

The Correlation of Maternal Leukocyte and NLR with APGAR Score in Caesarean Section at RSUD Dr. Soetomo 2023

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ABSTRACT

Background: Excessive inflammation can lead to morbidity and mortality in pregnant women and infants. The level of inflammation can be indicated by leukocyte levels and NLR. Caesarean section is performed to save both mother and baby, but it is associated with poor neonatal outcomes, as evidenced by lower APGAR scores. Research on the correlation between leukocyte levels, NLR, and APGAR scores in neonates born via caesarean section is still limited. Therefore, this study is important to conduct. **Method:** This is an observational retrospective study. The object of this study was patients who underwent caesarean section delivery with the following characteristics: no premature rupture of membranes or prolonged stages of labor, no signs of infection, no congenital anomalies, and a single, full-term, live pregnancy. The variables of this study were maternal NLR and APGAR score. **Result:** The median leukocyte counts for elective and emergency caesarean section was $9.48 \times 10^9/L$, while the median NLR for both groups was 4.14 and 5.21, respectively. The median first-minute APGAR score for elective and emergency caesarean sections were 7 and 6, respectively, while the fifth-minute APGAR score was 8 in both groups. In the elective group, no significant correlation was found between leukocyte levels and NLR with first and fifth-minute APGAR scores ($p > 0.05$). In the emergency caesarean section group, no significant correlation was found between leukocyte levels and the first-minute APGAR score ($p > 0.05$), but a significant correlation was found for the fifth-minute APGAR score ($p < 0.05$). A significant correlation was found between NLR and both first and fifth-minute APGAR scores ($p < 0.05$). **Conclusion:** There are significant correlations between maternal leukocyte and NLR with APGAR score in emergency caesarean section, particularly in 5-minute APGAR score.

Keywords: Leukocyte; NLR; APGAR score.

INTRODUCTION

Inflammation is an essential immune response during pregnancy, particularly in implantation, placentation, fetal growth, and parturition.[1] However, excessive inflammation can lead to maternal and neonatal morbidities, such as preeclampsia, intrauterine growth restriction, and preterm birth.[2] This response involves increased immune cells, including leukocytes (neutrophils, lymphocytes, monocytes, eosinophils, and basophils), which play critical roles in immunity and inflammation triggered by infection or tissue damage.[3] Neutrophils are one of the key players in innate immunity, while lymphocytes are pivotal in adaptive immunity. The neutrophil-to-lymphocyte ratio (NLR) serves as an inflammation marker representing both immune systems.[4]

Caesarean section is a surgical procedure to deliver a baby via abdominal and uterine incisions, often indicated for maternal or fetal conditions like

hypertension, fetal distress, or cephalopelvic disproportion.[5] Caesarean section carries risks such as infection, bleeding, and prolonged recovery.[6] Post-delivery, neonatal health is assessed using the APGAR score at 1 and 5 minutes, evaluating skin color, heart rate, reflexes, muscle tone, and respiration.[7] Several studies associate caesarean section with increased NICU admissions, respiratory complications, and low 5-minute APGAR scores, which are linked to neonatal mortality risk.[8,9]

Research indicates maternal inflammation impacts neonatal outcomes. A study found that elevated systemic inflammation in preeclamptic mothers is associated with lower neonatal APGAR scores.[10] Other studies reported increased maternal NLR correlating with low 5-minute APGAR scores and low birth weight. [11,12] The research about the correlation of maternal inflammatory markers, particularly leukocytes and NLR, with neonatal

APGAR scores in caesarean deliveries are limited. This study investigates the correlation of maternal leukocyte and NLR with the APGAR score of neonates delivered through caesarean section at Dr. Soetomo General Hospital in 2023.

METHOD

Study Design

This study used a retrospective observational design using secondary data obtained from medical records.

