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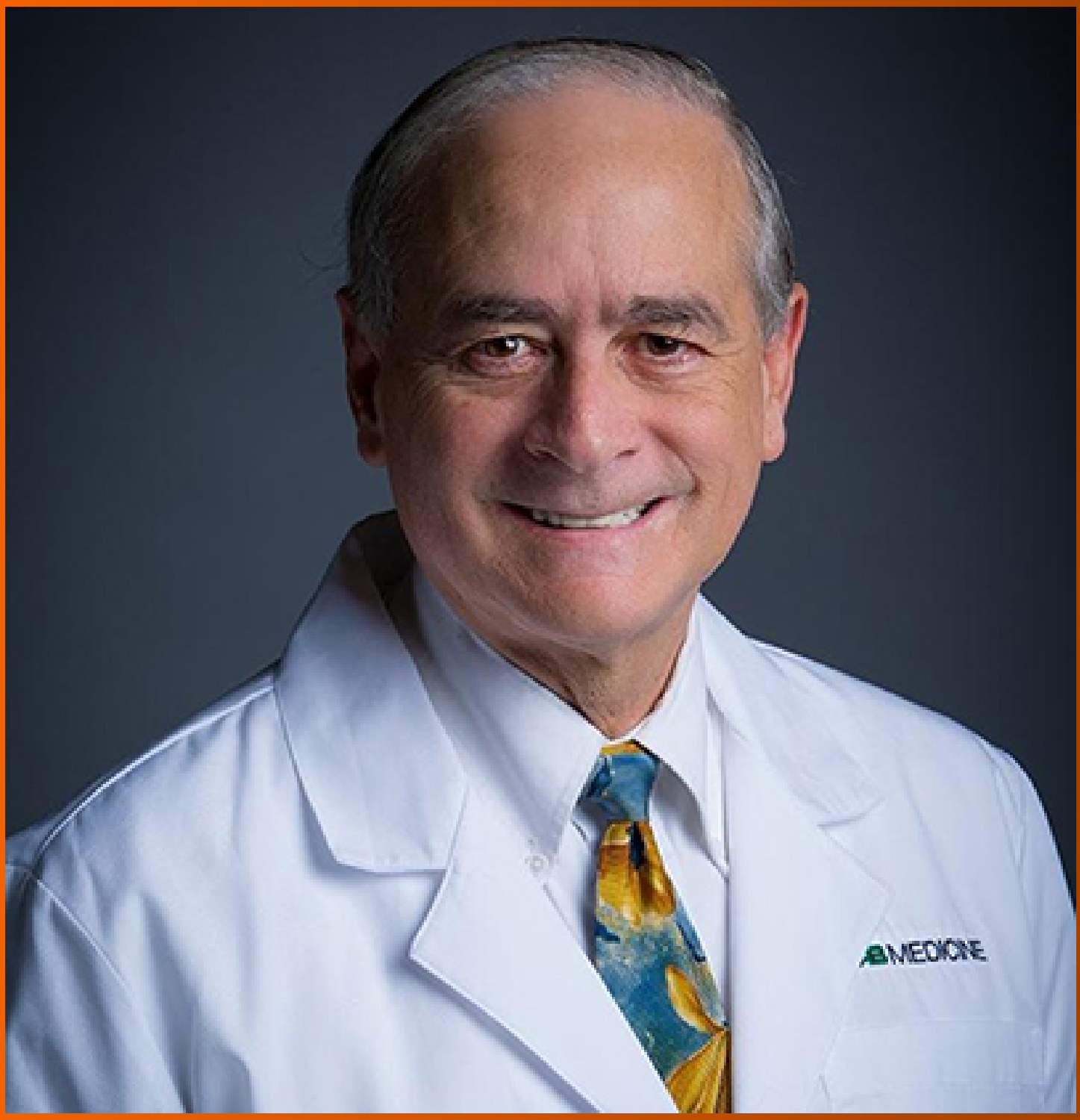

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Contents

Continuous Publication Volume 12 Number 3 May 11, 2023

ORIGINAL ARTICLE

Observational Study

CASE REPORT

World Journal of Obstetrics and Gynecology

Continuous Publication Volume 12 Number 3 May 11, 2023

Contents

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The primary aim of *World Journal of Obstetrics and Gynecology* (*WJOG*, *World J Obstet Gynecol*) is to provide scholars and readers from various fields of obstetrics and gynecology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

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ORIGINAL ARTICLE

Observational Study

Clinical implication of platelet to lymphocyte ratio in early onset preeclampsia: A single-center experience

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Abstract

BACKGROUND

Preeclampsia (PE) is a pregnancy syndrome of undetermined etiology; inflammation was one of the proposed theories for its development.

AIM

To examine the platelet to lymphocyte ratio (PLR), an inflammatory biomarker, as a marker to predict poor maternal-neonatal outcomes in early-onset PE (EoPE).

METHODS

A cross-sectional study enrolled 60 pregnant women with EoPE (at 32-30 wk of gestation) at a university hospital. Demographic criteria and hematological indices were collected, including platelet counts and indices (mean platelet volume and platelet distribution width), PLR, and the Doppler study, which calculated estimated fetal weight (EFW), amniotic fluid index (AFI), resistance index (RI), and pulsatility index (PI). Participants were followed until delivery, where maternal outcomes were recorded, including; delivery mode and reason for cesarean section, and neonatal outcomes, including fetal growth restriction (FGR), meconium-stained liquid, the 5-min Apgar score, and admission to the intensive care unit.

RESULTS

There was a trend of insignificant increases in cesarean sections. Sixty-one-point two percent (37/60) fetuses were admitted to the neonatal care unit; 70.0% of admitted fetuses were meconium-stained liquor, and 56.7% of them had FGR. PLR was positively correlated with AFI and EFW as r = 0.98, 0.97, P < 0.001; PLR showed negative correlations with PI and RI as r = -0.99, -0.98, P < 0.001. The Apgar score and the number of days admitted to the intensive care unit had a positive and negative correlation (0.69, -0.98), P < 0.0001, respectively. Receiver

operating characteristic calculated a PLR cutoff value (7.49) that distinguished FGR at 100% sensitivity and 80% specificity.

CONCLUSION

Strong, meaningful relationships between PLR and FGR parameters and a poor neonatal outcome with a significant *P* value make it a recommendable biomarker for screening EoPE-related complications. Further studies are suggested to see the impact on maternal-neonatal health.

Key Words: Preeclampsia; Early onset; Maternal complication; Adverse perinatal outcome; Apgar score

Core Tip: Women with preeclampsia (PE) suffer increased morbidity and mortality; their offspring endure higher risks in the early neonatal period and later life. Despite extensive research into PE, the only definitive treatment is to terminate the pregnancy. Many seek efficient prediction methods that may reduce expected risk. Platelet to lymphocyte ratio (PLR), an inflammatory biomarker, was studied in PE; however, little is known about its role in early-onset PE, a subtype with serious consequences for fetal and maternal health. Herein, we examine the role of PLR, which showed a strong, meaningful relationship between fetal growth restriction and poor neonatal outcome, making PLR a recommendable screening parameter.

