THE CLINICAL SIGNIFICANCE OF COMPLETE BLOOD COUNT, NEUTROPHIL-TO-LYMPHOCYTE RATIO, AND MONOCYTE-TO-LYMPHOCYTE RATIO IN GESTATIONAL DIABETES MELLITUS

G. Liu[1], J. Geng[1], R. Jin[1], N. Zhang[1,*], L. Mei[1]

[1]Obstetrical Department, Fu Yang People's Hospital Affiliated to Anhui Medical University, Anhui FuYang, China

Abstract

Background. To investigate the association between inflammatory factors, such as complete blood count (CBC) components, neutrophil/lymphocyte ratio (NLR), monocyte/lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), and gestational diabetes mellitus (GDM).

Methods. A total of 635 pregnant women with GDM and 296 with normal pregnancies at 7–13 weeks of gestation who underwent prenatal examinations in the obstetrics department were enrolled (June 2020–December 2020). CBC parameters, including WBC, neutrophil, lymphocyte (LYM), monocyte (MON), red blood cell (RBC), hemoglobin (HGB), mean corpuscular volume (MCV), platelet (PLT), platelet accumulation (PCT), mean platelet volume (MPV), NLR, MLR, PLR, alanine transaminase (ALT), aspartate transaminase (AST), gamma-glutamyl transferase (GGT), and other parameters were assessed. The receiver operating characteristic (ROC) curve was used to analyze the screening effects of the variables on the development of GDM.

Results. There were significant differences in the blood levels of WBC, NEU, LYM, MON, RBC, HGB, PCT, ALT, AST, GGT, NLR, and MLR between the GDM and control groups (P<0.05). The diagnostic level of MON was the highest among all factors.

Conclusion. Inflammatory factors (WBC, NEU, LYM, MON, NLR, and MLR counts) were correlated with GDM.

Keywords: Gestational diabetes mellitus, Leukocyte, Pregnancy, Monocyte/lymphocyte ratio, Neutrophil/lymphocyte ratio.

INTRODUCTION

Gestational diabetes mellitus (GDM) refers to abnormal glucose metabolism that occurs for the first time during pregnancy, excluding type 2 diabetes mellitus that is diagnosed before pregnancy. Although its pathogenesis remains unknown, the main recognized causes are increased glucose demand during pregnancy, increased insulin resistance (IR), and relative or absolute insulin deficiency (1). The GDM rate is rising in China owing to changes in fertility policies and increasing recognition of the significance of the disease. However, the precise prevalence of GDM remains unclear. Studies from the United States have reported prevalence rates ranging from 1% to 14% of pregnancies, whereas research in China has suggested a prevalence of over 5.07% (2), with some researchers estimating a much higher incidence of 17.5% (3).

Predictive approaches have been extensively adopted to assist clinicians in their decision-making processes by estimating the likelihood of a patient experiencing different outcomes (4, 5). Recent studies have indicated that routine complete blood count (CBC) components, specifically the platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), and monocyte-to-lymphocyte ratio (MLR), have the potential to serve as innovative indicators of the systemic inflammatory response in a range of medical conditions, including pregnancy complications (6-9), cerebral hemorrhage (10, 11), ischemic stroke (10), cardiac events (12, 13), sepsis and infectious pathologies (14, 15), cancers (16, 17), and other diseases. These cost-effective and easily accessible inflammatory markers can assist in assessing patient risk and modifying treatment strategies in routine clinical practice.

There is increasing evidence that inflammatory markers, such as NLR, MLR, PLR, and CBC indices, can be used to predict the risk of preeclampsia and the spread of gestational trophoblastic disease (18). Additionally, these markers may be helpful in

*Correspondence to: Ningzhi Zhang MD, Anhui Medical University, Obstetrical Department, Fu yang People's Hospital Affiliated to Anhui Medical University, Anhui FuYang, Hefei, 236000, China, E-mail: fyniyanghe@163.com

the diagnosis of GDM, intrahepatic cholestasis of pregnancy, HELLP syndrome, and hyperemesis (6-9). However, only a limited number of studies have assessed the predictive significance of PLR, MLR, and NLR in GDM. In this study, the association between routinely ordered inflammatory factors, including WBC, NEU, NLR, PLR, MLR-related levels, and other liver- and kidney-relevant indices, and the development of GDM was investigated.