Population and Sample

The population of this study is mothers who underwent caesarean section at RSUD Dr. Soetomo in 2023 and their newborns. The sample consisted of mothers and neonates that met the inclusion criteria. The inclusion criteria are mothers with singleton pregnancies at term (>37 weeks of gestation) and neonates delivered through caesarean section at RSUD Dr. Soetomo in 2023. The exclusion criteria consisted of the following characteristics: mothers with premature rupture of membranes (PROM), prolonged labor, signs of infection (fever) or diagnosed infections (COVID-19, pneumonia, tuberculosis, or hepatitis), and neonates with congenital anomalies.

Total sampling was used, including all eligible mothers and neonates who underwent caesarean sections in January to December 2023.

Variables and Operational Definitions

The independent variables in this study are maternal leukocyte count and NLR prior to caesarean section. Maternal leukocyte was defined as the total number of leukocytes circulating in the blood. The reference value of leukocyte count in the third trimester is $5,6 - 14,9 \times 10^9/L$. [13]

The NLR was defined as the ratio of neutrophils to lymphocytes. The NLR classification in this study was based on the NLR reference value according to a study by Zahorec (2021). [14]

- 0.1-0.7: Below the normal range.
- 1-2: Normal range.
- 2-3: Gray zone, indicating low inflammation and stress.
- 3-7: Mild to moderate inflammation and stress.
- 7-11: Moderate inflammation and stress.
- 11-17: Severe inflammation and stress.
- 17-23: Critical systemic inflammation and high stress.
- 23+: Critical systemic inflammation and supraphysiological stress.

The dependent variable in this study is the APGAR score of neonates at 1 and 5 minutes. The APGAR score was defined as a method to assess the clinical status of neonates at 1 and 5 minutes of life and the need for intervention to maintain respiration. It includes five components: color, heart rate, reflex, muscle tone, and respiration. Each component is scored 0, 1, or 2 and totaled. A normal APGAR score is defined as a score of 7 or more.

APGAR scores of 4-6 indicates a moderate asphyxia. APGAR scores of 1-3 indicates a severe asphyxia.[15]

Data Collection

The maternal demographic data consisted of age, body mass index, and parity. The obstetric data consisted of the gestational age, type, and indication of caesarean section. Maternal laboratory data consisted of leukocyte and NLR. Neonatal APGAR scores at 1 and 5 minutes were also collected. These data were obtained from the medical records.

Data Analysis

The data analysis was conducted using IBM SPSS Statistics version 22. A normality test was used to determine the distribution of the data. If the distribution is not normal, Spearman's rank correlation test is used. P-value of < 0,05 means the correlation is significant. The comparisons between caesarean section types (elective vs emergency) were conducted using Mann-Whitney U test. P-value of < 0,05 means there is a significant difference.

Ethical Clearance

This study received ethical approval from the Health Research Ethics Committee (ITKI) of RSUD Dr. Soetomo with reference number 1649/LOE/301.4.2/V/2024.

RESULTS

Throughout the study period (January-December 2023) there were 566 caesarean sections conducted at RSUD Dr. Soetomo in 2023. Out of 566 operations, 105 patients fit the inclusion criteria as explained in the study method. There were 52 elective caesarean sections and 53 emergency caesarean sections conducted.

TABLE 1: Maternal Demographics.

Variables	Elective Caesarean Section N (%)	Emergency Caesarean section N (%)
Age (years)		
<20	0 (0%)	3 (5,7%)
20-35	34 (65,4%)	38 (71,7%)
>35	18 (34,6%)	12 (22,6%)
Body Mass Index		
Underweight	0 (0%)	3 (5,7%)
Normal	4 (7,7%)	10 (18,9%)
Overweight	16 (30,8%)	21 (39,6%)
Obese class I	13 (25%)	9 (17%)
Obese class II	15 (28,8%)	4 (7,5%)
Obese class III	4 (7,7%)	6 (11,3%)
Parity		
Primiparous	10 (19,2%)	27 (50,9%)
Multiparous	42 (80,8%)	26 (49,1%)

Most patients in this study were aged 20-35 years in both elective (65.4%) and emergency (71.7%) caesarean groups.

This study found that overweight mothers dominated both groups, with a higher prevalence in the emergency caesarean section group (39.6% vs. 30.8% in elective caesarean section).