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INTRODUCTION

Preeclampsia (PE) is identified as new-onset hypertension in formerly normotensive pregnant women, combined with proteinuria, after the 20th wk of gestation; it affects 7% to 10% of all pregnancies. PE is primarily a placenta disease that can be early-onset or late-onset PE according to its onset below or above 32 wk of gestation[1,2]. Early-onset PE (EoPE) is a severe form of PE with a 0.35%-0.50% prevalence caused by inadequate recasting of the uterine spiral arteries and poor placental implantation. The hypoxic placenta produces excessive inflammatory mediators in maternal circulation as the pregnancy proceeds. As a result, vascular integrity is disrupted, and endothelial dysfunction occurs. The latter leads to hypertension, proteinuria, and other PE-related symptoms. The decreased perfusion to the fetus will reduce fetal growth rates; indeed, PE is a major cause of fetal growth restriction (FGR)[2-4].

FGR is linked to adverse obstetric effects, including higher cesarean sections (C-sections), poor neonatal outcomes; such as low Apgar scores, admission to the neonatal intensive care unit (NICU), and meconium-stained liquor, in addition to long-term health effects such as delayed neurodevelopmental milestones and adult cardiovascular disease[5-7].

Diagnosing FGR is made *via* serial ultrasound examination, which needs follow-up and patient compliance[3,8]. As a result, there was a necessity for prediction modules to assess current placental activity. Inflammation is a proposed cause of PE, and numerous inflammatory markers were examined to define PE severity and its related consequences[9-11]. Platelet turnover increases in the maternal circulation of PE women, which eventually reduces their numbers along with alterations in platelet size, and functionality; lymphocytes, on the other hand, will be increased in PE cases[12] owing to a maladaptive immune response and a hyper-inflammatory state in PE[13]. Therefore, the platelet to lymphocyte ratio (PLR) will decrease in severe PE cases as the numerator (platelets) decreases when divided by the increased denominator (lymphocyte). PLR has been studied for prognostic and predictive roles in various diseases, including PE and cancer prognosis. However, they presented inconsistent and sometimes contradicting results[11-13]. Moreover, PLR was not tested in EoPE.

We hypothesized that the reduction in PLR would predict poor obstetrical and neonatal outcomes in early-onset PE. We aimed to predict FGR through biological and ultrasonic markers for patients with EoPE as a primary goal. The secondary aim was to examine the correlation of PLR with predictors of maternal-fetal outcome.

MATERIALS AND METHODS

At the University Hospital in Baghdad, Iraq, a longitudinal study with a cross-sectional design recruited 60 eligible participants in June 2019 and ended in October 2020. The ethical committee of Mustansiriyah University approved the study (IRB 160, February 2019). The Declaration of Helsinki was followed in the study; all participants gave informed consent after we explained the study aims and methods prior to enrollment. The study participants were women with early-onset PE (less than 34 wk). Only women with severe PE were recruited (Figure 1).

Inclusion criteria

Pregnant between the ages of 18 and 40, with a gestational age of 30-32 wk, as determined by history and/or confirmed by an early ultrasound scan. They should not have started treatment. We aimed to have a narrow window in recruitment to make the study's demographics more uniform.

Exclusion criteria

Pregnant women with gestational age outside reference gestational age (> 32 wk and < 30 wk). Medical disorders like kidney and liver diseases, a personal or family history of thyroid, diabetes, or cardiovascular diseases, a personal history of chronic hypertension, blood dyscrasias, and anemia**.** Those with twin pregnancies and congenital fetal anomalies. Smoking mothers and those on aspirin or steroids were also excluded. Non-severe PE cases have been excluded.

Our hospital is a tertiary center that receives many cases of PE in addition to referred cases from the periphery of Baghdad. Admission, assessment of fetomaternal wellbeing, blood pressure control, accelerated lung maturity, and close follow-up for any deterioration of a pregnant mom or her unborn baby necessitating pregnancy termination are all part of the policy for managing severe EoPE.

Maternal assessment

A detailed history and general and obstetrical exams were conducted on the day of admission. In every case, maternal age, weeks of gestation, and systolic and diastolic blood pressure (SBP, DBP) were recorded while the patients were at rest. Lab tests were ordered, including blood biochemistry (serum creatinine, blood urea, alanine aminotransferase, and aspartate aminotransferase); a complete blood count to assess hematological indices hematocrit (10%), platelet distribution width, mean platelet volume, platelet counts, lymphocyte count, where the PLR was created; and a urine sample for evaluating total protein excreted.

Fetal assessment

On the same day of admission, an ultrasound scan was arranged to assess fetal wellbeing [gestational age, amniotic fluid index (AFI), estimated fetal weight (EFW), signs of fetal growth resection (FGR)]. A color Doppler spectral study measured uterine artery pulsatility and resistance index (PI and RI).

Cases were followed until delivery, at which point the maternal outcomes, including; the mode of delivery and reason for a C-section, were recorded. In addition, the neonatal outcome included meconium-stained liquor, a 5-min Apgar score, and admission to the NICU. The information was saved on an Excel sheet so that it could be analyzed later.

Defining study parameters

PE was defined according to the ACOG technical bulletin No. 219 (American College of Obstetricians and Gynecologists), which includes patients with a systolic blood pressure of 140 mmHg or a diastolic blood pressure of 90 mmHg following 20 wk of gestation and albuminuria of > 300 mg or a sustained 1+ dipstick at 24 h. A gestational age of less than 32 wk defines EoPE[1].

Cases of severe PE had a systolic blood pressure of 160 mmHg or a diastolic blood pressure of 110 mmHg. In the absence of proteinuria, the diagnostic criteria for severe PE comprise hypertension plus thrombocytopenia, impaired liver function, pulmonary edema, new development of renal insufficiency, or new-onset cerebral or visual problems[2].

The early-onset FGR was defined as ultrasonic EFW or fetal abdomen circumference less than the 3rd percentile using a population chart, or EFW or fetal abdominal circumference less than the 10th percentile correlated with umbilical artery PI more than the 95th percentile, or cerebroplacental ratios less than the 5th percentile[3,8].

The sample size was calculated according to the following equation for a cross-sectional study with quantitative variables[14]: Z1-α/2 = is a standard normal variate which is equal to 1.96; SD = standard deviation of a variable calculated by earlier published works; d = the precision level decided by the operator; sample size = $(1.96)^2$ $(0.35)^2/(0.1)^2$ = (3.84 × 0.1225)/0.01 = 43 patients. So, the sample size is 43 patients; we recruited 60 cases.

