Importance of haemogram parameters for prediction of the time of birth in women diagnosed with threatened preterm labour

Harun Egemen Tolunay[1] 🔾 and Erkan Elci[2]

Abstract

Objective: This study aimed to estimate the importance of complete blood count parameters for predicting the timing of birth in threatened preterm labour cases.

Methods: We performed a retrospective study of 92 patients who were diagnosed with threatened preterm labour (24–34 gestational weeks). The patients were divided into two groups according to the time of birth (group 1: delivered within the first week after diagnosis; group 2: delivered later than 1 week). We compared characteristics and complete blood count parameters between these two groups.

Results: There were no significant differences in maternal age, body mass index, gravida, parity, haemoglobin levels, and gestational weeks between the two groups. The mean cervical length was 24.24 ± 3.60 mm in group 1 and 30.70 ± 5.32 mm in group 2. There were significant differences in the neutrophil to lymphocyte ratio, white blood cell count, red cell distribution width (RDW), absolute lymphocyte cell count, and absolute neutrophil cell count between the two groups.

Conclusion: Maternal serum RDW, the neutrophil to lymphocyte ratio, white blood cell count, absolute lymphocyte cell count, and the absolute neutrophil cell count profile could guide clinicians in predicting the time of birth in threatened preterm labour cases.

[1]Department of Perinatology, Etlik Zübeyde Hanım Maternity and Women's Health Teaching and Research Hospital, Ankara, Turkey
[2]Van Training and Research Hospital, Department of Obstetrics and Gynecology, Van, Turkey

Corresponding author:
Harun Egemen Tolunay, Etlik Zübeyde Hanım Maternity and Women's Health Teaching and Research Hospital, Etlik Caddesi 55, Ankara 06010, Turkey.
Email: harunegementolunay@gmail.com

Introduction

Preterm birth is the leading cause of perinatal morbidity and mortality worldwide. Determining the risk of preterm birth in pregnant women can be difficult because of its multifactorial aetiology. Prediction of preterm birth is important for saving time for health workers and pregnant women to perform the necessary interventions. Many markers have been used to predict preterm labour. These include the patient's history, evaluation of maternal signs and symptoms, a clinical examination, biochemical markers, and cervical length. Cervical evaluation by transvaginal sonography, and foetal fibronectin and interleukin-6 levels appear to be the best method for predicting preterm birth.[1,2] Although preterm labour is the most common cause of perinatal morbidity and mortality, its aetiology is still unclear. Although tocolytic drugs are used for preterm labour, there has been no significant decrease in the frequency of preterm birth in the world. Markers for preterm birth may contain any factor that can be used to predict subsequent spontaneous preterm labour, such as the medical history, demographic factors, personal behaviour, physical characteristics, physical examination findings, evaluation of cervical length by ultrasonography, and measurement of a specific substance in a biological fluid.[3]

A complete blood count (CBC) is simple and inexpensive, and it contains important parameters for many diseases. The red cell distribution width (RDW) is a measure of the distribution of erythrocytes depending on the diameter or volume within the CBC parameters. A positive correlation between RDW levels and inflammatory processes, especially C-reactive protein levels and sedimentation, has been found in recent cohort studies.[4] RDW is a marker of anisocytosis and is related to various inflammatory conditions, such as thyroiditis,[5] ulcerative colitis,[6] rheumatoid arthritis,[7] chronic obstructive pulmonary disease,[8] irritable bowel syndrome,[9] and chronic renal failure.[10] The neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) are inexpensive to measure and are easily calculated indices that correlate with the prognosis of systemic inflammatory diseases. They are particularly useful in inflammatory, cardiovascular, and oncological diseases.[11–14] Mean platelet volume (MPV) is a parameter that is indicative of platelet function and activity.[15] MPV plays an important role in immunological and inflammatory events.[16] The PLR is associated with various conditions, including diabetes mellitus.[17] The NLR is associated with diabetes mellitus,[18] thyroiditis,[19] and thyroid nodules.[20] Similarly, MPV is associated with diabetes mellitus,[21] inflammatory conditions,[22] cardiac conditions,[23] and thyroid conditions.[24] Use of CBC parameters in the field of obstetrics and perinatology has recently been investigated. Orgul et al.[25] found that increased first trimester WBC and neutrophil counts may be predictive for early-onset preeclampsia.

In this study, we aimed to investigate whether CBC parameters can be used for predicting the timing of preterm birth.

