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Relationship between Antenatal Maternal Neutrophil-to-Lymphocyte Ratio and Early Onset Neonatal Sepsis in Preterm Neonates

Thitiphan Chayawongrungreung, M.D.*,
Jiraporn Luengmettakul, M.D.*,
Aungsumalin Srilar, M.D.*.

** Department of Obstetrics and Gynecology, Chareonkrung Pracharak Hospital, Medical Service Department, Bangkok Metropolitan Administration, Bangkok, Thailand*

ABSTRACT

Objectives: To determine the relationship between maternal neutrophil to lymphocyte ratio (NLR) and early onset neonatal sepsis (EONS) in preterm neonates.

Materials and Methods: Between 2012 to 2016, a total of 485 cases of preterm delivery were retrospectively reviewed. Study group consisted of 97 neonates diagnosed with EONS and other 388 without EONS were randomly selected as a comparison group (1:4 ratio). Data were extracted from medical records, including baseline characteristics, obstetric and delivery data. Maternal NLR was calculated from laboratory results within 72 hours prior to delivery.

Results: Neonates with EONS were significantly more likely to deliver at < 34 weeks ($p < 0.001$), had preterm premature rupture of membranes ($p = 0.043$), and had maternal fever ($p = 0.016$). White blood cell and neutrophil counts were significantly higher in EONS group while lymphocyte counts were comparable. Median NLR was significantly higher in EONS group (4.7 vs. 4.1, $p = 0.005$). NLR of > 5 significantly increased the risk of EONS (26.8% vs. 16.4%, $p = 0.007$). Logistic regression analysis showed that delivery at < 34 weeks and maternal fever were independently associated with EONS (adjusted odds ratio (ORs) 11.5, 95% confidence interval (CI) 6.7-19.7, and 3.4, 95% CI 1.1-11.3, respectively). Subgroup analysis showed that NLR of ≥ 5 independently increased the risk of EONS in those delivered at < 34 weeks (adjusted ORs 3.5, 95% CI 1.4-9.1) and maternal fever independently increased the risk of EONS in those delivered at ≥ 34 weeks (adjusted ORs 6.1, 95% CI 1.8-20.3).

Conclusion: Maternal NLR was significantly associated with EONS in preterm neonates, especially those delivered at < 34 weeks.

Keywords: preterm neonates, early onset neonatal sepsis, neutrophil to lymphocyte ratio.

Correspondence to: *Aungsumalin Srilar, M.D., Department of Obstetrics and Gynecology, Chareonkrung Pracharak Hospital, Medical Service Department, Bangkok Metropolitan Administration, Chareonkrung Road, Bangkholaem, Bangkok 10250, Thailand, Email: m_aungsu@gmail.com*

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ความสัมพันธ์ระหว่างอัตราส่วนเม็ดเลือดขาวชนิดนิวโตรฟิลล์ต่อลิมโฟไซต์ของมารดากับการเกิดภาวะติดเชื้อแรกเกิดระยะแรกในทารกคลอดก่อนกำหนด

ฐิติพรรณ ชยวงศ์รุ่งเรือง, จิรพร เหลืองเมตตากุล, อังสุมาลิน ศรีหล้า

บทคัดย่อ

วัตถุประสงค์: *เพื่อหาความสัมพันธ์ระหว่างอัตราส่วนเม็ดเลือดขาวชนิดนิวโตรฟิลล์ต่อลิมโฟไซต์ของมารดากับการเกิดภาวะติดเชื้อแรกเกิดระยะแรกในทารกคลอดก่อนกำหนด*