MATERIALS AND METHODS

Participants and study design

In this cross-sectional study, a total of 635 singleton pregnant women who underwent regular antenatal checkups in the obstetrics department of Fuyang People's Hospital affiliated with Anhui Medical University, Anhui, China, using simple random sampling were included (June 2020 to December 2020). Of these, 339 women were diagnosed with GDM by OGTT (GDM group), excluding 47 cases of preterm delivery who were not included in the statistical analysis, while 296 women displayed normal OGTT results (control group). The diagnostic criteria for GDM in this study were based on the 9th edition of Obstetrics and Gynecology, which involves measuring blood glucose levels at 24-28 weeks of gestation after an overnight fast and a 75 g oral glucose tolerance test. GDM was diagnosed if the blood glucose levels were equal to or greater than 5.1 mmol/L, 10.0 mmol/L, and 8.5 mmol/L after fasting, 1 h, and 2 h, respectively.

The exclusion criteria were as follows: (1) a known history of diabetes mellitus; (2) the presence of additional cardiovascular risk factors, such as hypertension, hyperlipidemia, or coronary artery disease; and (3) the presence of other factors that may affect leukocyte subpopulations and information ratios, such as corticosteroids, acetylsalicylic acid, smoking, impaired liver and renal function, a history of trauma, signs of active infection, peritonitis, pancreatitis, and pelvic inflammation.

Clinical information and biochemical examination

The anthropometric and clinical data of the pregnant women, including age, height, pre-pregnancy weight, pre-pregnancy body mass index (BMI), weight gain during pregnancy, 24-hour vaginal bleeding, and other general conditions, were collected. Fasting venous blood was collected from pregnant women at 37–39 weeks of gestation, the relevant indices (such

as WBC, NEU, MON, RBC, HGB, and PLT) in routine blood were detected, and the levels of NLR, PLR, and MLR were calculated. The levels of urinary leukocytes, urinary bacteria, ALT, AST, urea nitrogen, and creatinine in the liver and kidney were measured and calculated in the early morning after fasting (10–12 h). The WBC, NEU, RBC, and HGB levels in routine blood tests were measured using an automatic blood cell analyzer, and liver and kidney function tests were performed using an automatic biochemical analyzer.

Statistical analysis

Statistical analyses were conducted using the SPSS software (version 22.0; IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was used to determine data normality. Continuous data are shown as mean ± standard deviation (SD) and were compared using an independent Student's t-test. Categorical data were expressed as frequencies and percentages using the Chi-squared or Fisher's exact test. To examine the prognostic significance of factors for improved risk stratification of GDM, we performed receiver operating characteristic (ROC) analysis to determine the area under the curve (AUC) of each component and evaluated the efficacy of a combination of these factors. P-values less than 0.05 (P < 0.05) were considered significant.

RESULTS

Between June and December 2020, our hospital recorded a total of 4,245 deliveries, of which 339 were full-term deliveries complicated by GDM, resulting in an overall incidence of 7.74% in infants with gestational age. The incidence rate of GDM was 9.09% (386/4,245). A comparison of the baseline and clinical characteristics of the pregnant women is presented in Table 1. The mean maternal age, pre-pregnancy weight, pre-pregnancy BMI, weight gain during pregnancy, mean newborn weight, and 24-hour vaginal bleeding were significantly different between the two groups (P<0.05) (Table 1).