Materials and methods

The medical records of Van Training and Research Hospital were reviewed from January 2017 to March 2018. Ninety-two patients who were diagnosed with threatened preterm labour (TPL) were enrolled in the study. This study was designed as a retrospective assessment of data, and therefore, ethics committee approval and informed consent were not required.

In this study, pregnant women at 24 to 34 gestational weeks who were diagnosed with TPL were enrolled. TPL was defined as regular uterine contractions with or without other symptoms, such as pelvic

pressure, backache, increased vaginal discharge, menstrual-like cramps, bleeding, and cervical changes.[26] Pregnant women with preeclampsia, idiopathic thrombocytopenia, urinary tract infection, diabetes, and rheumatic disease were excluded from the study. All patients were hospitalized after the diagnosis of TPL was made and followed up at the hospital. After a foetal ultrasound examination and routine tests, hydration treatment was applied. Additionally, tocolytic treatment was provided with a calcium channel blocker (nifedipine). Prophylactic corticosteroid treatment was performed in all pregnant women.

Haemogram parameters were evaluated using blood samples that were taken before steroid treatment. These parameters included haemoglobin levels, the NLR, white blood cell (WBC) count, RDW, and MPV.

Patients who delivered within the first week after diagnosis of TPL were included in group 1 and those who delivered later than 1 week were included in group 2.

Statistical analyses

The Statistical Package for the Social Sciences (SPSS) version 21.0 for Windows (IBM Corp., Armonk, NY, USA) was used for all statistical analyses. The Shapiro–Wilk test was used to test for the distribution of normality. According to the results of data distribution, non-parametric tests were preferred. We used the Mann–Whitney U test to compare continuous variables. A p value < 0.05 was considered statistically significant.

Results

There were 46 patients in group 1 and 46 patients in group 2. Age, haemoglobin levels, gravidity, parity, body mass index, and gestational weeks were similar between the groups. The mean cervical length of patients in group 1 was significantly lower than that of patients in group 2 ($p < 0.001$, Table 1).

Table 2 summarizes the haemogram parameters of the two groups. There were no significant differences between the platelet count and MPV between the two groups. However, the NLR, WBC, RDW, and absolute neutrophil cell count were significantly higher in group 1 than in group 2 (all $p < 0.05$). Additionally, the absolute lymphocyte cell count was significantly lower in group 1 than in group 2 ($p = 0.027$, Table 2).

Discussion

In this study, we investigated the possible association of the time of birth and

Table 1. Demographic variables of the groups.

	Group 1	Group 2	*p* value
Age (years)	29.74 ± 3.52	29.52 ± 4.59	0.518
Parity	1.54 ± 0.84	1.57 ± 0.98	0.947
Gestational weeks	31.28 ± 2.02	31.20 ± 1.50	0.161
Gravida	2.78 ± 1.03	2.74 ± 1.31	0.491
Body mass index (kg/m²)	24.30 ± 3.89	24.42 ± 2.42	0.753
Haemoglobin (mg/dL)	10.88 ± 0.98	10.84 ± 1.10	0.739
Cervical length (mm)	24.24 ± 3.60	30.70 ± 5.32	<0.001

Values are mean ± standard deviation. Group 1: birth occurred within 1 week after hospitalization with diagnosis of threatened preterm labour; group 2: birth occurred later than 1 week after hospitalization with diagnosis of threatened preterm labour.

Table 2. Differences in haemogram parameters between the groups.

	Group 1	Group 2	*p* value
Platelet number ($\times 10^3/mm^3$)	268.93 ± 40.83	271.35 ± 33.56	0.549
Mean platelet volume (fL)	8.38 ± 0.72	8.36 ± 0.81	0.223
Absolute neutrophil count (cell/mm^3)	4794.65 ± 121.27	4091.39 ± 105.72	<0.05
Absolute lymphocyte count (cell/mm^3)	2167.24 ± 203.73	2170.48 ± 172.11	0.027
RDW (%)	14.84 ± 0.77	13.90 ± 1.09	<0.05
NLR (%)	2.85 ± 0.40	2.16 ± 0.28	<0.05
WBC count (/μL)	8.0 ± 0.99	6.85 ± 0.76	<0.05

Values are mean ± standard deviation. Group 1: birth occurred within 1 week after hospitalization with diagnosis of threatened preterm labour; group 2: birth occurred later than 1 week after hospitalization with diagnosis of threatened preterm labour. RDW: red cell distribution width; NLR: neutrophil to lymphocyte ratio; WBC: white blood cell.

maternal CBC variables in patients with TPL. The main findings in our study were as follows. We found that the NLR, WBC count, RDW, and absolute neutrophil cell count were higher in group 1 (those who delivered 1 week after hospitalization with the diagnosis of TPL) than in group 2 (those who did not deliver within 1 week after the hospitalization). We also found that the absolute lymphocyte cell count was lower in group 1 than in group 2. Platelet number and MPV were not different between these two groups. Additionally, cervical length was significantly lower in group 1 than in group 2.