วัสดุและวิธีการ: *การศึกษาย้อนหลังโดยศึกษาสตรีที่คลอดก่อนกำหนดในช่วงปี พ.ศ.2555 จนถึง ปี พ.ศ.2559 โดยพิจารณาค่าผลเลือดอัตราส่วนเม็ดเลือดขาวชนิดนิวโตรฟิลล์ต่อลิมโฟไซต์ของมารดาก่อนคลอด 72 ชั่วโมง กับการเกิดภาวะติดเชื้อแรกเกิดระยะแรกของทารก กลุ่มประชากร ได้แก่ ทารกคลอดก่อนกำหนดที่มีภาวะติดเชื้อแรกเกิดระยะแรกจำนวน 97 คน และทารกคลอดก่อนกำหนดที่ไม่มีภาวะติดเชื้อแรกเกิดระยะแรกจำนวน 388 คน (อัตราส่วน 1 ต่อ 4)*

ผลการศึกษา: *การเพิ่มขึ้นของอัตราส่วนเม็ดเลือดขาวชนิดนิวโตรฟิลล์ต่อลิมโฟไซต์ของมารดาก่อนคลอดสัมพันธ์กับการเกิดภาวะติดเชื้อแรกเกิดระยะแรกในทารกที่คลอดก่อนกำหนดอย่างมีนัยสำคัญทางสถิติ โดยค่ามัธยฐานของอัตราส่วนเม็ดเลือดขาวชนิดนิวโตรฟิลล์ต่อลิมโฟไซต์ของมารดาในกลุ่มที่ทารกมีภาวะติดเชื้อแรกเกิดระยะแรกเท่ากับ 4.7 ในขณะที่ค่ามัธยฐานของอัตราส่วนดังกล่าวของกลุ่มมารดาที่ทารกไม่มีภาวะติดเชื้อแรกเกิดระยะแรกเท่ากับ 4.1 ($p = 0.005$) ปัจจัยสำคัญที่ทำให้เกิดภาวะการติดเชื้อแรกเกิดระยะแรก ได้แก่ อายุครรภ์คลอดที่คลอดน้อยกว่า 34 สัปดาห์ ($p < 0.001$) ภาวะน้ำเดินก่อนเจ็บครรภ์คลอด ($p = 0.043$) และการที่มารดามีไข้ก่อนคลอด ($p = 0.016$) และเมื่อพิจารณาค่าการตรวจนับเม็ดเลือดอย่างสมบูรณ์ของมารดาพบว่า กลุ่มมารดาที่ทารกมีภาวะติดเชื้อแรกเกิดระยะแรกจะมีจำนวนเม็ดเลือดขาวทั้งหมด และจำนวนเม็ดเลือดขาวชนิดนิวโตรฟิลล์ก่อนคลอดสูงกว่า ($p = 0.041$ และ 0.001 ตามลำดับ) แต่จำนวนเม็ดเลือดขาวชนิดลิมโฟไซต์ไม่ต่างกันในสองกลุ่ม นอกจากนี้ความเสี่ยงที่ทารกแรกเกิดที่คลอดก่อนกำหนดจะมีภาวะติดเชื้อแรกเกิดระยะแรกเพิ่มมากขึ้น เมื่อค่าอัตราส่วนเม็ดเลือดขาวชนิดนิวโตรฟิลล์ต่อลิมโฟไซต์ของมารดาก่อนคลอด ≥ 5 (ร้อยละ 26.8 vs 16.4, $p = 0.007$) การวิเคราะห์ถดถอยแบบโลจิสติก พบว่าปัจจัยที่สัมพันธ์กับการเกิดภาวะการติดเชื้อแรกเกิดระยะแรกคือการคลอดที่อายุครรภ์ที่น้อยกว่า 34 สัปดาห์ และการที่มารดามีไข้ก่อนคลอด (adjusted ORs 11.5, 95% CI 6.7-19.7 และ 3.4, 95% CI 1.1-11.3 ตามลำดับ) และเมื่อวิเคราะห์แยกกลุ่มพบว่าอัตราส่วนดังกล่าวของมารดาที่ ≥ 5 จะเพิ่มความเสี่ยงของภาวะการติดเชื้อแรกเกิดระยะแรกในกรณีที่ทารกคลอดก่อน 34 สัปดาห์ (adjusted ORs 3.5, 95% CI 1.4-9.1) และการที่มารดามีไข้ก่อนคลอดจะเพิ่มความเสี่ยงของการเกิดภาวะการติดเชื้อแรกเกิดระยะแรกในทารกที่คลอดตั้งแต่ 34 สัปดาห์ขึ้นไป (adjusted ORs 6.1, 95% CI 1.8-20.3)