Table 2 shows the comparison of blood and urinary parameters and inflammatory markers between the GDM and control groups. Among the CBC factors, WBC, NEU, MON, RBC, HGB, and PCT levels were significantly lower in the GDM group than in the control group (P<0.05), while there were no significant differences in LYM, MCV, PLT, and MPV (P<0.05). The combined inflammatory indices NLR and MLR, but not PLR, were significantly lower in the GDM

group than in the control group (P<0.05). Moreover, ALT, AST, and GGT levels were significantly higher in the GDM group than in the control group (P<0.05); however, there were no statistically significant differences between the two groups in the kidney markers creatinine and uric acid (P<0.05). With respect to urinary parameters, urinary leukocyte and bacterial counts were not significantly different between the GDM and control groups (P<0.05) (Table 2).

Table 3 and Figure 1 show the predictive values of blood sugar, urine sugar, liver and kidney function, and levels of all inflammatory factors for GDM in late pregnancy. The AUC of WBC, NEU, LYM, MON, RBC, urine bacterial count, and ALT were 0.623, 0.621, 0.547, 0.614, 0.548, 0.557, 0.555, and 0.574, respectively, which were statistically significant (P<0.05). The maximum AUC of the MON was 0.619, its cutoff value was 0.435, and the Jordan index was 0.207. Sensitivity and specificity were 70.61% and 50.15%, respectively (Table 3 and Fig. 1).
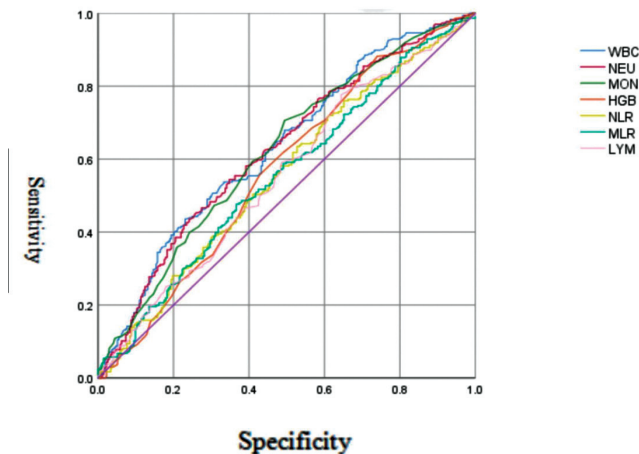

Figure 1. Receiver–operating characteristics (ROC) curve analysis for WBC, NEU, MOM, HGB, NLR, MLR, and LYM levels in predicting GDM during the third trimester of pregnancy.

DISCUSSION

Although GDM is becoming increasingly well-known, its pathogenesis remains unclear. Recent evidence suggests that inflammatory factors are involved in the process of IR and indirectly in the occurrence and development of GDM (19). Routine blood tests are common laboratory procedures used in the initial assessment of GDM and are part of the free maternity tests provided by the state during pregnancy. Elevated NEU and WBC counts are associated with both chronic and acute inflammation and have been implicated in GDM pathogenesis (6, 20, 21).

Studies have shown that insulin sensitivity is associated with peripheral blood WBC counts, which, as one of the most common indicators of the inflammatory response, can cause IR by activating inflammatory response signaling pathways through structure recognition receptors when the body is stimulated by infections, chemical alterations, etc. (22). Recent research has suggested that inflammatory factors may reflect a high risk of developing gestational diabetes. WBC count is a widely used biomarker of systemic inflammation, and platelets and red blood cells also play an important role in the inflammatory response. Activated platelets release numerous chemokines and express a large number of membrane receptors involved in inflammation (23, 24). Several studies have confirmed that elevated WBC, RBC, and PLT counts are associated with the GDM development (4). A retrospective analysis by Zhao *et al.* demonstrated that WBC count was significantly correlated with the development of GDM. The authors further reported that when the WBC count of pregnant women with GDM was 7.965×10^9/L, diagnostic sensitivity and specificity were 79.4% and 31.3 %, respectively, while evaluation by the homeostatic insulin assessment model revealed a positive correlation between the insulin resistance index and WBC count (25).