Statistical analysis

The statistical analysis of the data was carried out through Microsoft Office Excel 2016 and the SPSS 26 program. The numerical data were expressed as mean, standard deviation. Categorical data were

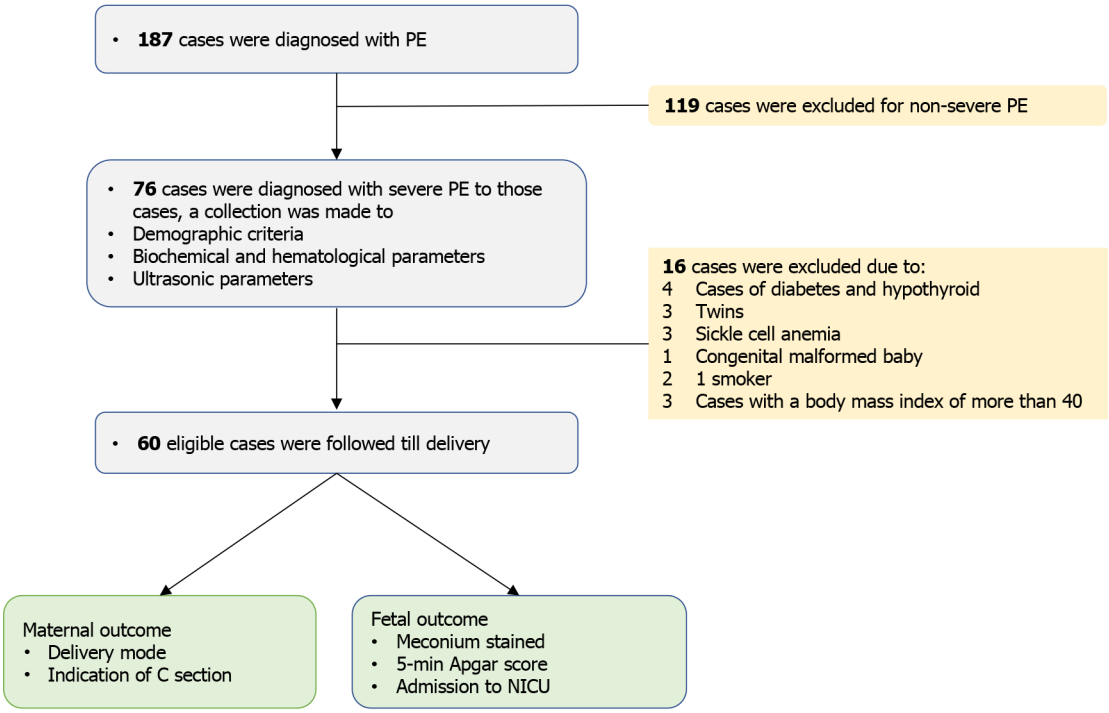

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Figure 1 Study flow chart. PE: Preeclampsia; NICU: Neonatal intensive care unit.

presented as numbers and percentages. Linear regression assessed the correlation between PLR and the study parameters, including maternal and neonatal outcomes. The receiver operating characteristic (ROC) curve was constructed to calculate the PLR that correlates with FGR at the highest sensitivity and specificity. All tests were considered significant when the *P* value was 0.05.

RESULTS

This study examined 60 pregnant women diagnosed with severe PE at a gestational age of 32-30 wk. Table 1 shows the primary criteria of the study. The mean maternal age was 27.0 years ± 2.6 years, the PLR ratio was 7.86 ± 1.75, the EFW was 1.30 ± 0.08, the days of admission to the NICU were 7.09 d ± 2.05 d, and the mean Apgar score was 6.54 ± 1.60. Table 2 describes the maternal outcome in terms of cesarean section (C-section), which showed a trend toward a higher percentage *vs* vaginal delivery with no statistical significance (65% *vs* 35%). Table 3 describes the neonatal outcome of the delivered newborn. Of the total fetuses studied, 37/60 (61.2%) were admitted to the NICU. Seventy percent of admitted fetuses were meconium-stained liquor. The occurrence of meconium-stained liquor was significantly higher among admitted cases. The FGR was reported in 56.7% of the admitted fetuses, which is significantly higher in admitted fetuses. The lowest Apgar scores were found in the admitted cases to the NICU. A statistically significant difference was confirmed in the admission to the NICU between different Apgar scores. The percentage of dead fetuses is not statistically significant between admitted and unadmitted fetuses in Table 4. PLR, taken as an independent variable, was correlated with the FGR parameters (AFI, EFW, PI, and RI). All correlations were strongly significant, as the correlation coefficients (*r*) were (0.98, 0.97, -0.99, -0.98), respectively, with $P < 0.001$. As for newborn parameters, the Apgar score showed a positive correlation of 0.69, while admission days to the NICU showed a strong inverse correlation of -0.98; both had a $P < 0.0001$. The ROC curve calculated a PLR cutoff value < 7.49, an AUC of 0.8, and $P < 0.001$, which was correlated at 100% sensitivity and 80% specificity with FGR, as described in Table 5.

DISCUSSION

Analysis showed a strong, meaningful correlation of PLR to parameters that define FGR, which indicates PLR reliability in FGR prediction. The strong link between PLR and neonatal outcomes, such as Apgar score and number of days in the NICU, suggests that PLR is a good predictor of neonatal outcome.

Table 1 Primary characteristics of the studied group

Maternal demographic and biochemical parameter, *n* = 60	
Maternal age in yr	27.0 ± 2.6
Mean systolic BP in mL/Hg	160.2 ± 5.2
Mean diastolic BP in mL/Hg	105.2 ± 4.7
Urine for albumin in gm/dL	2.89 ± 0.09
Serum creatinine in mg/dL	0.86 ± 0.52
Blood urea in mg/dL	29.38 ± 14.04
Alanine aminotransferase in U/L	27.43 ± 5.32
Aspartate aminotransferase in U/L	21.80 ± 4.49
Maternal hematological indices, *n* = 60	
Hematocrit, 10%	36.58 ± 2.81
Platelet count as × 10^9	182.40 ± 47.42
MPV in fL	10.52 ± 0.23
PDW in fL	16.68 ± 1.37
PLR ratio	7.86 ± 1.75
Fetal demographic criteria, *n* = 60	
Fetal AFI in cm	6.60 ± 1.19
Estimated fetal weight FW in kg	1.360 ± 0.08
PI UA Doppler	3.29 ± 0.59
RI UA Doppler	3.13 ± 0.55
Admission to NICU in d	7.09 ± 2.05
Mean Apgar score	6.54 ± 1.60

Data are mean ± SD. AFI: Amniotic fluid index; BP: Blood pressure; FW: Fetal weight; MPV: Mean platelet volume; NICU: Neonatal intensive care unit; PDW: Platelet distribution width; PI: Pulsatility index; PLR: Platelet to lymphocyte ratio; RI: Resistance index; UA: Uterine artery.