This study found that 80% of elective caesarean section patients were multiparous, while 50.9% of emergency caesarean patients were primiparous.

TABLE 2: The Indications of The Caesarean Section.

Indications	Elective Caesarean Section N (%)	Emergency Caesarean Section N (%)
Maternal Indication		
Abnormal Placentation	13 (24,5%)	3 (5,7%)
Previous caesarean section	25 (47,2%)	8 (15,1%)
Uterus Dehiscence	1 (1,9%)	1 (1,9%)
Cardiorespiratory Disease	5 (9,61%)	21 (39,6%)
Obstructive mass in the genital tract	1 (1,9%)	0 (0%)
Maternal-fetal Indication		
Cephalopelvic Disproportion	0 (0%)	2 (3,7%)
Fetal Indication		
Fetal Distress	3 (5,7%)	13 (24,5%)
Malpresentation	4 (7,5%)	5 (9,4%)

The most common indication for elective caesarean section was a history of prior SC (47.2%), while the cardiorespiratory disease was the leading indication for emergency caesarean section (39.6%).

TABLE 3: The Median of Maternal Leukocyte, NLR, and APGAR Score.

Variables	Elective Caesarean section Median (Min-Max)	Emergency Caesarean section Median (Min-Max)	p-value
Leukocyte ($\times 10^9/L$)	9,48 (4,83 - 20,10)	11,21 (4,32 - 25,34)	0,001
NLR	4,14 (2,04 - 12,20)	5,21 (1,55 - 41,44)	0,038
1-minute APGAR score	7 (3-8)	6 (1-8)	0,010
5-minute APGAR score	8 (5-9)	8 (3-9)	0,090

The median leukocyte count was higher in emergency SC ($11.21 \times 10^9/L$) than in the elective caesarean section group ($9.48 \times 10^9/L$), with significant differences ($p < 0.05$). The median NLR was also higher in the emergency group (5,21 vs 4,14 in the elective group).

Significant differences were observed in the median 1-minute APGAR scores between elective caesarean section (median: 7) and emergency caesarean section (median: 6, $p < 0.05$). However, no significant differences were found in the 5-minute APGAR scores (median: 8 for both groups, $p > 0.05$).

TABLE 4: The Distribution of Maternal Leukocyte, NLR, and APGAR Score.

Variable	Elective Caesarean Section N (%)	Emergency Caesarean Section N (%)
Leukocyte		
<5,6	1 (1,92%)	1 (1,89%)
5,6 - 14,9	48 (92,31%)	40 (75,47%)
>14,9	3 (5,77%)	12 (22,64%)
NLR		
0,1 - 0,7	0 (0%)	0 (0%)
1-2	0 (0%)	1 (1,89%)
2-3	6 (11,54%)	7 (13,21%)
3-7	40 (76,92%)	28 (52,83%)
7-11	3 (5,77%)	10 (18,87%)
11-17	3 (5,77%)	2 (3,77%)
17-23	0 (0%)	3 (5,66%)
23	0 (0%)	2 (3,77%)
1-minute APGAR score		
1-3	1 (1,92%)	8 (15,09%)
4-6	13 (25%)	19 (35,85%)
7-10	38 (73,08%)	26 (49,06%)
5-minute APGAR score		
1-3	0 (0%)	3 (5,66%)
4-6	3 (5,77%)	6 (11,32%)
7-10	49 (94,23%)	44 (83,02%)

The patients in both groups mostly had normal leukocyte. The emergency caesarean section has more frequent cases of leukocytosis than the elective group (22,64% vs 5,77%). In both groups, NLR of 3-7 was most frequently found (76,92% in elective and 52,83% in emergency group). Higher NLR (>7) results were found in the emergency group.

Over 70% of the neonates had >7 1-minute APGAR scores in the elective group. In the emergency group, more than half of the neonates had <7 1-minute APGAR score. In both of the groups, the 5-minute APGAR score was found mostly >7 (94,23% in the elective and 83,02% in the emergency group).

TABLE 5: The Correlation Between Maternal Leukocyte and NLR with APGAR Score.