Table 1. Comparison of baseline and clinical characteristics of pregnant women between the GDM and control groups

	GDM group n=339	Control group n=296	P-value
Age (years)	30.53±4.92	26.46±3.27	P<0.0001
Prepregnancy weight (kg)	63.17±11.20	56.29±8.87	P<0.0001
Prepregnancy BMI (kg/m²)	24.11±3.96	21.24±3.11	P<0.0001
Weight gain (kg)	13.09±6.23	15.32±5.36	P<0.0001
University culture	127 (37.46)	193 (65.20)	P<0.0001
Macrosomia incidence	54 (15.92)	25 (8.44)	P=0.004
Mean newborn weight (g)	3539±421.40	3382±434.30	P<0.0001
Average body weight of macrosomia (g)	4233±212.10	4284±284.90	P=0.372
Postpartum hemorrhage rate	7 (2.06)	6 (2.02)	P=0.804
24-hour vaginal bleeding	338.50±179.30	296±140.60	P=0.001

Continuous and categorical data are presented as mean ± SD and number (percentage), respectively. Remarks: All births were full term, excluding premature births. GDM: gestational diabetes mellitus; BMI: body mass index.

NLR and PLR are simple, fast, and inexpensive markers of inflammation and have been used as markers of inflammation or metastasis in cancer and inflammatory bowel disease, as prognostic markers for ischemic heart disease, and for screening for diabetes-related complications (5, 26). Yilmaz *et al.* reported a significant association between NLR and GDM, with a threshold value of 2.93. The sensitivity and specificity of the NLR for diagnosing GDM were 76% and 94%, respectively (6). Moreover, Hudzik *et al.* first evaluated PLR in relation to GDM and concluded that PLR was associated with poor outcomes in patients (27). Another study showed that PLR is useful in predicting inflammation in patients with diabetic nephropathy (28). Furthermore, elevated MLR may be a favorable prognostic factor for clinical outcomes in patients with hyperglycemia during pregnancy (29). Increased MLR values are thought to be a metabolic response to overwhelming systemic inflammation or immune dysfunction; inflammation, primarily changes in inflammatory cytokine release in the placenta, may cause fetal dysplasia through epigenetic alterations (30).

Several studies have concluded, however, that blood NLR and PLR are not recommended in screening for GDM, but they propose that an increased WBC count is an important marker of gestational diabetes because it provides evidence of subclinical inflammation. A study by Ozyer *et al.* indicated that WBC count and CRP and IL-6 levels were not associated with the development of GDM at mid-or late gestation (31), which was not in agreement with the present study. Our study found that WBC, NEU, MON, PCT, NLR, and MLR were significantly lower in the GDM group than those in the control group. We found no significant differences in the MCV, PLT, PCT, and PLR factors between the two groups. The results of this study were partly in line with the above-mentioned

Table 2. Comparison of blood and urinary parameters and inflammatory indicators between the GDM and control groups

	GDM group n=339	Control group n=296	P-value
WBC ($*10^9$/L)	8.18±2.01	9.07±2.09	P<0.0001
NEU ($*10^9$/L)	6.05±1.75	6.86±1.94	P<0.0001
LYM ($*10^9$/L)	1.560±0.44	1.641±0.52	P=0.035
MON ($*10^9$/L)	0.45±0.13	0.52±0.27	P<0.0001
RBC ($*10^{12}$/L)	4.00±0.36	4.06±0.34	P=0.020
HGB (g/L)	119.40±11.26	121.50±9.83	P=0.013
MCV (fL)	92.07±5.75	91.45±10.06	P=0.338
PLT ($*10^9$/L)	196.70±56.85	203.90±48.85	P=0.093
PCT (%)	0.20±0.04	0.22±0.12	P=0.047
MPV (fL)	10.94±5.46	10.42±1.63	P=0.117
NLR	4.16±1.64	4.57±2.17	P=0.006
PLR	134.40±49.02	133.80±48.67	P=0.962
MLR	0.30±0.10	0.34±0.19	P=0.005
ALT (U/L)	18.66±28.88	13.32±8.76	P=0.002
AST (U/L)	21.32±26.87	17.45±6.46	P=0.016
GGT (U/L)	14.49±11.48	12.62±7.70	P=0.018
Creatinine (umol/L)	41.72±7.28	41.58±7.41	P=0.810
Uric acid (μmmol/L)	301.00±74.45	292.20±65.90	P=0.117
Urinary leukocyte count	21.73±54.36	20.32±51.47	P=0.739
Urinary bacterial count	8.55±20.61	7.017±13.88	P=0.279