สรุป: *ค่าอัตราส่วนเม็ดเลือดขาวชนิดนิวโตรฟิลล์ต่อลิมโฟไซต์ของมารดาก่อนคลอดสัมพันธ์กับการเกิดภาวะการติดเชื้อแรกเกิดระยะแรกในทารกที่คลอดก่อนกำหนด โดยเฉพาะกรณีที่คลอดก่อน 34 สัปดาห์*

คำสำคัญ: *ทารกคลอดก่อนกำหนด, ภาวะการติดเชื้อแรกเกิดระยะแรก, อัตราส่วนเม็ดเลือดขาวชนิดนิวโตรฟิลล์ต่อลิมโฟไซต์*

Introduction

Early onset neonatal sepsis (EONS) is an acquired infection according to peripartum vertical mother-to-newborn transmission[1]. The most important neonatal factor of mortality from such condition is prematurity or low birth weight (LBW). According to National Institute of Child Health and Human Development neonatal research network data, the incidence rate of infection is 3 to 10-fold higher in LBW infant comparing to full term normal weight infant and their consequence complications are more hazardous such as respiratory distress syndrome, intraventricular hemorrhage, necrotizing enterocolitis or even death[2]. Current evidence suggests that intraamniotic or intrauterine infection is the major cause of preterm labor accounting for 25-40% of preterm birth with intact membranes[3]. Although the inflammation is subclinical or occurs without clinical signs of chorioamnionitis, there are histological evidence of inflammation in the fetal membranes, umbilical cord or decidua. In order to identify definite intrauterine or placental inflammation, invasive procedures, such as amniocentesis or cordocentesis are needed. Several maternal serum biomarkers have been investigated for their use in predicting in-utero inflammation, including white blood cell (WBC) count, C-reactive protein (CRP), procalcitonin, interleukin (IL)-6, IL-8, IL-10, interferon gamma and others[4-6].

Neutrophil to lymphocyte ratio (NLR) is a marker of inflammatory disease and prognostic value in several types of cancers or cardiovascular diseases[7-11]. It is a simple, inexpensive and safe test which can be obtained from maternal peripheral blood. However, information on the use of NLR in women with preterm delivery to predict or identify neonates at risk for EONS is limited and controversial. Therefore, the primary objective of this study was to determine the relationship between antenatal maternal NLR and EONS in preterm neonates. Secondary objective was to identify factors associated with EONS among preterm neonates. In addition, appropriate cut-off value of NLR to predict EONS was also evaluated.

Materials and Methods

After approval of ethics committee of Medical Service Department, Bangkok Metropolitan Administration, a study was conducted in 485 preterm neonates who were born between 2012 to 2016 in Chareonkrung Pracharak Hospital, Bangkok, Thailand. Inclusion criteria were singleton, preterm infants who delivery between 24 and 36^{+6} weeks of gestation and had maternal complete blood count data within 72 hours prior to delivery. Exclusion criteria were neonates with chromosomal anomalies or metabolic syndrome, mother with preeclampsia, chorioamnionitis, hepatitis, cardiovascular disease, rheumatoid disease, cancer, polycystic ovary syndrome, connective tissue disease, Crohn's disease and history of cervical excision procedure or cervical cerclage.

This study was a retrospective study. Sample size was estimated from data of pilot study that showed NLR in mothers of EONS of 6.8 ± 4.8 and 5.2 ± 4.5 in those without EONS. At 95% confidence level (CI) and 80% power and 1:4 ratio, at least 87 neonates with EONS and 348 without EONS were required.