Variables	p-value
Leukocyte and APGAR score	
AS 1 min	
Elective	0,353
Emergency	0,088
AS 5 min	
Elective	0,179
Emergency	0,046
NLR and APGAR score	
AS 1 min	
Elective	0,885
Emergency	0,047
AS 5 min	
Elective	0,656
Emergency	0,033

Maternal leukocyte was significantly correlated with a 5-minute APGAR score in emergency caesarean section ($p < 0,05$). Maternal NLR was significantly correlated with 1-minute and 5-minute APGAR score in the emergency caesarean section ($p < 0,05$). Leukocyte and NLR were not significantly correlated with APGAR scores in the elective group ($p > 0,05$).

DISCUSSION

Maternal Demographics

Most patients were aged 20–35 years in both elective (65.4%) and emergency (71.7%) caesarean section groups. These findings align with research by Norbaiti et al. (2024), which showed that women aged 20–35 years represented the majority of deliveries. [16] Maternal age outside this range (too young or too old) is considered high risk and associated with increased maternal and neonatal morbidity and mortality. Studies by Hochler et al. (2023) and Khalil et al. (2013) indicate that advanced maternal age is linked to higher incidences of comorbidities, such as hypertension, diabetes, and obesity, which contribute to complications like preeclampsia, preterm delivery, NICU admission, and neonatal asphyxia.[17,18] Biological immaturity and emotional instability in younger mothers can negatively affect prenatal care and nutrition, increasing risks of preeclampsia, anemia, and preterm delivery. [19,20]

Overweight mothers dominated both groups, with a higher prevalence in the emergency group (39.6% vs. 30.8% in elective caesarean section). According to Burnie et al. (2022), underweight mothers have a lower risk of complications like preeclampsia but are at higher risk for anemia and delivering low birth-weight infants.[21] Obese mothers are at increased risk of gestational diabetes, preeclampsia, and caesarean section, as well as neonatal complications such as congenital anomalies and macrosomia.[22] These findings emphasize the importance of BMI as a factor influencing maternal and neonatal outcomes.

This study found that 80% of elective caesarean section patients were multiparous, while 50.9% of emergency caesarean section patients were primiparous. These results align with a study by Benzouina et al. (2016), who reported a higher prevalence of primiparous women in emergency caesarean section cases.[23] Primiparous mothers face increased risks of complications such as preeclampsia, IUGR, and fetal distress.[24] Multiparity, on the other hand, can weaken the uterus and increase the risks of complications such as uterine rupture during delivery.[25]

Maternal Leukocyte and NLR

This study found that the median leukocyte count in the elective group was $9.48 \times 10^9/L$, while in the emergency group, it was $11.21 \times 10^9/L$. The median leukocyte counts in this study were within the normal range for the third trimester, according to Abbassi-Ghanavati (2009), which is $5.6\text{--}14.9 \times 10^9/L$. [13] When compared to the reference range for the general adult population ($3.5\text{--}10.5 \times 10^9/L$, Kemenkes RI, 2022), the median leukocyte counts in emergency caesarean group were higher.[26] This could be attributed to hematologic changes during pregnancy due to physiological stress, particularly concerning leukocyte levels. Leukocyte levels increase early in pregnancy and remain elevated throughout, ranging between $6\text{--}16 \times 10^9/L$ in healthy pregnancies. This increase results from a heightened inflammatory response during normal pregnancy, which may be due to fetal tolerance, immunosuppression, and immunomodulation.[27]

The median NLR in elective caesarean group was 4.14, whereas in emergency caesarean group, it was 5.21. The median NLR in both SC types falls within the range of 3–7, indicating mild to moderate inflammation and stress. These results are higher than the normal reference NLR range of 1–2. It is important to note that the NLR classification used in this study follows Zahorec (2021), which is based on the general population, as no specific literature on NLR classification in third-trimester pregnant women has been found.[14]

NLR consists of the ratio between two leukocyte components: neutrophils and lymphocytes. The increase in NLR observed in this study could be caused by changes in leukocyte levels during pregnancy, induced by physiological stress.

