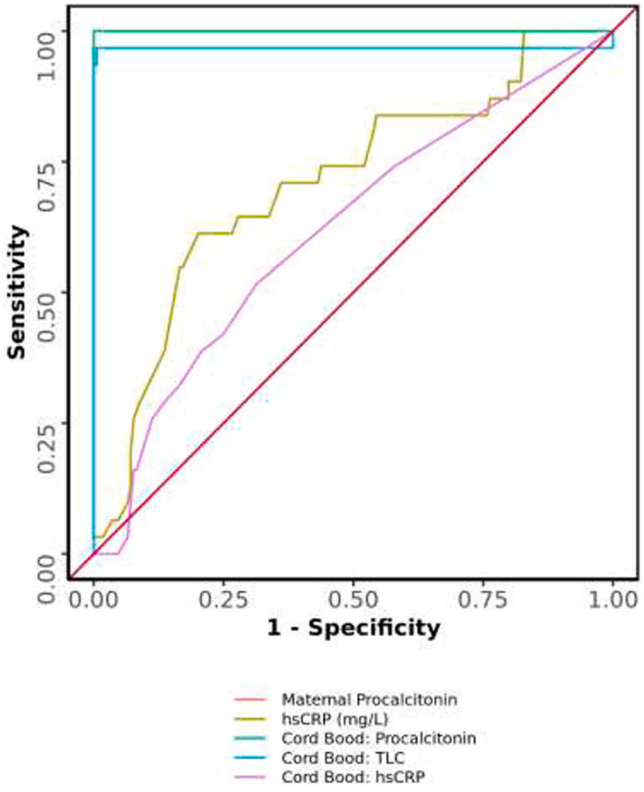


**Fig. 2.** ROC curve comparing all laboratory parameters of sepsis.

## Discussion

Neonatal sepsis is one of the leading causes of neonatal morbidity and mortality. Screening the mothers and testing of cord blood for inflammatory markers such as WBC, hs-CRP and PCT aids the pediatrician to suspect sepsis and institute relevant interventions. The present study of 200 women found foul smelling liquor, LPV > 18 h, MSL, > 4 PV examinations, intrapartum fever, prematurity and low birth weight to have statistically significant association with EONS. Similar risk factors for EONS i.e. premature rupture of membranes, meconium stained liquor, maternal infections, prematurity and low birth weight have been reported in various studies [10–14]. Along with the above-mentioned risk factors, Noah et al. [10] found maternal age < 20 yrs and > 30 yrs, male sex and Alam et al. [12] discovered thrombocytopenia to be additional risk factors for EONS.

The present study found maternal procalcitonin had a sensitivity of 100% i.e. it detected all cases of EONS and specificity of 98.8% with diagnostic accuracy of 99% in predicting EONS. Maternal hs-CRP had sensitivity and specificity of 61% and 79% respectively with diagnostic

**Table 3**
Diagnostic performance of various lab parameters in predicting sepsis.

| Laboratory parameters | Predicted cut-off by ROC curve | Sensitivity | Specificity | Positive predictive value | Negative predictive value | Diagnostic accuracy |
|---|---|---|---|---|---|---|
| Maternal TLC (/mm$^3$) | - | 83.9% | 90% | 60.5% | 96.8% | 89.10% |
| Maternal hs-CRP (mg/l) | $\geq 10$ | 61% | 79% | 35.2% | 91.8% | 76.6% |
| Maternal procalcitonin (ng/ml) | $\geq 0.078$ | 100% | 98.8% | 93.9% | 100% | 99% |
| Cord blood TLC (/mm$^3$) | $\geq 12{,}000$ | 96.8% | 99.4% | 96.8% | 99.4% | 99% |
| Cord blood hs-CRP (mg/l) | $\geq 0.30$ | 51.6% | 68.8% | 23.2% | 88.6% | 66.2% |
| Cord blood procalcitonin (ng/ml) | $\geq 0.35$ | 100% | 94.1% | 75.6% | 100% | 95% |

accuracy of 76.6%. Sensitivity and specificity of maternal TLC in predicting EONS were 83.9% and 90% respectively with diagnostic accuracy of 89.1%. In agreement with our work, Cetin O et al. [6] in prospective observational study of 57 pregnancies found maternal PCT sensitivity 85.2%, specificity 86.7%, maternal blood CRP sensitivity and specificity in predicting EONS was 77.8% and 80% respectively, maternal TLC count sensitivity and specificity was 67.9% and 72.4% respectively. Similar results of sensitivity and specificity of maternal blood CRP and TLC for prediction of EONS have been seen in other studies [11,15,16]. There has been no other study on prediction of EONS by maternal blood PCT. However, studies have shown association of maternal blood PCT levels with maternal infection/chorioamnionitis [17–19]. The present study found maternal procalcitonin has a superior diagnostic accuracy compared to maternal TLC and hs-CRP. Similar to our study, Cetin O et al. [6] study also showed maternal blood PCT levels to be more accurate in predicting EONS compared with blood CRP and TLC.