Table 2 Maternal outcome for the enrolled participants, *n* = 60

Parameter	Study participants presented	*n* (%)	*P* value
Mode of delivery	Vaginal delivery	21 (35)	< 0.407
	Cesarean delivery	39 (65)	
Indication for CS delivery	Previous scar	13 (22.5)	< 0.190
	Fetal distress	12 (20)	
	Failed induction	11 (17.5)	
	Malpresentation	3 (5)	

According to Mannaerts *et al*[15], PLR was low among the EoPE group compared to healthy controls. They confirmed that PLR tends to decrease after 20 wk of gestation in patients destined to have PE. Their results were in good agreement with the Yücel *et al*[16], which confirmed a lower PLR among severe PE cases compared to mild PE and healthy controls. Sisti *et al*[17] examined PLR in a case-control study involving cases of HELLP syndrome and healthy controls. Their analysis confirmed lower PLR among affected patients. They suggested that the ratio be included in the HELLP syndrome prediction mode.

Our results showed a strong positive link between PLR and AFI. Less blood flow to the placenta and ischemia cause less blood flow to the fetal kidneys, which lowers AFI[10].

The PLR showed a significant positive correlation with the EFW. Likewise, Can *et al*[18] investigated PLR and NLR in relation to birth weight in healthy and malnourished term babies. Both ratios were

Table 3 Neonatal outcome of the delivered newborn (*n* = 60) presented as numbers and percentage

Variable		Admitted, *n* = 37	Not admitted, *n* = 23	*P* value
Meconium	Meconium stain	26 (70%)	0 (0%)	0.000
	No meconium	11 (30%)	23 (100%)	
Occurrence of FGR	FGR	21 (56.7%)	0 (0%)	0.000
	No FGR	16 (43.3%)	23 (100%)	
Apgar score	> 7	0 (0%)	19 (51.3%)	0.000
	5-7	5 (21.7%)	18 (48.7%)	
	< 5	23 (78.3%)	0 (0%)	
Occurrence of dead fetus	Dead fetus	2 (5%)	0 (0%)	0.257
	Not dead fetus	35 (95%)	23 (100%)	

FGR: Fetal growth restriction.

Table 4 Correlation between the platelet to lymphocyte ratio and the studied variables

PLR *vs* variables	Correlation coefficient	*P* value
AFI	0.98	< 0.001
EFW	0.97	< 0.001
PI	-0.99	< 0.001
RI	-0.98	< 0.001
Apgar score	0.69	< 0.0001
Admission days to NICU	-0.98	< 0.0001

AFI: Amniotic fluid index; EFW: Estimated fetal weight; NICU: Neonatal intensive care unit; PI: Pressure index; PLR: Platelet to lymphocyte ratio; RI: Resistance index; UA: Uterine artery.

Table 5 Receiver operating characteristic curve defined the platelet to lymphocyte ratio cutoff value that discriminated fetal growth restriction with the utmost sensitivity and specificity

Parameter	Cutoff value	Sensitivity	Specificity	AUC	*P* value
PLR	< 7.49	100%	80%	0.9	< 0.001

AUC: Area under the curve; PLR: Platelet to lymphocyte ratio.

significantly high in the malnourished study division; they were recommended as reliable markers.

Akgun *et al*[19] investigated PLR with birth weight and gestational age. Their results show a significant correlation with birth weight. Furthermore, a significant correlation was found between infants' birth weight and gestational age. Kırmızı *et al*[20] examined PLR and NLR in late onset FGR in a case-control study. They did not recommend PLR as its levels were statistically insignificant compared to the NLR. Their study had a small sample size, which may explain the shortcomings of their results.

Both PI and RI were strongly correlated with PLR, which was consistent with previous research linking changes in PI and RI waveforms of uterine arteries to the development of PE and FGR[21]. A Cochrane review also showed that the use of a doppler can help reduce the number of C-sections, labor inductions, and perinatal deaths in FGR babies[22].

Platelet indices, along with PI and RI, were suggested by Abdel Razik *et al*[23] as a way to measure the severity of PE rather than predict its onset.

In terms of obstetric outcomes, 60.0% of cases were ended by C-section, 61.2% of fetuses were admitted to the neonatal care unit, 70.0% were meconium-stained, and 56.7% of the meconium-stained fetuses had FGR, which led to a lower Apgar score among admitted cases. Our results were in line with the study of Jha *et al*[24], where significant differences were seen in the PE groups they examined. In

addition to low Apgar scores at 1st and 5th min and on admission days to the NICU[24].

In the current study, the Apgar score showed a significant *P* value among newborns with a positive correlation to PLR. Okoye *et al*[25] discussed lower PLR in neonates of PE women, which correlates with hypertension severity. PLR has also been linked to poor birth outcomes, as evidenced by low Apgar scores. Their study examined PLR and other blood indices in the cord blood of neonates born to PE mothers. No meaningful association was seen between PLR and neonatal birth weight; it only correlated with 1st and 5-min Apgar scores in newborns.

Kim *et al*[26] discussed a considerably low PLR in women with severe PE. It was most strongly related to the time of admission to the delivery interval.

According to the Özdemirci *et al*[27], PLR in late-onset FGR cases did not show a significant increase. They suggested that an exaggerated inflammatory response was proposed to be a cause for FGR and to be absent in late-onset FGR cases, emphasizing our findings and forming the novelty of our study.

PE is a major risk factor for growth restriction; insufficient spiral artery penetration during early implantation has been blamed for early-onset FGR. To supply the fetus with nutrients, the diseased placenta will develop a mechanism to overcome increased resistance to blood flow and decreased placenta perfusion[5]. Since blood is a primary interface between the fetus and mother, any stressful event will cause blood parameters passing through the placenta to be altered. Therefore, many researchers addressed blood indices, searching for biomarkers that correlate with PE and consequent FGR[10,28].

Different pathophysiologic mechanisms underlie PE sub-types. EoPE is the result of impaired placenta development and improper innate immune system activation that trigger a systemic inflammatory response as early as the second trimester. The injured endothelial cells secrete many cytokines and inflammatory markers into the circulation that cause changes in the complete blood film parameters in PE cases[29,30].

Platelet numbers will be reduced due to consumption. Lymphocyte numbers, key players in systemic inflammation, will be increased. These changes are thought to be responsible for maternal and fetal complications[11]. Hence, PLR forecasts an impending or ongoing inflammatory pathology.

The current study result may have a clinical implication by preventing PE-related complications. Patients with known inflammatory biomarkers may benefit from prophylactic doses of low molecular weight heparin, which has immunomodulatory and anti-inflammatory properties. Low-molecular-weight heparin was recommended to prevent adverse obstetrical problems[31].

We have to acknowledge some of the inconsistencies in earlier studies regarding the value of PLR. Morisaki *et al*[32] technical report explained that different blood ratios were caused by different gestational ages, attributing these inconsistencies to different maternal criteria, gestational age, and inflammatory responses among pregnant women. Our findings clearly demonstrated that there was no statistical correlation between the PLR and the mode of delivery or the indication of the delivery, which was consistent with previous studies that criticized the insignificant role of blood ratios in predicting maternal outcomes[33,34]. Since delivery is the only treatment for PE progression, we must evaluate maternal risk against newborn problems. For that, early and accurate detection is necessary[35,36].