A short cervical length can be predictive for preterm birth, and when coupled with appropriate preterm birth prevention strategies, it is associated with a reduction in spontaneous preterm birth in asymptomatic women with a singleton gestation. Our finding of a short cervical length in group 1 is consistent with previous published studies.[27]

CBC parameters significantly vary in number and quality in inflammatory events; in particular, neutrophil and platelet counts increase, and lymphocyte counts decrease.[28,29] Neutrophils are precursor cells of the immune system and are synthesized in the bone marrow. Many cytokines, chemokines, and growth factors are responsible for synthesis of neutrophils, apart from antimicrobial agents produced in defence.[30] Platelets increase secretion of cytokines (similar to neutrophils) at the onset of inflammation, and increased cytokine levels contribute to increased inflammation by increasing new neutrophil and platelet synthesis. Accumulation of neutrophils and platelets leads to sterile inflammation in tissues and increases tissue damage by synthesizing protease and growth factors in immunological conditions.[31,32] Use of an index is more practical than evaluating individual parameters and can provide reliable information on disease severity by estimating predictive values based on their relationship with the disease. Indices, such as the NLR and PLR, are useful in the prognostic follow-up of diseases, such as acute coronary syndrome, ulcerative colitis, diabetes, obstructive sleep apnoea, Sjögren syndrome, and systemic lupus erythematosus with predominant inflammatory activity.[33–35] The PLR has a significant relationship with cancer and inflammatory diseases, similar to the NLR.[36,37]

Preterm birth is among the most important causes of perinatal morbidity and mortality. There have been many studies on the aetiology of preterm labour and prevention of preterm labour.[38] The exact aetiology of preterm birth is unknown. However, in

more than half of preterm cases, the aetiological factor is subclinical intrauterine infection and inflammation, which can be detected by increased concentrations of cytokines and prostaglandins in amniotic fluid and maternal blood.[39–41]

Maternal inflammation and organization of the vascular bed, which are indicated by the NLR, are associated with foetal development and preterm delivery. Consistent with our findings, previous studies have also shown that an increased maternal inflammatory response is accompanied by preterm delivery.[42–44]

Few studies have investigated CBC parameters in the field of obstetrics and perinatology. The NLR can be used in combination with existing markers to improve detection rates of preterm birth, as shown by Gezer et al.[45] In another study conducted by Özel et al.,[46] the accuracy of the NLR was detected in pregnancies with preterm premature rupture of the membranes. Several studies have shown that maternal and maternal–foetal inflammation may trigger premature labour.[47,48] Previous studies have also shown that maternal inflammation affects birth weight either directly or via preterm labour.[49–51] In light of these findings, an increased NLR and PLR can be a result of preterm labour or insufficiency of the maternal–placental–foetal unit. A study that investigated the NLR and PLR in preeclamptic patients found a correlation between the PLR, but not the NLR, and the severity of preeclampsia.[52] These authors concluded that the PLR could indicate maternal immune activation in preeclampsia. Monitoring the symptoms observed in pregnant women who have preterm labour and being able to predict preterm birth, and managing complications and neonatal outcomes are important.

To the best of our knowledge, this retrospective study is the first to investigate the associations of the NLR, RDW, absolute neutrophil cell count, and absolute lymphocyte cell count in patients who deliver within 1 week of diagnosis of TPL. Our study suggests that the maternal NLR, RDW, WBC, and absolute neutrophil cell count are positively associated with birth within 1 week of diagnosis of TPL. Additionally, absolute lymphocyte cell count levels are higher in pregnant women who do not deliver in 1 week after diagnosis of TPL.

There is no proven method for prediction of preterm birth. Evaluation of cervical length is relatively successful for predicting preterm birth. A haemogram test is an inexpensive and effective method, but a larger dataset is required to clarify the issue of predicting preterm birth. The combined use of markers may be more useful in predicting preterm delivery.

