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Research Article

Correlation of NLR, PLR, Platelet Parameters and D-Dimer with Venous Thromboembolism (VTE) in Pregnancy: A Retrospective Study

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Abstract

This retrospective study aimed to evaluate the correlation between the Neutrophil-Lymphocyte Ratio (NLR), Platelet-Lymphocyte Ratio (PLR), platelet parameters (Mean Platelet Volume [MPV], Platelet Distribution Width [PDW]), and D-dimer levels with venous thromboembolism (VTE) during pregnancy. Data were collected from electronic medical records and laboratory reports from January 2022 to December 2023, including 298 healthy pregnant women and 24 women who experienced VTE during pregnancy. The analysis revealed that women with VTE exhibited wider variability in the parameters studied, even though their age ranges were comparable to the control group. Pregnant women with VTE showed increased MPV, NLR, PLR, and D-dimer levels, while PDW was reduced compared to healthy pregnant women. Significant correlations were observed between MPV, PDW, NLR, PLR, and D-dimer levels in the VTE group, with strong correlations between MPV and PDW, D-dimer, and NLR ($r = .94, .76$, and $.78$, $p < .01$), and PDW with D-dimer and NLR ($r = .79$ and $.72$, $p < .01$). Moderate correlations were also found between PDW and Pct ($r = 0.45$), Pct and NLR ($r = 0.48$), MPV and PLR ($r = 0.44$), and PDW and PLR ($r = 0.48$) at $p < .05$.

Keywords: Venous thromboembolism; NRL; Platelet-lymphocyte ratio; Platelet parameters-Mean platelet volume; Platelet distribution width; Platelet crit; D- dimer

Introduction

Venous thromboembolism (VTE) is a condition where clots form in deep veins and pulmonary embolisms [1]. Pregnancy is a significant risk factor for VTE, with DVT accounting for approximately 80% of cases and PE affecting the remaining 20% of pregnant women. The global incidence of VTE during pregnancy is estimated to be approximately 2 cases per 1,000 births, while for Chinese women, the incidence rate is 1.88 per 1,000 [2,3]. VTE is responsible for 1.1 fatalities per 100,000 births but contributes to approximately 10% of maternal mortality [4]. Pregnant women have a 4- to 5-fold increased risk of developing VTE compared to non-pregnant women [5]. The increased risk of VTE in pregnancy is attributed to hormonal changes that reduce venous capacity, physical obstruction caused by the enlarging uterus, and decreased mobility, which hinders proper blood circulation [6,7].

The formation of VTE is based on the inflammation and platelet activity and interaction between them [8]. Inflammation is a central factor in clot formation, accompanied by hypercoagulability and endothelial damage [9,10]. These inflammatory mediators bind to and activate platelets, significantly contributing to thrombus formation in both venous and arterial thrombosis [11,12]. The MPV indicates platelet activation and activation potential in patients and is highly associated with VTE [13-16]. The platelet-to-lymphocyte ratio (PLR) is equally valuable since that is an indication of both hemostatic and inflammatory activity, in contrast to the simple platelet count [17-20].

There is no in-depth analysis of pregnancy-specific factors correlating for NLR, PLR, platelet parameters, and D-dimer with physiological vascular and hormonal changes [21]. It also does not monitor these biomarkers across trimesters and consequently misses likely fluctuations, which would refine VTE risk assessment [22]. Furthermore, while existing research discusses correlations, it does not fully explore the real-world clinical utility of these biomarkers in VTE prevention, early detection, or risk stratification. This study aims to determine a correlation between VTE and neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), platelet parameters, and D dimer levels in pregnancy. The objectives include examining the association of these biomarkers with VTE risk, evaluating these biomarkers for predicting VTE in pregnant women, and managing VTE to improve maternal health outcomes.

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Methodology

Study Design

This study employed a retrospective cohort design to analyze medical records of pregnant women diagnosed with VTE and healthy pregnant women at Lanzhou University Second Hospital between January 1, 2022, and December 31, 2023. This study design evaluated the relationships between NLR, PLR, platelet measurements, and D-dimer levels alongside VTE pregnancy outcomes. This approach provides access to preexisting clinical data compared to prospective studies' time and cost reduction procedures [23]. A retrospective study effectively serves biomarker correlation analysis because VTE occurs infrequently during pregnancy but enables the identification of cases without extended follow-up requirements.

Inclusion and exclusion criteria

Inclusion criteria

Participants had to meet the following conditions:

- Pregnant women aged 20 to 45 years with a singleton pregnancy.
- Completion of required laboratory tests.
- Voluntary consent to participate in the study.
- Both healthy pregnant women and patients diagnosed with VTE, confirmed through Doppler ultrasonography, were included.