Umbilical cord hs-CRP in present study had sensitivity and specificity of 51.6% and 68.8% respectively with diagnostic accuracy of 66.2%. Contrary to our study, study by Patrick et al. [20] on 103 babies, out of which 12 were found to have sepsis found cord blood CRP to have sensitivity of 100% and specificity of 90%. The better diagnostic accuracy in this study could be because our study had a comparatively bigger sample size. In the present study, umbilical cord hs-CRP falsely predicted 53 cases. In agreement with our study, Kumar et al. [21] found that even in absence of infection, raised cord CRP levels were found to be strongly linked with protracted labour $> 12$ h, maternal fever and rupture of membranes $> 24$ h ($p < 0.005$). They suggested that apart from infections, other stimuli like hypoxia, trauma and metabolic changes can induce production of CRP. Hence, they inferred that CRP from cord blood is not a reliable predictor of EONS. The present study found sensitivity and specificity of umbilical cord TLC in predicting EONS were 96.8% and 99.4% respectively with diagnostic accuracy of 99%. As opposed to our study, Hornik et al. [22] in study on 2177 participants discovered EONS to be linked with low rather than high TLC levels. They found TLC count of $< 5000$/mm$^3$ to have sensitivity and specificity of 50% and 94% respectively. The difference in results could be because of our small sample size.

The present study found umbilical cord blood procalcitonin had a sensitivity of 100% and specificity of 94.1% with diagnostic accuracy of 95% in predicting EONS. Similar results have been seen in other previous studies on cord blood PCT for predicting EONS [7,23]. A meta-analysis which evaluated PCT in suspected EONS cases found pooled sensitivity to be 78% in cord blood PCT compared to pooled value of 70% in studies measuring PCT at 24–48 h after birth [3]. They suggested that evaluating cord blood PCT for predicting EONS may lead to increased diagnostic accuracy as it avoids confounding factors like physiological rise of PCT following birth and PCT rise due to perinatal events like respiratory distress, hypoxic ischemic encephalopathy, intracranial hemorrhage, pneumothorax etc [3]. A systemic review and meta-analysis [24] concluded that either maternal TLC or CRP was inadequate for diagnosis of EONS and cord blood PCT can be used as valid rule-in and rule-out test. Huetz N et al. [2] determined the possible effects of umbilical cord blood procalcitonin based algorithm. They found a substantial decrease in antibiotic prescription rate in neonates. They concluded that PCT could assist in early start of antibiotic therapy in babies at high risk of infection and also decrease the antibiotic prescription in non-infected neonates.

The strength of our study is that we evaluated levels of inflammatory markers in both maternal and cord blood to predict EONS. Ours is the first study till date, to the best of our knowledge to correlate the diagnostic accuracy of both maternal and cord blood PCT in the detection of EONS. The limitation is small sample size of our study.

## Conclusion

Procalcitonin in both maternal as well as cord blood is a promising biomarker to detect EONS with high diagnostic accuracy. We recommend that a PCT- based algorithm must be made to reduce empirical antibiotic use for EONS.

## Declaration of Competing Interest

There are no conflicts of interest.