Acknowledgement

Declaration of conflicting interest

Funding

ORCID iD

Harun Egemen Tolunay ![ORCID icon] https://orcid.org/0000-0002-8922-4400

References

1. MacDorman MF. Race and ethnic disparities in fetal mortality, preterm birth, and infant mortality in the United States: an overview. *Semin Perinatol* 2011; 35:

200–208. DOI: 10.1053/j.semperi.2011.02.017.

2. Russell RB, Green NS, Steiner CA, et al. Cost of hospitalization for preterm and low birth weight infants in the United States. *Pediatrics* 2007; 120: e1–e9. DOI: 10.1542/peds.2006-2386

3. Goldenberg RL, Iams JD, Mercer BM, et al. What we have learned about the predictors of preterm birth. *Semin Perinatol* 2003; 27: 185–193. DOI: 10.1016/s0146-0005(03)00017-x

4. Lippi G, Targher G, Montagnana M, et al. Relation between red blood cell distribution width and inflammatory biomarkers in a large cohort of unselected outpatients [published correction appears in Arch Pathol Lab Med. 2009 Aug; 133(8): 1186]. *Arch Pathol Lab Med* 2009; 133: 628–632. DOI: 10.1043/1543-2165-133.4.628

5. Aktas G, Sit M, Dikbas O, et al. Could red cell distribution width be a marker in Hashimoto's thyroiditis? *Exp Clin Endocrinol Diabetes* 2014; 122: 572–574. DOI: 10.1055/s-0034-1383564

6. Molnar T, Farkas K, Szepes Z, et al. RDW can be a useful additional marker in diagnosing Crohn's disease and ulcerative colitis. *Dig Dis Sci* 2008; 53: 2828–2829. DOI: 10.1007/s10620-008-0345-4

7. Cakir L, Aktas G, Berke-Mercimek O, et al. Are red cell distribution width and mean platelet volume associated with rheumatoid arthritis? *Biomed Res* 2016; 27: 292–294.

8. Sincer I, Zorlu A, Yilmaz MB, et al. Relationship between red cell distribution width and right ventricular dysfunction in patients with chronic obstructive pulmonary disease. *Heart Lung* 2012; 41: 238–243. DOI: 10.1016/j.hrtlng.2011.07.011

9. Aktas G, Alcelik A, Tekce BK, et al. Red cell distribution width and mean platelet volume in patients with irritable bowel syndrome. *Prz Gastroenterol* 2014; 9: 160–163. DOI: 10.5114/pg.2014.43578

10. Tekce H, Kin Tekce B, Aktas G, et al. The evaluation of red cell distribution width in chronic hemodialysis patients. *Int J Nephrol* 2014; 2014: 754370.

11. Pichler M, Hutterer GC, Stoeckigt C, et al. Validation of the pre-treatment neutrophil-lymphocyte ratio as a prognostic factor in a large European cohort of renal cell carcinoma patients. *Br J Cancer* 2013; 108: 901–907. DOI: 10.1038/bjc.2013.28

12. Tamhane UU, Aneja S, Montgomery D, et al. Association between admission neutrophil to lymphocyte ratio and outcomes in patients with acute coronary syndrome. *Am J Cardiol* 2008; 102: 653–657. DOI: 10.1016/j.amjcard.2008.05.006

13. de Jager CP, van Wijk PT, Mathoera RB, et al. Lymphocytopenia and neutrophil-lymphocyte count ratio predict bacteremia better than conventional infection markers in an emergency care unit. *Crit Care* 2010; 14: R192. DOI: 10.1186/cc9309

14. Templeton AJ, Ace O, McNamara MG, et al. Prognostic role of platelet to lymphocyte ratio in solid tumors: a systematic review and meta-analysis. *Cancer Epidemiol Biomarkers Prev* 2014; 23: 1204–1212. DOI: 10.1158/1055-9965.EPI-14-0146

15. Bath PM and Butterworth RJ. Platelet size: measurement, physiology and vascular disease. *Blood Coagul Fibrinolysis* 1996; 7: 157–161.