Preterm neonate was defined as neonate who were born between 24 and 36^{+6} weeks of gestation. EONS was defined as the presence of confirmed or suspected sepsis within 72 hours after birth which was diagnosed by one of the following criteria 1.) positive culture in peripheral blood or cerebrospinal fluid 2.) absence of positive culture but consisting of two or more following: 2.1) body temperature < 36.5°C or >37.5°C; 2.2) respiratory rate > 60/min or grunting or retraction or nasal alar flaring or partial pressure of oxygen (PaO_2) < 70 mmHg; 2.3) heart rate < 100 beats per minute or > 180 beats per minute or capillary refill more than 3 seconds or blood pressure less than 2 time standard deviation at that age; 2.4) perfusion abnormalities; altered mental status or oliguria or acidosis (venous blood pH < 7.25); 2.5) immature to total neutrophil ratio ≥ 0.2 or neutropenia or thrombocytopenia; platelet < 150,000/mm^3 or CRP > 5 mg/mL after birth 6 hours or more[12, 13].

Maternal demographic data including antepartum, intrapartum, mode of delivery and neonatal outcome

data were extracted from medical records. The clinical data included baseline characteristics, obstetric data, labor and delivery data, treatment, and neonatal outcomes. Complete blood count data were retrieved from the latest laboratory results within 72 hours prior to delivery using sysmex XE-5000 and XT-20001 automatic analyzer in all patients. The neutrophil to lymphocyte ratio (NLR) was defined as the ratio of absolute neutrophil count and absolute lymphocyte count.

All statistical analyses were achieved using SPSS version 14.0 software (SPSS Inc, Chicago, IL, USA). Descriptive statistics including mean, standard deviation, number, and percentages were used to describe various characteristics as appropriate. Comparisons of various characteristics between cases and controls were performed with student's t test, chi-squared test, and Mann-Whitney U test as appropriate. NLR was compared between groups to determine its association with EONS, both as continuous data and categorical data with selected cut-off. Logistic regression analysis was used to determine independent associated factors of EONS, adjusting for potential confounders. A p value of < 0.05 was considered statistical significance.

Results

A total of 485 preterm neonates were included, 97 with EONS and 388 without EONS. Various baseline characteristics were compared between the 2 groups and the results are shown in Table 1. Mothers whose neonates had EONS were significantly more likely to have preterm premature rupture of membranes (34% vs. 24%, $p = 0.043$), received antenatal corticosteroids (53.6% vs. 14.4%, $p < 0.001$), received tocolytics (26.8% vs. 7.7%, $p < 0.001$), and had maternal fever (7.2% vs. 2.3%, $p = 0.016$).

Table 1. Comparison of clinical characteristics between the 2 groups.

Clinical characteristics	Early onset neonatal sepsis		p value
	Present (n = 97)	Absent (n = 388)	
Mean maternal age ± SD (years)	27.36 ± 7.3	27.27 ± 6.7	0.904*
Mean BMI ± SD (kg/m^2)	23.07 ± 6.39	24.88 ± 5.06	0.020*
Nulliparity, n (%)	37 (38.1%)	160 (41.2%)	0.579**
Previous preterm birth, n (%)	13 (13.4%)	31 (8.0%)	0.097**
Preterm PROM, n (%)	33 (34.0%)	93 (24.0%)	0.043**
Antenatal corticosteroid use, n (%)	52 (53.6%)	56 (14.4%)	< 0.001**
Antenatal antibiotic use, n (%)	92 (94.8%)	370 (95.4%)	0.831**
Tocolytic use, n (%)	26 (26.8%)	30 (7.7%)	< 0.001**
Maternal fever, n (%)	7 (7.2%)	9 (2.3%)	0.016**

BMI: body mass index; SD: standard variation; PROM: premature rupture of membranes; n: number of patients. * = independent samples t test, ** = chi-squared test.

Table 2 showed comparisons of neonatal outcomes between the 2 groups. Neonates with EONS significantly had worse outcomes than those without EONS, including lower gestational age (GA) at delivery, early preterm birth (< 34 weeks), lower birth weight, lower Apgar score, and higher rate of neonatal intensive care unit admission.