Study limitations

The cross-sectional nature of this study is one since the causal effect cannot be elucidated[37]. A case-control study may perform better in confirming the link between PLR and EoPE. We aimed to collect a higher sample size; however, the COVID-19 pandemic limited many work aspects. It is worth mentioning that risk analysis for the prevention of PE was not done; we think that the current analysis served our aim well. The fact that the current study was a single-center experience may limit the globalization of its results.

Study strengths

Although PLR was examined in late-onset PE, its role in EoPE was not addressed earlier. This paper emphasizes the significance of PLR in predicting early-onset PE associated with FGR[38-40]. PLR was intimately linked to FGR parameters; moreover, it correlated with important predictors of neonatal outcome; its significant correlation to FGR EoPE with high sensitivity and specificity (100%, 80%) and a significant AUC of 0.9, $P < 0.001$ makes it a valuable predictor. Since PLR was already validated for PE and its related co-morbidities, we needed no external validation. FGR is responsible for 50% of unexplained stillbirths. Its implications extend beyond postpartum, as it increases neonatal morbidity and the risk of cardiovascular diseases in the offspring[41]. PLR is simple, inexpensive, and can guide clinicians and assist with the timely referral of affected women to tertiary care centers to halt adverse fetal outcomes. Further studies are needed to explore the future implications of PLR on fetal and maternal health and their predictive value for early childhood and adult-onset diseases.

CONCLUSION

PLR is a reliable predictor of adverse fetal outcomes, including FGR parameters, a poor Apgar score,

and admission to the neonatal care unit among pregnant women with EoPE. PLR had high sensitivity and specificity with no added expanders, making it a recommendable marker in their prediction. In light of the promising role of anti-coagulant use in preventing obstetrical-related complications, PLR may be used in predicting, categorizing, and preventing early-onset PE-related complications.

ARTICLE HIGHLIGHTS

Research background

Preeclampsia (PE) is a pregnancy condition with an unknown origin that includes two subtypes based on 34 wk of gestation: Early and late onset PE; inflammation was postulated as an explanation. The platelet to lymphocyte ratio (PLR), an inflammatory biomarker, was investigated as a predictor of poor maternal-neonatal outcome in patients with early-onset PE (EoPE).

Research motivation

Much research has shown that inflammation may be an underlying pathology that triggers PE development. There is an increased need for new methods with enhanced predictive ability. Demonstrating changes in blood indices, PLR seems an appealing option given the promising results declared by earlier work.

Research objectives

To ascertain if PLR in cases with early-onset PE can be linked to essential predictors of fetomaternal wellbeing during the intrapartum period. The second goal is to analyze the reliability of PLR as a helpful marker for monitoring prenatal predictors in women with early-onset PE.

Research methods

Cross-sectional research at University Hospital involved 60 pregnant women with EoPE (at 32-30 wk of gestation). Platelet counts and indices (mean platelet volume and platelet distribution width), PLR, Doppler study, which produced estimated fetal weight (EFW), amniotic fluid index (AFI), resistance index (RI), and pulsatility index (PI) were all gathered. Participants were tracked until birth, when maternal outcomes such as delivery style and reason for cesarean section were documented, as well as newborn outcomes such as fetal growth restriction (FGR), meconium-stained fluids, five-minute Apgar score, and admission to the critical care unit.

Research results

A cesarean section trend has been noted. Sixty-one-point two percent (37/60) fetuses were hospitalized to the newborn care unit, 70% had meconium-stained liquid, and 56.7% had FGR. PLR was shown to be favorably connected with AFI and EFW (r = 0.98, 0.97, P < 0.001), and negatively correlated with PI and RI (r = -0.99, -0.98, P < 0.001). The Apgar score and the number of days admitted to the critical care unit had a positive and negative connection (r = 0.69, -0.98, P < 0.001), respectively. The PLR cutoff value derived by receiver operating characteristic (7.49) differentiated FGR with 100% sensitivity and 80% specificity.

Research conclusions

PLR had substantial P value associations with FGR measures and poor neonatal outcomes, making it a promising biomarker for screening EoPE-related problems. More research is needed to determine the influence on maternal-neonatal health.

Research perspectives

Defining reliable biomarkers that are antenatal clinics based with no added expense can be a promising option, especially for low-resource settings.

FOOTNOTES

Author contributions: Akram W contributed to conception and statistical analysis; Abdullah Hussein Z and Hameed Humadi M contributed to data collection and scientific editing; Nori W wrote, edited, and drafted the final version; all authors read and approved the final version.

Institutional review board statement: The study was reviewed and approved by the ethical committee of Mustansiriyah University (No. 160).

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REFERENCES

1 **Hypertension in pregnancy**. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. *Obstet Gynecol* 2013; **122**: 1122-1131 [PMID: 24150027 DOI: 10.1097/01.AOG.0000437382.03963.88]
2 **He Y**, Xu B, Song D, Yu F, Chen Q, Zhao M. Correlations between complement system's activation factors and anti-angiogenesis factors in plasma of patients with early/late-onset severe preeclampsia. *Hypertens Pregnancy* 2016; **35**: 499-509 [PMID: 27315511 DOI: 10.1080/10641955.2016.1190845]
3 **Audette MC**, Kingdom JC. Screening for fetal growth restriction and placental insufficiency. *Semin Fetal Neonatal Med* 2018; **23**: 119-125 [PMID: 29221766 DOI: 10.1016/j.siny.2017.11.004]
4 **Bellos I**, Fitrou G, Pergialiotis V, Papantoniou N, Daskalakis G. Mean platelet volume values in preeclampsia: A systematic review and meta-analysis. *Pregnancy Hypertens* 2018; **13**: 174-180 [PMID: 30177049 DOI: 10.1016/j.preghy.2018.06.016]
5 **Pastén V**, Tapia-Castillo A, Fardella CE, Leiva A, Carvajal CA. Aldosterone and renin concentrations were abnormally elevated in a cohort of normotensive pregnant women. *Endocrine* 2022; **75**: 899-906 [PMID: 34826118 DOI: 10.1007/s12020-021-02938-0]
6 **Womersley K**, Ripullone K, Hirst JE. Tackling inequality in maternal health: Beyond the postpartum. *Future Healthc J* 2021; **8**: 31-35 [PMID: 33791457 DOI: 10.7861/fhj.2020-0275]
7 **Andraweera PH**, Lassi ZS. Cardiovascular Risk Factors in Offspring of Preeclamptic Pregnancies-Systematic Review and Meta-Analysis. *J Pediatr* 2019; **208**: 104-113.e6 [PMID: 30876753 DOI: 10.1016/j.jpeds.2018.12.008]
8 **Gordijn SJ**, Beune IM, Thilaganathan B, Papageorghiou A, Baschat AA, Baker PN, Silver RM, Wynia K, Ganzevoort W. Consensus definition of fetal growth restriction: a Delphi procedure. *Ultrasound Obstet Gynecol* 2016; **48**: 333-339 [PMID: 26909664 DOI: 10.1002/uog.15884]
9 **Perucci LO**, Corrêa MD, Dusse LM, Gomes KB, Sousa LP. Resolution of inflammation pathways in preeclampsia-a narrative review. *Immunol Res* 2017; **65**: 774-789 [PMID: 28391374 DOI: 10.1007/s12026-017-8921-3]
10 **Nori W**, Ali IA, Akram W. The Value of Serum Fibrinogen/Uric Acid Ratio as a Novel Marker of Fetal Growth Restriction in Preeclampsia at 34 wk. *Current Women's Health Reviews* 2023; **19**: e010322201543 [DOI: 10.2174/1573404818666220301125216]
11 **Nori W**, Roomi AB, Akram W. Platelet indices as predictors of fetal growth restriction in Preeclamptic Women. *Revista Latinoamericana de Hipertension* 2020; **15**: 280-285 [DOI: 10.5281/zenodo.4442971]
12 **Triggianese P**, Perricone C, Chimenti MS, De Carolis C, Perricone R. Innate Immune System at the Maternal-Fetal Interface: Mechanisms of Disease and Targets of Therapy in Pregnancy Syndromes. *Am J Reprod Immunol* 2016; **76**: 245-257 [PMID: 27108670 DOI: 10.1111/aji.12509]
13 **Harmon AC**, Cornelius DC, Amaral LM, Faulkner JL, Cunningham MW Jr, Wallace K, LaMarca B. The role of inflammation in the pathology of preeclampsia. *Clin Sci (Lond)* 2016; **130**: 409-419 [PMID: 26846579 DOI: 10.1042/CS20150702]
14 **Chow SC**, Shao J, Wang H, Lokhnygina Y. Sample size calculations in clinical research. *Biometrics* 2017; **64**: 1307-1308 [DOI: 10.1111/j.1541-0420.2008.01138_10.x]
15 **Mannaerts D**, Heyvaert S, De Cordt C, Macken C, Loos C, Jacquemyn Y. Are neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), and/or mean platelet volume (MPV) clinically useful as predictive parameters for preeclampsia? *J Matern Fetal Neonatal Med* 2019; **32**: 1412-1419 [PMID: 29179639 DOI:

