Advanced Medical Journal, Vol.10, No.4, P.73-79,2025 https://doi.org/10.56056/amj.2025.400

The Association of Inflammatory Biomarkers of Neutrophil-to-Lymphocyte Ratio with Spontaneous Preterm Delivery

Tavan Adnan Khdhir* Sallama Nasir Kamil**

Abstract

Background and objectives: Preterm birth is a significant contributor to infant mortality that is closely associated with the inflammatory process. The neutrophil-to-lymphocyte ratio reflects the balance between pro-inflammatory neutrophils and anti-inflammatory lymphocytes. This study assessed the relationship between the neutrophil-to-lymphocyte ratio and spontaneous preterm delivery.

Methods: A case-control study was conducted at Sulaimani Maternity Teaching Hospital from May 2022 to May 2023 on 100 women (50 with preterm labour and 50 with full-term labour). In-person interviews were conducted to collect patients' data. White blood cell, neutrophil, and lymphocyte counts were determined, and then the neutrophil-to-lymphocyte ratio was calculated during the second trimester and at labour onset.

Results: The preterm group had significantly elevated white blood cell and neutrophil counts throughout the second trimester and at labour than the control group ($p \leq 0.05$). The lymphocyte and neutrophil-to-lymphocyte ratio in the preterm group was non-significantly ($p > 0.05$) increased throughout the second trimester and significantly ($p \leq 0.05$) increased at labour compared to the control group. Blood values were significantly ($p \leq 0.05$) lower in the preterm group during the second trimester than at labour for all parameters except for neutrophil-to-lymphocyte ratio ($p > 0.05$). All blood parameters were elevated during labour compared to the second trimester, with significant changes to WBC and lymphocyte counts ($p \leq 0.05$) and non-significant changes ($p > 0.05$) for neutrophils and NRL.

Conclusion: The laboratory blood parameters have variable impacts on clinical prediction and emphasizing the possible relevance of inflammatory biomarkers to preterm birth risks.

Keywords: Inflammatory biomarkers, Laboratory indicators, Neutrophil-lymphocyte ratio, Preterm birth

*MBChB, KHCMS/Obstetrics and Gynecology Trainee, Sulaimani Maternity Teaching Hospital, Sulaimani Directorate of Health, Sulaymaniyah, Iraq.
Email Adress: tavan.adnan@yahoo.com. (Corresponding Author).
**MBChB, HDOG, FICOG, GABOG, Assistant Professor of Obstetrics and Gynecology at Department of Clinical Sciences, College of Medicine, University of Sulaimani, Kurdistan Region/ Iraq. Email: sallam.nasir@univsul.edu.iq

Introduction

Preterm delivery is a critical issue in midwifery, defined as labour onset before the 37th week of pregnancy. It remains the leading cause of infant mortality within the first year, characterized by multifactorial aetiology.[1] The cause of over 60% of premature births remains unknown.[2] While medically induced preterm delivery may be prompted by fetal or maternal indicators, approximately 70% occur spontaneously without clear explanation. Inflammatory processes are implicated in childbirth, playing a significant role in both premature and full-term deliveries.[3,4] Preterm birth (PTB) imposes a substantial financial burden on global healthcare systems, encompassing direct medical costs and indirect expenses such as lost productivity and income. The World Health Organization (WHO) estimated the international price of PTB to be approximately three billion dollars in 2012. Effective prevention and management of PTB are crucial for improving maternal and infant health outcomes and reducing economic burdens on individuals and society. Globally, PTB incidence ranges from 5.0 - to 18%, with 15% occurring before the 32nd week of pregnancy. Each year, around 15 million neonates are born prematurely, contributing to one million deaths worldwide.[5, 6] In recent years, the neutrophil-to-lymphocyte ratio (NLR), a potential inflammatory biomarker, has been linked to adverse outcomes in various disorders, including obstetric complications. Research has explored its role in preeclampsia, intrahepatic cholestasis, coronavirus disease-19 (COVID-19), sepsis, and congenital infections.[7] The NLR, derived from a routine complete blood count test, is a cost-effective, readily available laboratory parameter in clinical settings. Despite numerous studies examining NLR in pregnancies complicated by preterm delivery, its specific role in this context remains under investigation.[8] Macrophages and neutrophils play pivotal roles in the inflammatory response during pregnancy and childbirth. While macrophages clear debris and pathogens, neutrophils combat bacterial infections. Although their functions may differ, both cell types increase in response to full-term and premature births. Neutrophils are notably abundant in the decidua of individuals experiencing preterm delivery, suggesting their heightened involvement in preterm labour. Dysregulation of macrophages and neutrophils has been associated with complications related to preterm delivery.[9] This study aims to compare levels of inflammatory biomarkers, specifically the neutrophil-to-lymphocyte ratio, in women with preterm and term labour and to identify associations between NLR and spontaneous preterm delivery.