## References

[1] Murthy S, Godinho MA, Guddattu V, Lewis LES, Nair NS. Risk factors of neonatal sepsis in India: a systematic review and meta-analysis. PloS One 2019;14:4.
[2] Huetz N, Launay E, Gascoin G, Leboucher B, Savagner C, Muller JB, et al. Potential impact of umbilical cord blood procalcitonin based algorithm on antibiotics exposure in neonates with suspected early-onset sepsis. Front Pediatr 2020;8:127.
[3] Gilfillan M, Bhandari V. Neonatal sepsis biomarkers: where are we now? Res. Rep. Neonatol. 2019;9:9–20.
[4] Mishra UK, Jacobs SE, Doyle LW, Garland SM. Newer approaches to the diagnosis of early-onset neonatal sepsis. Arch Dis Child Fetal Neonatal Ed 2006;91(3):208–12.
[5] Su H, Chang SS, Han CM, Wu KY, Li MC, Huang CY, et al. Inflammatory markers in cord blood or maternal serum for early detection of neonatal sepsis-a systemic review and meta-analysis. J Perinatol 2014;34(4):268–74.
[6] Cetin O, Aydın ZD, Verit FF, Zebitay AG, Karaman E, Elasan S, et al. Is Maternal blood procalcitonin level a reliable predictor for EONS in preterm premature rupture of membranes? Gynecol Obstet Investig 2017;82(2):163–9.
[7] Oria O, Beceiro J, Barrionuevo M, Ripalda MJ, Olivas C. Procalcitonina en sangre de cordón en la valoración del riesgo de sepsis neonatal precoz. Pedia (Barc) 2017;87:87–94.
[8] National Institute for Health and Care Excellence (NICE) Antibiotics for Early-onset Neonatal Infection: Antibiotics for the Prevention and Treatment of Early-Onset Neonatal Infection. London: Clinical guideline [CG149] (2012).
[9] Puopolo KM, Draper D, Wi S, Newman TB, Zupancic J, Lieberman E, et al. Estimating the probability of neonatal early-onset infection on the basis of maternal risk factors. Pediatrics 2011;128:e1155–63.
[10] Noah FN, Doya LJ, Jouni O. Perinatal risk factors and early onset of neonatal sepsis. Int J Pedia Res 2022;8:088.
[11] Panwar C, Kaushik SL, Kaushik R, Sood A. Correlation of neonatal and maternal clinico-hematological parameters as predictors of early onset neonatal sepsis. Int J Conte Pedia 2017;4(1):36–42.
[12] Alam MM, Saleem AF, Shaikh AS, Munir O, Qadir M. Neonatal sepsis following prolonged rupture of membranes in a tertiary care hospital in Karachi, Pakistan. J Infect Dev Ctries 2014;8(1):67–73.
[13] Jajoo M, Kapoor K, Garg LK, Manchanda V, Mittal SK. To study the incidence and risk factors of early onset neonatal sepsis in an out born neonatal intensive care unit of India. J Clin Neonatol 2015;4:91–5.
[14] Lekic E, Babovic S, Vukicevic J, Nesovic M, Dragas L. Early-onset neonatal sepsis and risk factors in the preterm infants. Perinat J 2019;27(3):143–9.
[15] Popowski T, Goffinet F, Maillard F, Schmitz T, Leroy S, Kayem G. Maternal markers for detecting early-onset neonatal infection and chorioamnionitis in cases of premature rupture of membranes at or after 34 weeks of gestation: a two-center prospective study. BMC Pregnancy Childbirth 2011;11:26.
[16] Suryavanshi A, Kalra R. Study of association of c-reactive protein with maternal chorioamnionitis and early-onset neonatal sepsis in premature rupture of

membranes deliveries: a diagnostic dilemma. Int J Appl Basic Med Res 2019;9(4):236–40.
[17] Oludag T, Gode F, Caglayan E, Saatli B, Okyay RE, Altunyurt S. Value of maternal procalcitonin levels for predicting subclinical intra-amniotic infection in preterm premature rupture of membranes. J Obstet Gynaecol Res 2013;40(4):954–60.
[18] Joyce CM, Deasy S, Abu H, Lim YY, O'Shea PM, O'Donoghue K. Reference values for C-reactive protein and procalcitonin at term pregnancy and in the early postnatal period. Ann Clin Biochem 2021;58(5):452–60.
[19] Agarwal R, Priyadarshini P, Mehndiratta M. Serum procalcitonin in pregnancy-associated sepsis: a case control study. South Afr J Obstet Gynaecol 2019;25(1):15–9.
[20] Patrick R, Rajan A, Soans ST, Shriyan A. Cord C-reactive protein as a marker for early onset neonatal sepsis children. Int J Conte Pedia Int J Conte Pedia [Internet] 2017;44(2):527–9.
[21] Kumar R, Deka A, Choudhury SN, Roy M. C-reactive protein—as an early diagnostic marker of early onset sepsis and its correlation with blood culture. N Indian J OBGYN 2016;2(2):78–82.
[22] Hornik CP, Benjamin DK, Becker KC, et al. Use of the complete blood cell count in early-onset neonatal sepsis. Pedia Infect Dis J 2012;31(8):799–802.
[23] Joram N, Muller J-B, Denizot S, Orsonneau J-L, Caillon J, Roze J-C, et al. Umbilical cord blood procalcitonin level in early neonatal infections: a 4-year university hospital cohort study. Eur J Clin Microbiol Infect Dis 2011;30(8):1005–13.
[24] Su H, Chang SS, Han CM, et al. Inflammatory markers in cord blood or maternal serum for early detection of neonatal sepsis-a systemic review and meta-analysis. J Perinatol 2014;34(4):268–74.