10.1080/14767058.2017.1410701]
16 **Yücel B**, Ustun B. Neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, mean platelet volume, red cell distribution width and plateletcrit in preeclampsia. *Pregnancy Hypertens* 2017; **7**: 29-32 [PMID: 28279444 DOI: 10.1016/j.preghy.2016.12.002]
17 **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 (Kaunas)* 2019; **55** [PMID: 31072037 DOI: 10.3390/medicina55050123]
18 **Can E**, Can C. The value of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) parameters in analysis with fetal malnutrition neonates. *J Perinat Med* 2019; **47**: 775-779 [PMID: 31318695 DOI: 10.1515/jpm-2019-0016]
19 **Akgun N**, Namli Kalem M, Yuce E, Kalem Z, Aktas H. 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 [PMID: 27678153 DOI: 10.1080/14767058.2016.1237497]
20 **Kırmızı DA**, Baser E, Onat T, Caltekin MD, Kara M, Yalvac ES. Can Inflammatory Hematological Parameters be a Guide to Late-onset Fetal Growth Restriction? *Z Geburtshilfe Neonatol* 2020; **224**: 262-268 [PMID: 32590874 DOI: 10.1055/a-1177-1516]
21 **Cnossen JS**, Morris RK, ter Riet G, Mol BW, van der Post JA, Coomarasamy A, Zwinderman AH, Robson SC, Bindels PJ, Kleijnen J, Khan KS. Use of uterine artery Doppler ultrasonography to predict pre-eclampsia and intrauterine growth restriction: a systematic review and bivariable meta-analysis. *CMAJ* 2008; **178**: 701-711 [PMID: 18332385 DOI: 10.1503/cmaj.070430]
22 **Dall'Asta A**, Brunelli V, Prefumo F, Frusca T, Lees CC. Early onset fetal growth restriction. *Matern Health Neonatol Perinatol* 2017; **3**: 2 [PMID: 28116113 DOI: 10.1186/s40748-016-0041-x]
23 **Abdel Razik M**, Mostafa A, Taha S, Salah A. Combined Doppler ultrasound and platelet indices for prediction of preeclampsia in high-risk pregnancies. *J Matern Fetal Neonatal Med* 2019; **32**: 4128-4132 [PMID: 29804487 DOI: 10.1080/14767058.2018.1481953]
24 **Jha UC**, Dangal G. Fetal Outcome in Cesarean Versus Normal Deliveries in Pregnancy with Meconium-stained Liquor: A Cross-sectional Study. *J Nepal Health Res Counc* 2021; **19**: 107-110 [PMID: 33934143 DOI: 10.33314/jnhrc.v19i1.2856]
25 **Okoye HC**, Madu AJ, Korubo K, Efobi C, Eze OE, Obodo O, Okereke K, Ilechukwu G. Correlates of neutrophil/lymphocyte, platelet/lymphocyte, and platelet/neutrophil ratios of neonates of women with hypertensive disease of pregnancy with neonatal birth outcomes. *Hypertens Pregnancy* 2019; **38**: 105-110 [PMID: 30835575 DOI: 10.1080/10641955.2019.1584819]
26 **Kim MA**, Han GH, Kwon JY, Kim YH. Clinical significance of platelet-to-lymphocyte ratio in women with preeclampsia. *Am J Reprod Immunol* 2018; **80**: e12973 [PMID: 29781540 DOI: 10.1111/aji.12973]
27 **Özdemirci Ş**, Başer E, Kasapoğlu T, Karahanoğlu E, Kahyaoglu I, Yalvaç S, Tapısız Ö. Predictivity of mean platelet volume in severe preeclamptic women. *Hypertens Pregnancy* 2016; **35**: 474-482 [PMID: 27314286 DOI: 10.1080/10641955.2016.1185113]
28 **Nori W**, Hamed RM, Roomi AB, Akram W. Alpha-1antitrypsin in pre-eclampsia; from a clinical perspective. *J Pak Med Assoc* 2021; **71** Suppl 8: S53-S56 [PMID: 35130219]
29 **Aneman I**, Pienaar D, Suvakov S, Simic TP, Garovic VD, McClements L. Mechanisms of Key Innate Immune Cells in Early- and Late-Onset Preeclampsia. *Front Immunol* 2020; **11**: 1864 [PMID: 33013837 DOI: 10.3389/fimmu.2020.01864]
30 **Örgül G**, Aydın Haklı D, Özten G, Fadiloğlu E, Tanacan A, Beksaç MS. First trimester complete blood cell indices in early and late onset preeclampsia. *Turk J Obstet Gynecol* 2019; **16**: 112-117 [PMID: 31360585 DOI: 10.4274/tjod.galenos.2019.93708]
31 **Beksac MS**, Tanacan A, Ozten G, Cakar AN. Low-dose low-molecular-weight heparin prophylaxis against obstetrical complications in pregnancies with metabolic and immunological disorder-associated placental inflammation. *J Matern Fetal Neonatal Med* 2022; **35**: 1546-1553 [PMID: 32354247 DOI: 10.1080/14767058.2020.1760834]
32 **Morisaki N**, Piedvache A, Nagata C, Michikawa T, Morokuma S, Kato K, Sanefuji M, Shibata E, Tsuji M, Shimono M, Ohga S, Kusuhara K; Japan Environment and Children's Study Group. Maternal blood count parameters of chronic inflammation by gestational age and their associations with risk of preterm delivery in the Japan Environment and Children's Study. *Sci Rep* 2021; **11**: 15522 [PMID: 34330940 DOI: 10.1038/s41598-021-93101-2]
33 **Yakiştiran B**, Tanaçan A, Altinboğa O, Erol A, Şenel S, Elbayiyev S, Yücel A. Role of derived neutrophil-to-lymphocyte ratio, uric acid-to-creatinine ratio and Delta neutrophil index for predicting neonatal outcomes in pregnancies with preeclampsia. *J Obstet Gynaecol* 2022; **42**: 1835-1840 [PMID: 35290156 DOI: 10.1080/01443615.2022.2040968]
34 **Aydoğan Kırmızı D**, Onat T, Başer E, Demir Çaltekin M. Letter to Editor. *Turk J Obstet Gynecol* 2019; **16**: 278-279 [PMID: 32231862 DOI: 10.4274/tjod.galenos.2019.93585]
35 **Melamed N**, Baschat A, Yinon Y, Athanasiadis A, Mecacci F, Figueras F, Berghella V, Nazareth A, Tahlak M, McIntyre HD, Da Silva Costa F, Kihara AB, Hadar E, McAuliffe F, Hanson M, Ma RC, Gooden R, Sheiner E, Kapur A, Divakar H, Ayres-de-Campos D, Hiersch L, Poon LC, Kingdom J, Romero R, Hod M. FIGO (international Federation of Gynecology and obstetrics) initiative on fetal growth: best practice advice for screening, diagnosis, and management of fetal growth restriction. *Int J Gynaecol Obstet* 2021; **152** Suppl 1: 3-57 [PMID: 33740264 DOI: 10.1002/ijgo.13522]
36 **Helou A**, Walker S, Stewart K, George J. Management of pregnancies complicated by hypertensive disorders of pregnancy: Could we do better? *Aust N Z J Obstet Gynaecol* 2017; **57**: 253-259 [PMID: 27396975 DOI: 10.1111/ajo.12499]
37 **Solem RC**. Limitation of a cross-sectional study. *Am J Orthod Dentofacial Orthop* 2015; **148**: 205 [PMID: 26232823 DOI: 10.1016/j.ajodo.2015.05.006]
38 **Cornelius DC**. Preeclampsia: From Inflammation to Immunoregulation. *Clin Med Insights Blood Disord* 2018; **11**: 1179545X17752325 [PMID: 29371787 DOI: 10.1177/1179545X17752325]
39 **Stojkovic Lalosevic M**, Pavlovic Markovic A, Stankovic S, Stojkovic M, Dimitrijevic I, Radoman Vujacic I, Lalic D, Milovanovic T, Dumic I, Krivokapic Z. Combined Diagnostic Efficacy of Neutrophil-to-Lymphocyte Ratio (NLR),