All data are presented as mean ± SD. GDM: gestational diabetes mellitus; WBC: white blood cell; NEU: neutrophil; LYM: lymphocyte; MON: monocyte; RBC: red blood cell; HGB: hemoglobin; MCV: mean corpuscular volume; PLT: platelet; PCT: platelet accumulation; MPV: mean platelet volume; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; MLR: monocyte-to-lymphocyte ratio; ALT: alanine transaminase; AST: aspartate transaminase; GGT: gamma-glutamyl transferase.

Table 3. Value of various inflammatory factors in predicting GDM in the third trimester of pregnancy

Category	AUC	95% CI	p-value	Cut-off value	Sensitivity (%)	Specificity (%)	Jordan index
WBC	0.623	0.580-0.666	<0.0001	9.315	43.58	75.81	0.193
NEU	0.621	0.578-0.665	<0.0001	7.005	43.58	76.4	0.199
LYM	0.547	0.503-0.592	0.037	1.325	77.7	34.81	0.125
MON	0.614	0.571-0.658	<0.0001	0.435	70.61	50.15	0.207
HGB	0.557	0.513-0.602	0.011	111.500	88.18	23.89	0.120
NLR	0.561	0.516-0.606	0.007	3.440	71.62	39.82	0.114
MLR	0.558	0.514-0.603	0.010	0.322	47.64	64.6	0.122

GDM: gestational diabetes mellitus; WBC: white blood cell; NEU: neutrophil; LYM: lymphocyte; MON: monocyte; HGB: hemoglobin; NLR: neutrophil-to-lymphocyte ratio; MLR: monocyte-to-lymphocyte ratio.

findings; however, the WBC, NLR, and MLR values were low, and PLR could not be used as a meaningful indicator and did not have diagnostic value.

Lao *et al.* found that the incidence of GDM in pregnant women with high HGB levels (≥130 g/L) in early pregnancy was as high as 18.7%, which was significantly higher than that in the group with HGB <130 g/L (10.9%) (32). Similarly, Gao *et al.* concluded through retrospective analysis that high HGB levels (≥130 g/L) in early pregnancy were significantly correlated with the occurrence of GDM (32). Tarim *et al.* found that the incidence of GDM was significantly higher in the ≥122 g/L HGB group than in the < 122 g/L HGB group, but high HGB levels were not found to be an independent risk factor for GDM development after logistic regression analysis (33). Chen *et al.* concluded that high HGB levels (> 130 g/L) did not increase the risk of developing GDM (34). Our study found lower erythrocyte levels and HGB concentrations in the GDM group than in the control group, which differs slightly from a previous study, ostensibly due to the late gestational stage of the participants. The current study concluded that whether there is a significant correlation between HGB levels and the occurrence of GDM is controversial (35).

The liver plays an irreplaceable role in the pathogenesis of diabetes as it is the main site and target of glucose and insulin metabolism. A study by Erdogan *et al.* (36) found that ALT and GGT levels were significantly higher in the GDM group than in healthy controls, which may be one of the early predictors of GDM. Another prospective study of 2,610 pregnant women diagnosed with GDM showed a correlation between maternal blood GGT levels, but not AST and ALT levels, and the occurrence of GDM in mid-pregnancy (37). However, a study by Liu *et al.* showed that liver metabolic levels of ALT, AST, total bilirubin, and fibrinogen in early pregnancy were closely related to the occurrence of GDM. These findings emphasize the importance of monitoring liver function in pregnant women, particularly in those at risk of GDM (38). Our study found that the levels of ALT, AST, and GGT were significantly higher in the GDM group than in the control group. We also found that there was no statistical difference between creatinine, urea nitrogen, urinary leukocytes, and urinary bacterial counts in the two groups; however, urinary leukocyte and urinary bacterial counts were higher than those in the healthy control group. These findings are consistent with the increased susceptibility of individuals with diabetes to infectious factors and highlight the need for increased attention to infectious risk in this population.