Maternal complete blood count results were compared between the 2 groups and the results are shown in Table 3. Mothers of EONS neonates had significantly lower hemoglobin and hematocrit levels. On the other hand, they had significantly higher mean WBC count, platelet counts, and neutrophil counts while mean lymphocytes count was comparable.

Comparison of NLR between the 2 groups are also demonstrated in Table 3. Neonates with EONS had significantly higher NLR than those without EONS [Median (interquartile range): 4.69 (3.32, 7.49) vs. 4.07 (2.95, 5.55), p = 0.005, respectively]. Using the cut-off value of 5 for NLR, the results showed that those with EONS were significantly more likely to have NLR ≥ 5 than those without EONS (46.4% vs. 31.7%, p = 0.007).

Table 2. Comparison of pregnancy outcomes between the 2 groups.

Characteristics	Early onset neonatal sepsis		p value
	Present (n = 97)	Absent (n = 388)	
Mean gestational age at delivery ± SD (days)	229.88 ± 22.48	249.29 ± 10.30	< 0.001*
Preterm birth			< 0.001**
Early preterm birth (< 34weeks), n (%)	54 (55.7%)	37 (9.5%)	
Late preterm birth (≥ 34weeks), n (%)	43 (44.3%)	351 (90.5%)	
Mean birth weight ± SD (grams)	1,985.13 ± 661.70	2,587.39 ± 444.64	< 0.001*
Apgar scores < 7			
At 1 min, n (%)	23 (23.7%)	11 (2.8%)	< 0.001**
At 5 min, n (%)	10 (10.3%)	1 (0.3%)	< 0.001**
Cesarean delivery, n (%)	33 (34.0%)	94 (24.2%)	0.050**
NICU admission, n (%)	52 (53.6%)	25 (6.4%)	< 0.001**

NICU: neonatal intensive care unit; n: number of patients. * = independent samples t test, ** = chi-squared test.

Table 3. Comparison of maternal laboratory results between the 2 groups.

Laboratory results	Early onset neonatal sepsis		p value
	Present (n = 97)	Absent (n = 388)	
Mean hemoglobin ± SD (g/dL)	11.51 ± 1.70	11.93 ± 1.35	0.026*
Mean hematocrit ± SD (%)	34.27 ± 4.51	35.61 ± 3.67	0.008*
Median white blood cell count (IQR) (cells/μL)	13,210 (10,710, 17,000)	11,930 (9,840, 14,000)	0.041**
Median neutrophil count (IQR) (cells/μL)	9,829 (7,679, 13,663)	8,827 (7,097, 10,752)	0.001**
Median lymphocyte count (IQR) (cells/μL)	2,068 (1,453, 2,719)	2,127 (1,687, 2,635)	0.417**
Median platelet count (IQR) (cells/μL)	262,000 (215,000, 301,500)	238,000 (205,000, 284,000)	0.018**
Median NLR (IQR)	4.69 (3.32, 7.49)	4.07 (2.95, 5.55)	0.005*
NLR category			0.007***
NLR < 5, n (%)	52 (53.6%)	265 (68.3%)	
NLR ≥ 5, n (%)	45 (46.4%)	123 (31.7%)	

SD: standard variation; g/dL: gram/deciliter; IQR: interquartile range; NLR: neutrophil to lymphocyte ratio; n: number of patients. * = independent samples t test, ** = Mann-Whitney U test, *** = chi-squared test.

Subgroup analysis was performed according to GA at delivery and the results are shown in Table 4. NLR ≥ 5 significantly increased the risk of EONS only among early preterm birth at < 34 weeks (72.7% vs. 46.8%, p = 0.012). On the other hand, such association was not observed among late preterm birth (10.5% vs. 11.1%, p = 0.853).

Table 5 showed the results of logistic regression analysis of all cases. The only 2 factors that independently associated with EONS were early preterm birth (< 34 weeks) with adjusted OR 11.53 (95% CI 6.74-19.73, p < 0.001) and maternal fever with adjusted OR 3.45 (95%CI 1.07-11.13, p = 0.038).