Platelet-to-Lymphocyte Ratio (PLR), and Mean Platelet Volume (MPV) as Biomarkers of Systemic Inflammation in the Diagnosis of Colorectal Cancer. *Dis Markers* 2019; **2019**: 6036979 [PMID: 30800188 DOI: 10.1155/2019/6036979]

40 **Biswas M**, Belle VS, Maripini N, Prabhu K. Neutrophil-lymphocyte ratio in pregnancy-associated maternal complications: A review. *Asian Pac J Reproduct* 2021; **10**: 252 [DOI: 10.4103/2305-0500.331262]

41 **Nardozza LM**, Caetano AC, Zamarian AC, Mazzola JB, Silva CP, Marçal VM, Lobo TF, Peixoto AB, Araujo Júnior E. Fetal growth restriction: current knowledge. *Arch Gynecol Obstet* 2017; **295**: 1061-1077 [PMID: 28285426 DOI: 10.1007/s00404-017-4341-9]

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CASE REPORT

Stone accumulation overlying vaginal mesh exposure: A case report

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Abstract

BACKGROUND

Vaginal stones are rare with current literature limited to case reports. Vaginal stones are classified as primary or secondary stones. Primary stones form in the vagina when there is urinary stasis. Secondary stones form in the presence of a vaginal foreign body that acts as a nidus for the deposition of urinary salts. Foreign bodies, such as surgical mesh, make vaginal stone formation more likely, particularly in patients with urinary incontinence and conditions that predispose them to urinary calculi formation.

CASE SUMMARY

A 71-year-old female with a history of sacrocolpopexy, hyperaldosteronism, and urgency urinary incontinence presented with vaginal stone accumulation overlying two areas of vaginal sacrocolpopexy mesh exposure. The vaginal stones were initially removed to permit examination, but the stones reaccumulated at the site of the exposed mesh, later requiring definitive surgical management.

CONCLUSION

Patients with vaginal mesh exposure and conditions that predispose them to kidney stones are not ideal candidates for expectant management of mesh exposure, particularly if they have coexisting urinary incontinence. These individuals should be counseled about possible vaginal stone accumulation, and surgical management should be considered.

Key Words: Vaginal stones; Urgency urinary incontinence; Sacrocolpopexy; Mesh complications; Mesh exposure; Case report

Core Tip: Patients with vaginal mesh exposure that have underlying conditions that predispose them to urinary calculi formation may be at increased risk of vaginal stone accumulation at the site of mesh exposure. Expectant management of the mesh exposure likely allows vaginal stones to accumulate as urine is persistently in contact with the foreign body. Definitive surgical management in the form of complete excision of the entire area of exposed mesh should be recommended to patients to avoid vaginal stone accumulation.

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INTRODUCTION

Vaginal foreign bodies, such as surgical mesh, are risk factors for the formation of secondary vaginal stones. When urine has prolonged contact with an exposed foreign body, secondary vaginal stones can form due to crystallization of stagnant urine. Urinary incontinence is therefore thought to contribute to vaginal stone formation[1]. We propose that individuals with exposed vaginal mesh and underlying medical conditions that place them at increased risk of kidney stones are prone to forming secondary vaginal stones. Following the CARE Checklist (2016) and with signed patient consent, we present the unique case of a patient with hyperaldosteronism and urgency urinary incontinence who had vaginal stone formation and later reaccumulation at the site of sacrocolpopexy mesh exposure.

CASE PRESENTATION

Chief complaints

A 71-year-old G4P4004 Caucasian female with known vaginal sacrocolpopexy mesh exposure that she previously opted to expectantly manage presented to urogynecology clinic with complaints of overactive bladder and urgency urinary incontinence.

History of present illness

The patient's symptoms of overactive bladder and urgency urinary incontinence had been worsening for about four years. Her urinary incontinence was nearly constant with dribbling throughout the day. Previous trials of oxybutynin, mirabegron, and solfenacin were ineffective.