16. Briggs C. Quality counts: new parameters in blood cell counting. *Int J Lab Hematol* 2009; 31: 277–297. DOI: 10.1111/j.1751-553x.2009.01160.x

17. Atak B, Aktas G, Duman TT, et al. Diabetes control could through platelet-to-lymphocyte ratio in hemograms. *Rev Assoc Med Bras (1992)* 2019; 65: 38–42. DOI: 10.1590/1806-9282.65.1.38

18. Duman TT, Aktas G, Atak BM, et al. Neutrophil to lymphocyte ratio as an indicative of diabetic control level in type 2 diabetes mellitus. *Afr Health Sci* 2019; 19: 1602–1606. DOI: 10.4314/ahs.v19i1.35

19. Aktas G, Sit M, Dikbas O, et al. Elevated neutrophil-to-lymphocyte ratio in the diagnosis of Hashimoto's thyroiditis. 2017; 63: 1065–1068. DOI: 10.1590/1806-9282.63.12.1065

20. Sit M, Aktas G, Erkol H, et al. Neutrophil to lymphocyte ratio is useful in differentiation of malign and benign thyroid nodules. *P R Health Sci J* 2019; 38: 60–63.

21. Aktas G, Kocak MZ, Duman TT, et al. Mean platelet volume (MPV) as an

inflammatory marker in type 2 diabetes mellitus and obesity. *Bali Med J* 2018; 7: 650–653.

22. Aktas G, Sit M, Tekce H, et al. Mean platelet volume in nasal polyps. *West Indian Med J* 2013; 62: 515–518.

23. Sincer I, Çekici Y, Cosgun M, et al. Does mean platelet volume decrease in the presence of coronary artery fistula? *Arq Bras Cardiol* 2019; 113: 71–76. Published 2019 Jun 27. DOI: 10.5935/abc.20190088

24. Sit M, Aktas G, Ozer B, et al. Mean platelet volume: an overlooked herald of malıgnant thyroıd nodules. *Acta Clin Croat* 2019; 58: 417–420. DOI: 10.20471/acc.2019.58.03.03

25. Örgül G, Aydın Haklı D, Özten G, et al. First trimester complete blood cell indices in early and late onset preeclampsia. *Turk J Obstet Gynecol* 2019; 16: 112.

26. Hwang HS, Na SH, Hur SE, et al. Practice patterns in the management of threatened preterm labour in Korea: a multicenter retrospective study. *Obstet Gynecol Sci* 2015; 58: 203–209. DOI: 10.5468/ogs.2015.58.3.203

27. Son M and Miller ES. Predicting preterm birth: cervical length and fetal fibronectin. *Semin Perinatol* 2017; 41: 445–451. DOI: 10.1053/j.semperi.2017.08.002

28. Gabay C and Kushner I. Acute-phase proteins and other systemic responses to inflammation [published correction appears in N Engl J Med 1999 Apr 29; 340(17): 1376]. *N Engl J Med* 1999; 340: 448–454. DOI: 10.1056/NEJM199902113400607

29. Kapçı M, Türkdoğan KA, Duman A, et al. Biomarkers in the diagnosis of acute appendicitis. *J Clin Exp Invest* 2014; 5: 250–255.

30. Mantovani A, Cassatella MA, Costantini C, et al. Neutrophils in the activation and regulation of innate and adaptive immunity. *Nat Rev Immunol* 2011; 11: 519–531. Published 2011 Jul 25. DOI: 10.1038/nri3024

31. McDonald B, Pittman K, Menezes GB, et al. Intravascular danger signals guide neutrophils to sites of sterile inflammation [published correction appears in Science. 2011 Mar 25; 331(6024): 1517]. *Science* 2010; 330: 362–366. DOI: 10.1126/science.1195491

32. Boilard E, Blanco P and Nigrovic PA. Platelets: active players in the pathogenesis of arthritis and SLE. *Nat Rev Rheumatol* 2012; 8: 534–542. DOI: 10.1038/nrrheum.2012.118

33. Durmus E, Kivrak T, Gerin F, et al. Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio are predictors of heart failure. *Arq Bras Cardiol* 2015; 105: 606–613. DOI: 10.5935/abc.20150126

34. Hu ZD, Sun Y, Guo J, et al. Red blood cell distribution width and neutrophil/lymphocyte ratio are positively correlated with disease activity in primary Sjögren's syndrome. *Clin Biochem* 2014; 47: 287–290. DOI: 10.1016/j.clinbiochem.2014.08.022

35. Bozan N, Kocak ÖF, Dinc ME, et al. Mean platelet volume, red cell distribution width, and neutrophil-to-lymphocyte ratio before and after surgery in patients with carotid body tumors. *J Craniofac Surg* 2017; 28: e649–e653. DOI: 10.1097/SCS.0000000000003786

36. Feng JF, Huang Y and Chen QX. Preoperative platelet lymphocyte ratio (PLR) is superior to neutrophil lymphocyte ratio (NLR) as a predictive factor in patients with esophageal squamous cell carcinoma. *World J Surg Oncol* 2014; 12: 58.