Table 4 . Subgroup analyses of relationship between maternal NLR and EONS according to gestational age at delivery.

Characteristics		Early onset neonatal sepsis		p value
		Present (n = 97)	Absent (n = 388)	
GA < 34 weeks	NLR < 5, n (%)	22 (22.7%)	25 (6.4%)	0.012*
	NLR ≥ 5, n (%)	32 (33.0%)	12 (3.1%)	
GA 34-36^{+6} weeks	NLR < 5, n (%)	30 (30.9%)	240 (61.9%)	0.853*
	NLR ≥ 5, n (%)	13 (13.4%)	111 (28.6%)	

GA: gestational age
NLR: neutrophil to lymphocyte ratio
EONS: early onset neonatal sepsis
n: number of patients
* = independent samples t test

Table 5. Logistic regression analyses to determine independent factors associated with EONS.

Variables	Adjusted ORs	95% Confidence Interval	p value
NLR ≥ 5	1.48	0.87 - 2.50	0.146
Gestational age < 34 weeks	11.53	6.74 - 19.73	< 0.001
PPROM	1.65	0.94 - 2.88	0.081
Antenatal antibiotics use	0.87	0.26 - 2.92	0.820
Maternal fever	3.45	1.07 - 11.13	0.038

EONS: Early onset neonatal sepsis
NLR: Neutrophil to lymphocyte ratio
PPROM: Preterm premature rupture of membranes
ORs: Odds ratio.

Logistic regression analysis was also performed separately between those with early and late preterm birth and the results are shown in Table 6. The only independent associated factor of EONS among early preterm birth was NLR ≥ 5 (adjusted OR 3.51, 95% CI 1.36-9.05, p = 0.009), while the only independent associated factor of EONS among late preterm birth was maternal fever (adjusted OR 6.06, 95% CI 1.80-20.34, p = 0.004).

Table 6. Logistic regression analyses to determine independent factors associated with EONS, stratified by gestational age at delivery.

Variables		Adjusted ORs	95% Confidence Interval	p value
GA < 34 weeks	NLR ≥ 5	3.51	1.36-9.05	0.009
	PPROM	1.91	0.70-5.20	0.204
	Antenatal antibiotics use	1.50	0.21-10.83	0.686
	Maternal fever	0.33	0.04-2.73	0.302
GA 34-36^{+6} weeks	NLR ≥ 5	1.01	0.50-2.04	0.986
	PPROM	1.37	0.67-2.80	0.389
	Antenatal antibiotics use	0.82	0.18-3.76	0.799
	Maternal fever	6.06	1.80-20.34	0.004

EONS: early onset neonatal sepsis
GA: gestational age
NLR: neutrophil to lymphocyte ratio
PPROM: preterm premature rupture of membranes

Discussion

In this study, increased maternal serum NLR was significantly increased in preterm neonates with EONS. NLR ≥ 5 was the only independent factor associated with EONS among early preterm birth (< 34 weeks) while maternal fever was the only independent factors associated with EONS among late preterm birth (≥ 34 weeks).

Intrauterine infection was one of the major causes of infection associated preterm labor or preterm premature rupture of membranes even in asymptomatic patient. EONS, by the definition, was the presence of confirmed or suspected sepsis within 72 hours after birth referred to acquired infection before or during delivery (vertical mother-to-child transmission). The fetus exposing to microorganism in utero may cause fetal inflammatory response syndrome, including funisitis[6]. Therefore, several studies have attempted to evaluate prenatal diagnosis of such intrauterine infection or funisitis. Previously reported tests included Gram staining and culture of amniotic fluid via amniocentesis, the measurement of leukoattractants, glucose concentration, WBC count, IL-6 and matrix metalloproteinase-8 (MMP-8) in amniotic fluid[5], cordocentesis for evaluation fetal plasma IL-6 concentration, and tumor necrotic factor-α. However, such procedures are invasive and difficult to achieve. Amniocentesis is related to a risk of fetal loss of approximately 0.2-2.9%[14, 15], and can possibly cause infection by itself. Moreover, histological study of chorioamnionitis can be done only after birth and delay diagnosis.