Patients and methods

This case-control research was conducted at Sulaimani Maternity Teaching Hospital, Sulaimaniyah, Iraq, from May 2022 to May 2023. A non-probability purposive sampling technique was used to select 100 pregnant women. Fifty women experienced preterm labour at 28 to 37 weeks of gestation, while the other 50 had full-term labour after 37 weeks of gestation. Inclusion criteria included women with singleton pregnancy, regardless of age and nationality. In contrast, exclusion criteria included those with gestational diabetes mellitus, hypertensive disorders complicating pregnancy, pre-eclampsia, intrauterine growth retardation, uterine and placental abnormalities, cervical insufficiency, history of cervical cerclage, microbial infection (bacterial, viral and parasitic), blood diseases, blood disorders and those on chronic medications for blood conditions. Structured in-person interviews with a standardized questionnaire were done with the women from May 30th 2022, to May 15th 2023, to collect their data, including age, residency, and pregnancy status.

https://doi.org/10.56056/amj.2025.400

Additionally, 5.0 mL of venous blood was collected from each patient during their 2nd trimester and at the onset of labour to conduct neutrophil count, lymphocyte count, white blood cell (WBC) count, and NLR at Hematology Laboratory of Sulaimani Maternity Teaching Hospital, Sulaimaniyah, Iraq using automated Hematological Analyzer (Swelab™ Alfa Plus, Stockholm, Sweden). Then, the obtained results were compared to the reference data.[10] Data analysis was performed using the Statistical Package for the Social Sciences (SPSS, version 25), involving descriptive and inferential statistical analyses. The entire dataset was coded and input into the SPSS software. Various essential statistical methods were employed to achieve the study's objectives. The t-test was used to compare CBC components between the two groups during the second trimester. A p-value of ≤0.05 was considered a significant difference, and p≤0.001 was a highly significant difference. The study proposal was approved by the Ethics Committee of the Kurdistan Higher Council of Medical Specialties (KHCMS) (No. 4915 on 11th November 2019). The written informed consent was obtained from each patient before data collection, while the patient's autonomy and dignity were kept confidential.

Results

As shown in Table (1), most patients in the preterm group (44%) and control group (52%) were aged 26 - 35 years old without significant difference between both groups (p=0.122). Regarding residency, most patients in the preterm group (62%) and control group (60%) were from urban areas without significant differences between both groups (p=0.1000). Regarding pregnancy status, the preterm group's mean gravida was 2.64 ± 1.30, while for the control groups, it was 2.70 ± 1.63 without significant difference (p=0.840). Furthermore, the preterm group had a parity mean of 1.40 ± 1.29, whereas the control group had 1.44 ± 1.31 with no significant difference (p=0.878).

Table (1): Characteristics of studied respondents.

Variables		Preterm group No. (%)	Control group No (%)	p-value
Age (Years)	18 - 25 26 - 35 36 - 45	19 (38.0) 22 (44.0) 9.0 (18.0)	10 (20.0) 26 (52.0) 14 (28.0)	0.122
Residency	Urban	31 (62.0)	30 (60.0)	1.000
	Rural	19 (38.0)	20 (40.0)	
Pregnancy status		Mean ± SD	Mean ± SD	
	Gravida	2.64 ± 1.30	2.70 ± 1.63	0.840
	Parity	1.40 ± 1.29	1.44 ± 1.31	0.878
Total		50 (100)	50 (100)	

Table (2) indicates that the preterm group exhibited significant elevation of WBC and neutrophil counts throughout the 2nd trimester (p=0.001 and p=0.005, respectively) and at labour compared to the control group (p=0.001). Despite the increased levels of lymphocytes and NLR in the preterm group throughout the 2nd trimester and at labour compared to the control group, no significant alterations (p=0.195 and p=0.09, respectively) were seen throughout the 2nd trimester, but substantial alterations were observed at labour (p=0.02 and p=0.004, respectively).

https://doi.org/10.56056/amj.2025.400

Table (2): Comparison of the blood parameters between two groups during the 2nd trimester and at labour.