37. Boilard E, Nigrovic PA, Larabee K, et al. Platelets amplify inflammation in arthritis via collagen-dependent microparticle production. *Science* 2010; 327: 580–583. DOI: 10.1126/science.1181928

38. Keelan JA, Newnham JP. Recent advances in the prevention of preterm birth. *F1000Res* 2017; 6: F1000 Faculty Rev-1139. Published 2017 Jul 18. DOI:10.12688/f1000research.11385.1

39. Puchner K, Iavazzo C, Gourgiotis D, et al. Mid-trimester amniotic fluid interleukins (IL-1β, IL-10 and IL-18) as possible predictors of preterm delivery. *In Vivo* 2011; 25: 141–148.

40. Vedovato S and Zanardo V. Corioamnionite e malattie infiammatorie del neonato pretermine [Chorioamnionitis and inflammatory disease in the premature newborn infant]. *Minerva Pediatr* 2010; 62: 155–156.

41. Kaczmarczyk K, Pituch-Zdanowska A, Wiszomirska I, et al. Long-term effects of premature birth on somatic development in women through adolescence and adulthood.

J Int Med Res 2018; 46: 44–53. DOI: 10.1177/0300060517714369

42. Rogers LK and Velten M. Maternal inflammation, growth retardation, and preterm birth: insights into adult cardiovascular disease. *Life Sci* 2011; 89: 417–421. DOI: 10.1016/j.lfs.2011.07.017

43. Guven MA, Coskun A, Ertas IE, et al. Association of maternal serum CRP, IL-6, TNF-alpha, homocysteine, folic acid and vitamin B12 levels with the severity of preeclampsia and fetal birth weight. *Hypertens Pregnancy* 2009; 28: 190–200. DOI: 10.1080/10641950802601179

44. Flo K, Blix ES, Husebekk A, et al. A longitudinal study of maternal endothelial function, inflammatory response and uterine artery blood flow during the second half of pregnancy. *Acta Obstet Gynecol Scand* 2016; 95: 225–232. DOI: 10.1111/aogs.12802

45. Gezer C, Ekin A, Solmaz U, et al. Identification of preterm birth in women with threatened preterm labour between 34 and 37 weeks of gestation. *J Obstet Gynaecol* 2018; 38: 652–657. DOI: 10.1080/01443615.2017.1399990

46. Ozel A, Alici Davutoglu E, Yurtkal A, et al. How do platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio change in women with preterm premature rupture of membranes, and threaten preterm labour? *J Obstet Gynaecol* 2020; 40: 195–199. DOI: 10.1080/01443615.2019.1621807

47. Oaks B, Stewart C, Laugero K, et al. Associations of maternal cortisol, inflammation, hemoglobin, iron status, and BMI with birth outcomes in pregnant women in Ghana. *FASEB J* 2015; 29: 579–581.

48. Stout MJ, Cao B, Landeau M, et al. Increased human leukocyte antigen-G expression at the maternal–fetal interface is associated with preterm birth. *J Matern Fetal Neonatal Med* 2015; 28: 454–459.

49. Fleischer NL, Merialdi M, van Donkelaar A, et al. Outdoor air pollution, preterm birth, and low birth weight: analysis of the world health organization global survey on maternal and perinatal health [published correction appears in Environ Health Perspect. 2014 Jun; 122(6): A151]. *Environ Health Perspect* 2014; 122: 425–430. DOI: 10.1289/ehp.1306837

50. Pringle KG, Rae K, Weatherall L, et al. Effects of maternal inflammation and exposure to cigarette smoke on birth weight and delivery of preterm babies in a cohort of indigenous Australian women. *Front Immunol* 2015; 6: 89. Published 2015 Mar 10. DOI: 10.3389/fimmu.2015.00089

51. Akgun N, Namli Kalem M, Yuce E, et al. Correlations of maternal neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) with birth weight. *J Matern Fetal Neonatal Med* 2017; 30: 2086–2091. DOI: 10.1080/14767058.2016.1237497

52. Toptas M, Asik H, Kalyoncuoglu M, et al. Are neutrophil/lymphocyte ratio and platelet/lymphocyte ratio predictors for severity of preeclampsia? *J Clin Gynecol Obstet* 2016; 5: 27–31.