Exclusion criteria

Participants were excluded if they had:

- A personal or family history of thromboembolism.
- A prior adverse pregnancy outcome, including miscarriage, placental rupture, or premature placental separation.
- Pre-existing medical conditions, such as:
  - Hypertension, diabetes, cardiovascular or cerebrovascular diseases (e.g., myocardial infarction, unstable angina, atherosclerosis, cerebral infarction).
  - Liver or kidney diseases.
  - Immune system disorders (e.g., antiphospholipid antibody syndrome, systemic lupus erythematosus).
  - Blood system disorders (e.g., idiopathic thrombocytopenic purpura, gestational thrombocytopenia).
- A history of surgery or trauma within the past month.
- Fever (body temperature ≥ 37.3°C) or active infection.
- Use of medications affecting coagulation or fibrinogen activity, including warfarin, aspirin, and heparin.
- Multiple pregnancies or pregnancies conceived through assisted reproductive technology.

Data Collection

Data were extracted directly from medical records for this retrospective study, which employed a total sampling method. A review examined patient records from healthy pregnant women and those diagnosed with VTE from January 2022 to December 2023. Laboratory test results were assessed for completeness and accuracy before analysis.

Statistical Analysis

The normality of the data was assessed using the Shapiro-Wilk test. Non- normally distributed data were presented as median (IQR). The Mann-Whitney test was employed to analyze the research subjects' characteristics and compare differences in platelet parameters, NLR, PLR, and D-dimer levels between healthy pregnant women and those with VTE. Univariate analysis (Spearman correlation) was done to identify variables that significantly correlate with VTE.

Results

The research evaluated health data from 298 pregnant women alongside data from 24 patients who received diagnoses of VTE. The study showed no statistical variations in age patterns or lymphocyte count measurements between these two groups. The neutrophil count was significantly higher in the VTE group ($p = 0.001$), while the mode of delivery showed a significant association with VTE ($p < 0.008$) (Table 1).

The analysis showed elevated levels of MPV, D-dimer, and NLR in pregnant women with VTE compared to healthy pregnant women, thus indicating these biomarkers' predictive capability for VTE assessment. PDW was decreased in pregnant women with VTE as compared to healthy pregnant women. The analysis of Table 2 indicates that Pct and PLR values fail to demonstrate meaningful variations between groups, suggesting their ineffectiveness as VTE assessment markers for pregnant women.

The findings reveal the comparative trends between platelet parameters to NLR, PLR, and D-dimer levels in pregnant women with VTE. The analysis of the correlation between MPV and other parameters revealed that MPV correlated well with PDW

Table 1: Characteristics between healthy pregnant women and those with VTE.

Variable	Total	Healthy Pregnant Women	Pregnant women with VTE	value
Age	30(28,33)	31(28,33)	29(28,31)	0.45
Neutrophil	7.34(5.8,8.8)	7.31(5.8,8.8)	9.46(7.6,11.9)	<0.001
Lymphocyte	1.47(1.14,1.77)	1.53(1.23,1.84)	1.42(1.1,1.6)	0.35
Method of Delivery				0.008
Normal	223	206	17	
Cesarean section	111	92	19	

Note: *Mann–Whitney difference test results.

Table 2: Differences in laboratory parameters between healthy pregnant women and women with VTE.

Variable	Total	Healthy Pregnant Women	Pregnant women with VTE	p-value*
Platelet crit (Pct)	0.21(0.18,0.25)	0.22(0.18,0.25)	0.19(0.15,0.22)	0.06
MPV	10.7(9,11.8)	11.2(10.7,12)	12(11,13.8)	<0.001
PDW	12(10.17,14)	14.9(12.3,16.9)	14(12,15)	0.013
D-dimer	1.36(1.02,1.95)	1.45(1.1,2.03)	2.24(1.96,3.23)	<0.001
NLR	4.99(3.67,6.86)	4.49(3.38,6.29)	7.1(6,7.7)	<0.001
PLR	136(111,183)	123.9(97.7,159)	143(130.75,152.7)	0.4

Note: *Mann–Whitney difference test results.

Table 3: Showing correlations between platelet parameters, NLR, PLR, and D-dimer in pregnant women with VTE.

Variables	MPV	PDW	Pct	D-dimer	NLR	PLR
MPV	-	-				
PDW	.94**	-	-			
Pct	.38	.45*	-	-		
D-dimer	.765**	.79**	.66**	-	-	
NLR	.786**	.72**	.48*	.789**	-	-
PLR	.44**	.48*	.52**	.60**	.52**	-

Note: **. Correlation is significant at the 0.01 level (2-tailed).

with a coefficient of 0.94 and had a statistically significant positive correlation with D-dimer and NLR ($r = 0.78$, $p < 0.01$). The statistical relationship between PDW and D-dimer is highly significant, with a coefficient of 0.79 and $p < 0.01$ and with NLR: 0.72 with $p < 0.01$, suggesting its involvement in thrombus formation (Table 3). Pct has a moderate inflammation relationship with D-dimer, about 0.66 at $p < 0.01$, and an inflammatory relationship with NLR of about 0.48 at $p < 0.05$. Moreover, the correlation of PLR with D-dimer is moderate, with a mean value of 0.60 and a significance level of <0.01. In contrast, NLR's correlation is also moderate, with a mean value of 0.52 and a significance level of <0.01.