Parameter	Preterm group	Control group	p-value
2nd Trimester	Mean ± SD	Mean ± SD	
WBC (10^9/L)	13432 ± 3291.203	10180 ± 2154.161	<0.001**
Lymphocyte (10^9/L)	2.1732 ± 0.57142	2.0320 ± 0.50928	0.195
Neutrophil (10^9/L)	8.424 ± 3.8056	6.446 ± 3.0725	0.005*
NLR	3.973 ± 1.8807	3.329 ± 1.9823	0.09
At Labor	Mean ± SD	Mean ± SD	
WBC (10^9/L)	16340 ± 4083.866	11460 ± 2643.513	<0.001**
Lymphocyte (10^9/L)	2.486 ± 0.7546	2.174 ± 0.5613	0.02*
Neutrophil (10^9/L)	9.412 ± 3.9840	6.432 ± 2.8550	<0.001**
NLR	4.041 ± 2.1219	3.024 ± 1.2043	0.004*

*Significant difference; **Highly significant difference using t-test.
CBC: Complete blood count, WBC: White blood cell, NLR: Neutrophil lymphocyte ratio

Table (3) illustrates that all blood parameters were lower in the preterm group during the second trimester than during labour, with highly significant differences in lymphocyte/WBC counts (p=0.001) and essential differences in neutrophil counts (p=0.006), while no significant changes were observed in the NLR (p=0.758).

Table (3): The blood parameters of the preterm group during their 2nd trimester and at labour.

Variables	2nd Trimester Mean ± SD	at Labor Mean ± SD	p-value
WBC (10^9/L)	13432 ± 3291.203	16340 ± 4083.866	<0.001**
Lymphocyte (10^9/L)	2.1732 ± 0.571	2.486 ± 0.754	<0.001**
Neutrophil (10^9/L)	8.424 ± 3.805	9.412 ± 3.984	<0.006*
NLR	3.973 ± 1.880	4.041 ± 2.121	0.758

*Significant difference; **Highly significant difference using t-test.
NLR: Neutrophil lymphocyte ratio, WBC: White blood cell.

The mean WBC and lymphocyte counts were elevated significantly during labour compared to the 2nd trimester (p<0.001 and p=0.002, respectively). Simultaneously, no significant alterations were observed for each neutrophil and NRL values (p=0.971 and p=0.256, respectively), as shown in Table (4).

Table (4): The blood parameters of the control group during their 2nd trimester and at labour.

Variables	2nd Trimester	at labour	p-value
WBC (10^9/L)	10180.00 ± 2154.161	11460.00 ± 2643.513	<0.001**
Lymphocyte (10^9/L)	2.0320 ± 0.50928	2.174 ± 0.5613	0.002*
Neutrophil (10^9/L)	6.446 ± 3.0725	6.432 ± 2.8550	0.971
NLR	3.329 ± 1.9823	3.024 ± 1.2043	0.256

*Significant difference; **Highly significant difference using t-test.
NLR: Neutrophil lymphocyte ratio, WBC: White blood cell.

https://doi.org/10.56056/amj.2025.400


Discussion

This study aims to compare inflammatory biomarkers, specifically the NLR, between women experiencing preterm and term labour to elucidate any potential association between NLR levels and spontaneous preterm delivery. Analysis of blood-derived inflammatory biomarkers during 2nd trimester and labour revealed notable variations in specific parameters among pregnant women in the preterm group. This study indicated that most patients in both groups were aged 26 - 35 (p=0.122) and from urban areas (p=0.100). Regarding pregnancy status, there were no significant differences between both groups in terms of gravida and parity (p>0.05). Similar results were observed by Nurfianto et al., who found no significant association between maternal age and gravidity in the preterm and control groups.[11] Furthermore, this study followed a substantial increase in the WBC, lymphocyte, and neutrophil counts. This observation is consistent with the findings of Cha et al., who investigated the prognostic significance of routine second-trimester blood parameters, including NLR, Lymphocyte-to-Monocyte Ratio (LMR), and platelet-lymphocyte ratio (PLR), to obstetric outcomes.[12] Moreover, Bain, reported significant increases in WBC count during normal pregnancies, which substantiates the findings of this study.[13] The present study contrasts with the findings of Kilic et al., who proposed a role for neutrophil s in promoting preterm birth, associating higher neutrophil levels in the early 2nd trimester with premature delivery.[14] Furthermore, our results diverge from those reported by Hershko et al., who identified a positive correlation between maternal age and peak levels of platelet-to-lymphocyte ratio (PLR) and normal NLR in the 2nd trimester.[15] Significant differences in neutrophil counts were observed between the two groups during their 2nd trimester, with the control group exhibiting lower white blood cell and neutrophil counts compared to the preterm group. Furthermore, the preterm group showed significantly elevated levels of white blood cells, lymphocytes, neutrophil, and NLR compared to the control group. These findings align with the observations of Li et al., who documented dynamic fluctuations in various blood parameters during pregnancy.[16] The present study demonstrates a strong correlation between WBC and lymphocyte counts among women delivering during the 2nd trimester compared to those in labour. Conversely, there were no significant differences in the NLR between the preterm and control groups. Deng et al. also observed comparable patterns of neutrophil and leukocytosis contributing to increased WBC levels during normal pregnancies, accompanied by a decline in lymphocyte counts during the 1st and 2nd trimesters, followed by an increase in the 3rd trimester. [17] Contrarily, Zhang et al reported elevated WBC, platelet, lymphocyte, and monocyte count with LMR in the spontaneous preterm birth group during the 1st trimester, alongside decreased PLR and NLR.[18]

Conclusions

The NLR value is not significantly higher in preterm-delivered women; however, other blood tests were significantly increased. Thus, laboratory biomarkers, cannot be used as crucial indicators for clinical prediction and the possible relevance of inflammatory biomarkers to preterm birth risks.