This study had certain limitations. Although we observed that inflammatory factors, such as WBC, NEU, LYM, and NLR, were significantly altered in pregnant women with GDM, we found that these tests were not very accurate. Our data showed that the maximum AUC value was < 0.7. We believe that there are three possible reasons for this finding. However, the sample size of this study was relatively small. These inflammatory indices are not specific to pregnancy, and fluctuate during pregnancy. They were chosen because they are inexpensive and easy to obtain, even in poor areas. Lastly, this study performed only the association analysis of inflammatory factors, such as WBC, NEU, NLR, MLR, and liver and kidney function-related indices in routine blood during pregnancy with GDM and did not combine the relevant indices in early pregnancy, such as fasting blood glucose and lipids, nor explored the mechanism of this in greater depth. Additional studies are needed to complement the results obtained in this study by conducting a prospective study to determine the relationship between early pregnancy-related inflammatory factors and the prognosis of pregnant women with GDM. Other risk factors for GDM should also be identified.

In conclusion, in our study, routinely ordered inflammatory factors, WBC, NEU, LYM, MON, NLR, and MLR counts were important markers involved in the development of GDM. The possible advantages of these markers include their availability and low cost compared to other sophisticated inflammatory markers that might not be available in all healthcare centers. The MON blood level requires particular attention, but further prospective demonstration in a larger sample is needed.

Conflict of interest
The authors declare that they have no conflict of interest.

References

1. McIntyre HD, Catalano P, Zhang C, Desoye G, Mathiesen ER, Damm P. Gestational diabetes mellitus. Nat Rev Dis Primers. 2019;5(1):47.
2. Wei Y-M, Yang H-X, Gao X-L. Investigation into the prevalence and suitable diagnostic criteria of gestational diabetes mellitus in China. Zhonghua Fu Chan Ke Za Zhi. 2008;43(9):647-650.
3. Wang C, Wei Y, Yang Y, Su R, Song G, Kong L, Yang H. Evaluation of the value of fasting plasma glucose in the first trimester for the prediction of adverse pregnancy outcomes. Diabetes Res Clin Pract. 2021;174:108736.

4. Tan P, Chai J, Ling L, Omar S. Maternal hemoglobin level and red cell indices as predictors of gestational diabetes in a multi-ethnic Asian population. Clin Exp Obstet Gynecol. 2011;38(2):150-154.

5. Celikbilek M, Dogan S, Ozbakır O, Zararsız G, Kücük H, Gürsoy S, Yurci A, Güven K, Yücesoy M. Neutrophil–lymphocyte ratio as a predictor of disease severity in ulcerative colitis. J Clin Lab Anal. 2013;27(1):72-76.

6. Yilmaz H, Celik H, Namuslu M, Inan O, Onaran Y, Karakurt F, Ayyildiz A, Bilgic M, Bavbek N, Akcay A. Benefits of the neutrophil-to-lymphocyte ratio for the prediction of gestational diabetes mellitus in pregnant women. Exp Clin Endocrinol Diabetes. 2014;122(01):39-43.

7. Panwar M, Kumari A, Arora R, Singh V, Bansiwal R. Raised neutrophil lymphocyte ratio and serum beta hCG level in early second trimester of pregnancy as predictors for development and severity of preeclampsia. Drug Discov Ther. 2019;13(1):34-37.

8. Sisti G, Faraci A, Silva J, Upadhyay R. Neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and routine complete blood count components in HELLP syndrome: a matched case control study. Medicina. 2019;55(5):123.

9. Wang J, Zhu Q-W, Cheng X-Y, Liu J-y, Zhang L-l, Tao Y-M, Cui Y-B, Wei Y. Assessment efficacy of neutrophil-lymphocyte ratio and monocyte-lymphocyte ratio in preeclampsia. J Reprod Immunol. 2019;132:29-34.