Neutrophils are the dominant type of leukocyte in differential counts. During pregnancy, apoptosis of neutrophils is impaired, leading to an increase in their numbers. However, their chemotactic and phagocytic activities decrease, likely due to inhibitory factors present in maternal serum. Unlike neutrophils, which increase during pregnancy, lymphocytes decrease during the first and second trimesters before increasing again in the third trimester. Additionally, stress during labor can lead to leukocytosis.[28]

This study found a significant difference in median leukocyte counts between mothers undergoing elective and emergency caesarean section ($p < 0.05$). The emergency caesarean group had a higher median leukocyte count ($11.21 \times 10^9/L$) compared to the elective group ($9.48 \times 10^9/L$). Additionally, although both groups were predominantly within the normal leukocyte range, elevated leukocyte levels were more common in the emergency group (22.64%) compared to the elective SC group (5.77%).

Similarly, a significant difference was observed in median NLR between mothers undergoing elective and emergency SC ($p < 0.05$). The emergency caesarean group had a higher median NLR (5.21) compared to the elective one (4.14). While both groups were dominated by NLR levels between 3–7, indicating mild to moderate inflammation and stress, the proportion was lower in the emergency SC group (52.83%) compared to the elective group (76.92%). The emergency group exhibited a more varied distribution, with higher NLR levels more frequently observed. For example, in the emergency SC group, 18.87% of cases had NLR levels between 7–11, compared to only 5.77% in the elective group. For NLR levels between 17–23, the emergency group accounted for 5.66% of cases, compared to 0% in the elective SC group. Similarly, NLR levels above 23 were found in 3.77% of emergency SC cases, but none in the elective SC group.

High leukocyte counts ($>14.9 \times 10^9/L$) and NLR levels >7 were more frequently observed in the emergency group, indicating higher levels of systemic inflammation. This elevated systemic inflammation is likely related to conditions prevalent in most emergency patients, such as heart disease and preeclampsia.

Neonatal APGAR Score

Significant differences were observed in the median 1-minute APGAR scores between elective and emergency caesarean groups ($p < 0.05$). The median 1-minute APGAR score in the emergency group was 6, lower than the 7 observed in the elective group. This result differs from the findings of Kulkarni et al. (2021), which reported a median 1-minute APGAR score of 7 in both groups.[29] However, no significant differences were found in the 5-minute APGAR scores between the two groups ($p > 0.05$), with both groups having a median score of 8. This result contrasts with the findings of Mendoza et al. (2021), who reported that the median 5-minute APGAR score was lower in the emergency caesarean group (8) compared to the elective one (9).[30]

Most neonates in the elective caesarean group had APGAR scores of 7–10 at both the 1-minute (73.08%) and 5-minute (94.23%) marks. The emergency group showed a different distribution, with a lower proportion of neonates scoring 7–10, especially at 1 minute (49.06%). More than 50% of neonates in the emergency caesarean group had APGAR scores <7 at the 1-minute mark. At 5 minutes, the proportion of neonates with APGAR scores of 7–10 increased to 83.02%.

The 1-minute APGAR score reflects a neonate's initial adaptation to extrauterine life.[31] A low 1-minute APGAR score, particularly <7 , indicates difficulties in adapting to life outside the uterus.[32] The lower scores in the emergency caesarean group suggest that neonates born via this procedure may require more time to adapt. Emergency caesarean section is often performed urgently, potentially leading to less preparation and increased stress for both the mother and neonate.[33] Acute stress may result in temporary hypoxia for the neonate, contributing to lower APGAR scores.[34]

The improvement in 5-minute APGAR scores compared to the 1-minute scores can be attributed to several factors influencing delivery, such as delivery type or perinatal complications. Neonates born via emergency caesarean section may have lower initial APGAR scores due to temporary asphyxia or the effects of medications used during delivery.[35] Over time, the 5-minute APGAR scores improve as neonates undergo resuscitation if needed and stabilize physiologically. Their breathing becomes more effective, and their heart rate stabilizes.[36]