Acknowledgements

The authors thank the healthcare staff at Sulaimani Maternity Teaching Hospital, Sulaimaniyah, Iraq, for their invaluable support and assistance throughout the study.

Conflict of interest

No conflict of interest has been declared.

https://doi.org/10.56056/amj.2025.400

References

1. Blencowe H, Cousens S, Ostergaard MZ, Chou D, Moller A-B, Narwal R, et al. National, regional, and worldwide estimates of preterm birth rates in 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. Lancet. 2012;379(9832):2162-2172.
2. Purisch SE, Gyamfi-Bannerman C. Epidemiology of preterm birth. Semin Perinatol. 2017;41(7):387-391.
3. Elgormus Y, Okuyan O, Uzun H. The relationship between haematological indices as indicators of inflammation and 25-hydroxyvitamin D3 status in newborns. BMC Pediatr. 2023;23(1):83.
4. Hamilton S, Oomomian Y, Stephen G, Shynlova O, Tower CL, Garrod A, et al. Macrophages infiltrate the human and rat decidua during the term and preterm labour: evidence that decidual inflammation precedes labour. Biol Reprod. 2012 ;86(2):39.
5. Chakaya J, Petersen E, Nantanda R, Mungai BN, Migliori GB, Amanullah F, et al. The WHO Global Tuberculosis 2021 Report–not-so-good news and turning the tide back to End TB. Int J Infect Dis. 2022;124.
6. Walani SR. Global burden of preterm birth. Int J Gynaecol Obstet. 2020;150(1):31-33.
7. Kang Q, Li W, Yu N, Fan L, Zhang Y, Sha M, et al. Predictive role of neutrophil-to-lymphocyte ratio in preeclampsia: A meta-analysis including 3982 patients. Pregnancy Hypertens. 2020; 20:111-118.
8. Ma M, Zhu M, Zhuo B, Li L, Chen H, Xu L, et al. Use of complete blood count for predicting preterm birth in asymptomatic pregnant women: A propensity score-matched analysis. J Clin Lab Anal. 2020;34(8).
9. Daglar HK, Kirbas A, Kaya B, Kilincoglu F. The value of complete blood count parameters in predicting preterm delivery. Eur Rev Med Pharmacol Sci. 2016;20(5):801-805.
10. Abdullah DA, Mahmood GA, Rahman HS. Haematology reference intervals for healthy adults of the city of Sulaymaniyah, Iraq. Int J General Med. 2020:1249-1254.
11. Nurfianto S, Hadi U, Purnomo W. Relationship between maternal age, gravida and gestational age with premature membrane rupture in adolescent pregnancy. Indian J Forensic Med Toxicol. 2019;13(4):756-760.
12. Cha HH, Kim JM, Kim HM, Kim MJ, Chong GO, Seong WJ. Association between gestational age at delivery and lymphocyte-monocyte ratio in the routine second-trimester complete blood cell count. Yeungnam Univ J Med. 2021;38(1):34-38.
13. Bain BJ. Haematology: 101 Morphology Updates. Wiley-Blackwell; 2023. Available from: https://doi.org/10.1394179812/
14. Kılıç Ç, Uğur M, Ünlü BS, Yıldız Y, Artar İ, Karli P, et al. Comparison of serum granulocyte colony-stimulating factor levels between preterm and term births. J Turk Ger Gynecol Assoc. 2014;15(4):208.
15. Hershko Klement A, Hadi E, Asali A, Shavit T, Wiser A, Haikin E, et al. Neutrophils to lymphocytes ratio and platelets to lymphocytes ratio in pregnancy: A population study. PLoS One. 2018;13(5): e0196706.
16. Li A, Yang S, Zhang J, Qiao R. Establishment of reference intervals for complete blood count parameters

https://doi.org/10.56056/amj.2025.400

during normal pregnancy in Beijing. J Clin Lab Anal. 2017;31(6): e22150.
17. Deng Q, Deng L, Chen C, Meng S, Pan Y, Qing C. Reference intervals of haematological variables for healthy antepartum and postpartum women. Obstet Gynecol Int J. 2014;1(3):63-65.
18. Zeng Y, Li L, Mao M, Liang X, Chen M, Xia Y, et al. Establishment of reference intervals of complete blood count for twin pregnancy. BMC Pregnancy Childbirth. 2021; 21:1-13.

https://doi.org/10.56056/amj.2025.400