Many studies have investigated more rapid, noninvasive testing, especially inflammation markers, for evaluation of the infection in effort to predict the EONS. These markers included WBC count, CRP, procalcitonin, IL-6, IL-8, IL-10, interferon gamma and others. Lee, et al., found that maternal serum CRP was significantly associated with funisitis and EONS[6]. Cetin, et al., also studied the prediction of EONS from antenatal non-invasive biomarkers and found that maternal blood procalcitonin level were superior to CRP and WBC count[4].

From a previous study, Kim, et al reported that NLR had a better overall diagnostic performance than maternal serum CRP levels in predicting placenta inflammatory response and distinguishing histologic chorioamnionitis from funisitis[16]. Once the microorganism invaded into intrauterine cavity or placental membranes, neutrophils were recruited into

the site of infection guided by extracellular chemoattractant, proinflammatory factors and several cytokines leading to neutrophilia in maternal blood circulation[3, 17, 18]. Contrary, both T and B lymphocytes were downregulated possibly because of the need to prevent priming of graft-versus-host-type reactivity, which could result in lymphocytopenia.

Therefore, the neutrophil to lymphocyte ratio (NLR) has been proposed to be a parameter of systemic inflammation and prognostic marker in various diseases, including oncologic diseases, septic shock, cardiovascular diseases, and many obstetrics conditions[9-11, 19, 20]. NLR was found to be increased in hyperemesis gravidarum, gestational diabetes, preeclampsia and spontaneous preterm delivery[21-25]. Importantly, NLR has been evaluated as a predictive marker for placental inflammatory response in preterm births[16].

The results of the present study showed that maternal NLR significantly increased among neonates with EONS. However, subgroup analysis showed that NLR of ≥ 5 significantly increased the risk of EONS only among early preterm birth (< 34 weeks) by 3.5 times. This was similar to previous reports by Kim, et al., and Hamiel, et al., which also reported that NLR alone or combined with absolute neutrophil count was a good tool for identification of serious bacterial disease, especially in neonates[16, 26]. On the other hand, no significant association was observed in late preterm birth (≥ 34 weeks) and only maternal fever was significantly increased the risk of EONS by 6 times. In terms of diagnostic performance of NLR, the cut-off value of NLR ≥ 5 had only 46% sensitivity, 68% specificity, 27% positive predictive value and 84% negative predictive value. In subgroup analyses in early preterm birth, NLR ≥ 5 had 59% specificity, 68% specificity, 73% positive predictive value and 68% negative predictive value.

This study was among a few studies determining the relationship between antenatal maternal NLR and EONS in preterm neonates. The results provided some additional information on the usefulness of NLR in preterm delivery. However, there were some limitations to be addressed. Some data might be incomplete due to the retrospective nature of the study. Sample size for subgroup analysis might be inadequate. The value of NLR could vary by GA and individually. Timing and severity of possible infections or inflammations could not be definitely determined and related to NLR. The cut-off value of NLR used in this study is arbitrary and the most appropriate one is still unknown. Further, larger studies are needed to elucidate the use of NLR in predicting EONS and other adverse outcomes in various obstetric conditions.

Nonetheless, from this study, NLR could possibly be useful in guiding the management and decision among women with early preterm labor where conservative treatment to prolong gestational period are commonly practiced. Awareness should be raised among obstetricians and paediatricians that high NLR could be a marker of intrauterine infections and increase the risk of EONS in the neonates. Appropriate management that offered in a timely manner could help reducing maternal and neonatal morbidities and mortalities.

Conclusion

In conclusion, maternal serum NLR was significantly associated with EONS in preterm neonates, especially those delivery at GA less than 34 weeks. It could be considered in clinical practice as a marker for development of EONS in preterm neonates.

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Potential conflicts of interest

The authors declare no conflict of interest.

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