10. Lattanzi S, Cagnetti C, Rinaldi C, Angelocola S, Provinciali L, Silvestrini M. Neutrophil-to-lymphocyte ratio improves outcome prediction of acute intracerebral hemorrhage. J Neurol Sci. 2018;387:98-102.

11. Lattanzi S, Brigo F, Trinka E, Cagnetti C, Di Napoli M, Silvestrini M. Neutrophil-to-lymphocyte ratio in acute cerebral hemorrhage: a system review. Transl Stroke Res. 2019;10:137-145.

12. Tamhane UU, Aneja S, Montgomery D, Rogers E-K, Eagle KA, Gurm HS. Association between admission neutrophil to lymphocyte ratio and outcomes in patients with acute coronary syndrome. Am J Cardiol. 2008;102(6):653-657.

13. Dentali F, Nigro O, Squizzato A, Gianni M, Zuretti F, Grandi AM, Guasti L. Impact of neutrophils to lymphocytes ratio on major clinical outcomes in patients with acute coronary syndromes: A systematic review and meta-analysis of the literature. Int J Cardiol. 2018;266:31-37.

14. de Jager CP, van Wijk PT, Mathoera RB, de Jongh-Leuvenink J, van der Poll T, Wever PC. Lymphocytopenia and neutrophil-lymphocyte count ratio predict bacteremia better than conventional infection markers in an emergency care unit. Crit Care. 2010;14:1-8.

15. Russell CD, Parajuli A, Gale HJ, Bulteel NS, Schuetz P, de Jager CP, Loonen AJ, Merekoulias GI, Baillie JK. The utility of peripheral blood leucocyte ratios as biomarkers in infectious diseases: A systematic review and meta-analysis. J Infect. 2019;78(5):339-348.

16. Templeton AJ, McNamara MG, Šeruga B, Vera-Badillo FE, Aneja P, Ocaña A, Leibowitz-Amit R, Sonpavde G, Knox JJ, Tran B. Prognostic role of neutrophil-to-lymphocyte ratio in solid tumors: a systematic review and meta-analysis. J Natl Cancer Inst. 2014;106(6):dju124.

17. Ethier J-L, Desautels DN, Templeton AJ, Oza A, Amir E, Lheureux S. Is the neutrophil-to-lymphocyte ratio prognostic of survival outcomes in gynecologic cancers? A systematic review and meta-analysis. Gynecol Oncol. 2017;145(3):584-594.

18. Guzel AI, Kokanali MK, Erkilinc S, Topcu HO, Oz M, Ozgu E, Erkaya S, Gungor T. Predictive role of the neutrophil lymphocyte ratio for invasion with gestational trophoblastic disease. Asian Pac J Cancer Prev. 2014;15(10):4203-4206.

19. Law KP, Zhang H. The pathogenesis and pathophysiology of gestational diabetes mellitus: Deductions from a three-part longitudinal metabolomics study in China. Clin Chim Acta. 2017;468:60-70.

20. Yang H, Zhu C, Ma Q, Long Y, Cheng Z. Variations of blood cells in prediction of gestational diabetes mellitus. J Perinat Med. 2015;43(1):89-93.

21. Fashami MA, Hajian S, Afrakhteh M, Khoob MK. Is there an association between platelet and blood inflammatory indices and the risk of gestational diabetes mellitus? Obstet Gynecol Sci. 2020;63(2):133-140.

22. Tzur T, Weintraub AY, Sergienko R, Sheiner E. Can leukocyte count during the first trimester of pregnancy predict later gestational complications? Arch Gynecol Obstet. 2013;287:421-427.

23. Qiu C, Sorensen TK, Luthy DA, Williams MA. A prospective study of maternal serum C-reactive protein (CRP) concentrations and risk of gestational diabetes mellitus. Paediatr Perinat Epidemiol. 2004;18(5):377-384.