Discussion

The study aims to establish the correlation between VTE and biomarkers, including NLR and PLR, in maternal pregnancy, as well as the absolute platelet count and D-dimer levels. These associations would assist in the early identification of the incidences of VTE and possible measures to contain it and, subsequently, minimize its impact on the mother's health. These complications include deep vein thrombosis and pulmonary embolism, which significantly affect both maternal and fetal morbidity and mortality [24]. Moreover, hypercoagulability and inflammation have been implicated in the development of VTE. Therefore, Zvetkova et al. (2024) have shifted their attention to the parameters of platelet (PLT), which can be determined through complete blood count [25]. They are relatively inexpensive biomarkers and rather easy to determine, which makes it possible to use them for VTE assessment. The findings highlighted below were deemed independent predictors of acute VTE since they demonstrate inflammation levels and prothrombotic activity [26,27]. Ming et al. (2018) have mentioned that NLR and PLR efficiently determine the risk in VTE patients as their level is high [28]. This evidence illustrates that both NLR and PLR were raised in pregnant women with VTE. In this respect, these associations add value to the role of these biomarkers in assessing risk and preventing VTE.

MPV levels show a connection to VTE risk for VTE throughout various patient populations, including pregnant women. According to Lippi et al. (2020), VTE patients show higher MPV values than controls, and MPV evaluation is a crucial method for assessing thrombotic risk potential [29]. Pregnancy-related activation and aggregation of platelets leads to elevated MPV levels, which serve as key molecular mechanisms during VTE development. Research findings demonstrated that MPV shows a significant correlation with VTE occurrences in pregnant women. Research by Udeh et al. (2024) showed that PDW functions as an activation and distribution marker for platelets while indicating higher VTE risk in pregnant women [30]. The current studies examining the link between PCT and VTE during pregnancy remain limited, but existing data shows PCT's potential to identify patients at risk for VTE development [31].

Endothelial dysfunction in pregnancy with VTE leads to microvascular fibrin deposits, which result in the production of fibrin clots and subsequently elevated levels of D-dimer. Increased D-dimer levels are associated with a higher risk of VTE during pregnancy. A recent study by researchers Van der Pol et al. (2017) emphasized D-dimer testing in pregnancy VTE diagnosis since combining it with clinical assessments gave it better accuracy [32]. Numerous studies have demonstrated that increased D-dimer levels are correlated with a greater risk of VTE both during pregnancy and the postpartum period [33,34]. Consistent with these findings, this study also observed significantly higher D-dimer levels in pregnant women with VTE. Similarly, Zhang et al. (2021) noted that increased D-dimer concentration is an independent risk factor for VTE during pregnancy and after childbirth [35]. These studies are in support of this study, as there were high D-dimer levels recorded from pregnant women who had VTE.

The strong correlations between the parameters emphasize the potential effectiveness of measuring platelet indices and inflammatory markers in assessing thrombotic risks during pregnancy, which further helps to get better outcomes for those at risk of thromboembolic complications. Ataullakhanov et al.'s (2016) study indicated that platelet indexes efficiently identify hypercoagulation state, including in pregnant women at risk of thromboembolic process [36].

Therefore, the examined forecast markers are potent in VTE as they include NLR and PLR, both of which are inflammatory markers that facilitate thrombus formation. Riondino et al. (2019) pointed out that, preceded by other investigations, their finding highlighted that the inclusion of the platelet indices to the models with inflammatory biomarkers could increase the predictive accuracy of VTE [37]. Based on the findings of this study, the parameters above are effective in identifying pregnant women at high risk for thromboembolic conditions about which intervention could be recommended.

Conclusion

The results of the presented study describe relationships of platelet counts, NLR, PLR, and D-dimer regarding VTE during pregnancy. These findings imply that pregnant women with VTE have a higher MPV, PDW, and D-dimer, higher NLR, and PLR, revealing an activated platelet and inflammatory state. These biomarkers have the potential to aid in recognizing patients at a high risk of VTE and improving VTE risk stratification. The results support assessing the clinical value of these parameters to enhance maternity health and derive effective preventive and curative measures for VTE during the prenatal period.

Declaration

This research study involves human participants and complies with the regulations and guidelines provided by the Clinical Research Center of Lanzhou University Second Affiliated Hospital.

Ethical Approval

The ethical committee of Lanzhou University Second Affiliated Hospital has approved this research. The written informed consent was sought and received from all the participants and/or their legal guardians.

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Authors Contributions

Shristy Manandhar and He Rong Xia developed and designed the study. Shristy Manandhar, Isha Manandhar, and Shiva Raj Pudasaini have done the data analysis and interpretation. Shristy Manandhar is the one who gathered the data and from whence prepared the raw manuscript. Moreover, it was appreciated that Kiran Acharya and Prajana Thapa contributed to critical revisions of the manuscript and gave final approval before submitting the final manuscript.

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