Correlation between Maternal Leukocyte and NLR with APGAR score

This study found no significant correlation between maternal leukocyte count or NLR and APGAR scores at both 1 and 5 minutes in the elective caesarean group ($p > 0.05$). Most mothers in the elective group had normal leukocyte levels ($5.6\text{--}14.9 \times 10^9/L$) and NLR values within the range of 3–7 (mild to moderate inflammation and stress), with APGAR scores of 7–10. Median APGAR scores were lower in neonates born to mothers with both normal and elevated leukocyte levels. However, the median APGAR scores were the same for NLR <7 and >7 . These findings suggest that optimal maternal conditions in elective SC support better neonatal adaptation to extrauterine life.

Elective caesarean section is typically performed in controlled settings, where the timing and conditions of delivery are planned to minimize stress for both mother and neonate. Such controlled conditions contribute to stable maternal and fetal states, reducing the impact of inflammatory biomarkers such as maternal leukocyte levels and NLR on neonatal outcomes. Overall, elective caesarean section generally results in better neonatal outcomes because it is less associated with complications that can arise in emergency settings.[37]

In the emergency caesarean group, a significant correlation was found between maternal leukocyte count and NLR with APGAR scores, particularly at 5 minutes ($p = 0.046$ for leukocyte count and $p = 0.03$ for NLR). The study revealed lower median APGAR scores as maternal leukocyte levels and NLR values increased. Higher leukocyte counts and NLR values indicate systemic inflammation, which correlates with lower 5-minute APGAR scores. Maternal inflammation is associated with the release of pro-inflammatory cytokines that negatively impact fetal development and adaptation. These cytokines can disrupt placental function and fetal homeostasis, leading to physiological responses that hinder neonatal adaptation, as reflected in lower APGAR scores.[38]

Most mothers in the emergency group had comorbid conditions such as valvular or septal heart disease and preeclampsia. These conditions increase systemic inflammation, explaining the higher leukocyte counts and NLR observed in this group. Emergency caesarean section is often performed following diagnoses such as obstructed labor, fetal distress, or maternal distress that pose immediate risks to the lives of both mother and baby.[39] In cases of preeclampsia, failed spiral artery remodeling leads to shallow placentation and reduced oxygen supply. In the late trimester, this results in endothelial damage and increased inflammatory cell activity.[40] Elevated maternal leukocyte counts and NLR, reflecting systemic inflammation, are influenced by maternal comorbidities such as heart disease or preeclampsia. These findings are consistent with Mihu et al. (2015), who reported higher leukocyte counts in mothers with preeclampsia and lower APGAR scores, birth weights, and gestational ages.[10] Similarly, Susilo et al. (2015) found that elevated leukocyte levels ($\geq 15,000/\mu\text{L}$), HELLP syndrome, and early-onset preeclampsia were independent risk factors for lower 1-minute APGAR scores.[41]

However, these findings differ from Wibowo (2018), who reported no significant effect of leukocyte levels on APGAR scores in cases of premature rupture of membranes.[42] Panwar et al. (2022) observed a negative correlation between second-trimester NLR and 5-minute APGAR scores.[12] Increased NLR levels have also been associated with a higher risk of chorioamnionitis in mothers delivering prematurely without signs of infection.[43] Conversely, Haliza et al. (2024) reported no correlation between NLR and neonatal mortality, delivery type, or APGAR scores in COVID-19-positive patients.[43]

Mild inflammation is common during pregnancy as part of normal physiological processes. However, excessive inflammation is associated with poor pregnancy outcomes. Inflammatory markers such as NLR and PLR were found to increase in neonates with APGAR scores < 7 during prolonged pregnancies, even in the absence of maternal comorbidities. This may be due to subclinical, low-grade inflammation.[11]

CONCLUSION

There was a significant correlation between maternal leukocyte and NLR with APGAR score in the emergency caesarean group ($p > 0,05$). Maternal comorbidities such as heart disease and preeclampsia can exacerbate the systemic inflammation in this group, which was reflected by an increase of the leukocyte and NLR.

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