24. Atta AA, AKABA GO, Nwegbu MM, Abdullahi HI, Ekele BA. A Prospective Cohort Study on the Association Between Elevated C-Reactive Protein and Gestational Diabetes Mellitus in a Nigerian Obstetric Population. Trop J Obstet Gynaecol. 2021;38(3):243-251.

25. He A, Zhou Z, Huang L, Yip KC, Chen J, Yan R, Li R. Association between serum iron and liver transaminases based on a large adult women population. J Health Popul Nutr. 2023;42(1):69.

26. Aygün F, Efe D. Association of neutrophil/lymphocyte ratio with obstructive coronary artery disease and coronary artery calcium score detected by multislice computed tomography in type 2 diabetes mellitus patients. Patient Prefer Adherence. 2015:1023-1031.

27. Hudzik B, Szkodzinski J, Gorol J, Niedziela J, Lekston A, Gasior M, Polonski L. Platelet-to-lymphocyte ratio is a marker of poor prognosis in patients with diabetes mellitus and ST-elevation myocardial infarction. Biomark Med. 2015;9(3):199-207.

28. Akbas EM, Demirtas L, Ozcicek A, Timuroglu A, Bakirci EM, Hamur H, Ozcicek F, Turkmen K. Association of epicardial adipose tissue, neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio with diabetic nephropathy. Int J Clin Exp Med. 2014;7(7):1794-1801.

29. Wang J, Zhu Q-W, Cheng X-Y, Sha C-X, Cui Y-B. Clinical significance of neutrophil–lymphocyte ratio and monocyte–lymphocyte ratio in women with hyperglycemia. Postgrad Med. 2020;132(8):702-708.

30. Bulka CM, Dammann O, Santos HP, VanderVeen DK, Smeester L, Fichorova R, O'Shea TM, Fry RC. Placental CpG methylation of inflammation, angiogenic, and neurotrophic genes and retinopathy of prematurity. Invest Ophthalmol Vis Sci. 2019;60(8):2888-2894.

31. Özyer Ş, Engin-Üstün Y, Uzunlar Ö, Katar C, Danışman N. Inflammation and glycemic tolerance status in pregnancy: the role of maternal adiposity. Gynecol Obstet Invest. 2014;78(1):53-58.

32. Lao TT, Chan LY, Tam K-F, Ho L-F. Maternal hemoglobin and risk of gestational diabetes mellitus in Chinese women. Obstet Gynecol. 2002;99(5):807-812.

33. Tarim E, Kilicdag E, Bagis T, Ergin T. High maternal hemoglobin and ferritin values as risk factors for gestational diabetes. Int J Gynaecol Obstet. 2004;84(3):259-261.

34. Chen X, Scholl TO, Stein TP. Association of elevated serum ferritin levels and the risk of gestational diabetes mellitus in pregnant women: The Camden study. Diabetes care. 2006;29(5):1077-1082.

35. Wang C, Lin L, Su R, Zhu W, Wei Y, Yan J, Feng H, Li B, Li S, Yang H. Hemoglobin levels during the first trimester of pregnancy are associated with the risk of gestational diabetes mellitus, pre-eclampsia and preterm birth in Chinese women: a retrospective study. BMC Pregnancy Childbirth. 2018;18:1-11.

36. Erdoğan S, Özdemir Ö, Doğan HO, Sezer S, Atalay CR, Yilmaz FM, Koca Y. Liver enzymes, mean platelet volume, and red cell distribution width in gestational diabetes. Turk J Med Sci. 2014;44(1):121-125.

37. Tan PC, Aziz AZ, Ismail IS, Omar SZ. Gamma-glutamyltransferase, alanine transaminase and aspartate transaminase levels and the diagnosis of gestational diabetes mellitus. Clin Biochem. 2012;45(15):1192-1196.

38. Liu G-L, Zhang N-Z. Routine blood tests in early pregnancy: their development and value in the early diagnosis of gestational diabetes mellitus. Clin Exp Obstet Gynecol. 2021;48(2):228-233.