History of past illness

In 2014, the patient underwent robotic-assisted supracervical hysterectomy, bilateral salpingo-oophrectomy, mesh sacrocolpopexy, posterior colporrhaphy, perineorrhaphy, retropubic midurethral sling insertion, and cystoscopy. One year after surgery, two areas of mesh exposure were identified at the anterior and posterior apices involving the sacrocolpopexy mesh. The patient was asymptomatic and opted to pursue expectant management. The patient was lost to follow-up until 2019 when she represented with the above chief complaint.

Personal and family history

Relevant personal history includes hyperaldosteronism, overactive bladder, urgency urinary incontinence, and tobacco use.

Physical examination

There was stone formation overlying the sacrocolpopexy mesh exposure sites at the anterior and posterior vaginal apices adjacent to the cervix. Given the degree of apical support maintained, office examination was difficult. Evaluation in the operating room was recommended.

In 2020, the patient underwent examination under anesthesia, cystourethroscopy, and vaginoscopy. On vaginoscopy, a midline anterior mesh exposure measuring approximately 3 cm (vertical) × 2 cm (transverse) × 3 mm (height) was identified with a 4 cm × 3 cm stone intermixed with the mesh fibers. A midline posterior mesh exposure measuring approximately 2.5 cm (vertical) × 0.5 cm (transverse) × 0.5 cm (height) was also identified with a 4 cm × 2 cm stone intermixed within the mesh fibers. Cystourethroscopy did not demonstrate any evidence of mesh exposure in the bladder or urethra, and vesicovaginal and urethrovaginal fistulae were specifically excluded. The majority of the calcifications were removed intraoperatively, which permitted improved visualization of the exposed mesh sites.

Laboratory examinations

Vaginal stone analysis was performed. The composition was noted to be 70% hydroxyapatite (calcium phosphate), 25% magnesium ammonium phosphate, and 5% ammonium acid urate.

Imaging examinations

None.

FINAL DIAGNOSIS

Following intraoperative evaluation, definitive surgical management with excision of the mesh exposure sites was planned. However, while awaiting surgery, the patient was in a motor vehicle accident requiring prolonged recovery. Additionally, factors related to coronavirus disease 2019 cases caused an approximately one-year delay in reevaluation. During this time, the vaginal stones reaccumulated at the exposed mesh sites. In 2021, mesh excision *via* a vaginal approach was performed. There was a 3 cm × 2 cm stone found anteriorly and a 2.5 cm × 0.5 cm stone found posteriorly. The stones were completely intermixed with the mesh strands (Figure 1). The patient was diagnosed with reaccumulation of vaginal stones at the site of exposed sacrocolpopexy mesh.

TREATMENT

The patient underwent excision of the entirety of the exposed mesh areas, concomitant removal of the stone material, and unremarkable cystourethroscopy. The stone analysis revealed a 100% hydroxyapatite composition.

OUTCOME AND FOLLOW-UP

The patient had no perioperative complications and did well postoperatively. On six-week follow-up examination, there was no evidence of continued mesh exposure or reaccumluation of vaginal stone material. The patient began intravesical onabotulinum toxin A injections for management of urgency urinary incontinence.

DISCUSSION

Sacrocolpopexy is a reconstructive surgical procedure that is performed to correct apical prolapse. A synthetic mesh is used to support the vagina, with or without the cervix, by affixing it to the anterior longitudinal ligament overlying the sacrum. The prevalence of mesh exposure following sacrocolpopexy is estimated to be as high as 10.5%[2]. While patients with mesh exposure may be asymptomatic, common presenting symptoms include pelvic pain, vaginal bleeding, and dyspareunia[3]. In this case, the patient was asymptomatic but was found to have vaginal stones on pelvic exam during follow-up examination. For a mesh exposure involving macroporous synthetic mesh, management strategies include expectant management, conservative management with the use of vaginal estrogen, or surgical management[3].

In general, data on vaginal stone formation are limited to case reports, and vaginal stones are therefore considered a rare phenomenon. Vaginal stones can be broadly categorized into primary or secondary stones. Primary stones typically result from urinary stasis within the vagina allowing for deposition of urinary salts. Some causes of primary stones include vaginal outlet obstruction, neurogenic bladder dysfunction, prolonged recumbent positioning such as in bedridden or paralyzed patients, and vesicovaginal, urethrovaginal, or ureterovaginal fistulae[4-7]. Secondary stones form in the vagina in the presence of a foreign body, such as contraceptive devices or exposed vaginal mesh, which acts as a nidus for urinary crystallization and subsequent stone formation[1].

Although limited data exist detailing the composition of vaginal stones, review of the current literature suggests that both primary and secondary vaginal stones are most commonly composed of struvite[1,4,5,8]. The proposed mechanism for struvite stone formation is that stasis of urine infected with urease-producing bacteria, such as *Klebsiella*, *Proteus mirabilis*, and *Escherichia coli*, causes the normally acidic environment of the vagina to become alkaline, which facilitates formation of struvite stones[9]. The first stone analysis for our patient revealed a predominantly hydroxyapatite composition (with a small struvite percentage), and the second stone analysis revealed 100% hydroxyapatite composition, which is a clear contrast to previously published cases of struvite vaginal stones. It is important to note that the composition of our patient's vaginal stones is more typical of kidney stones.

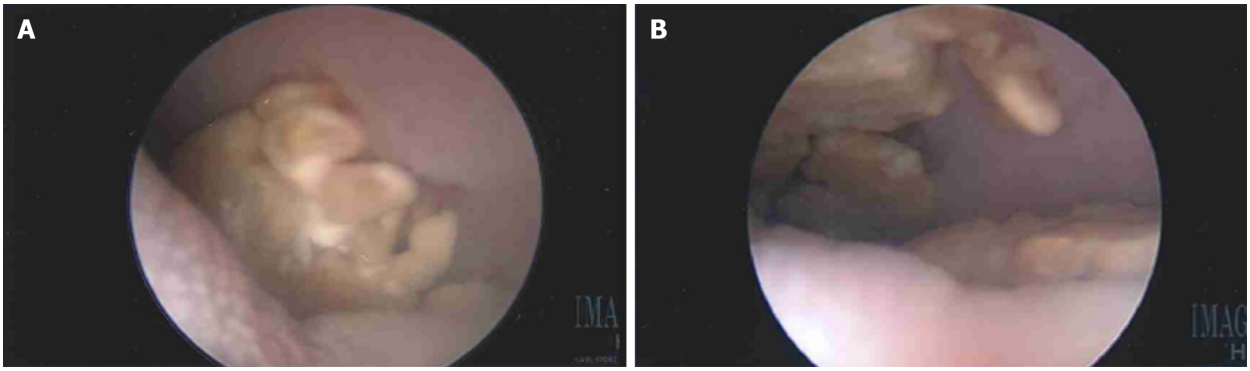

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Figure 1 Intraoperative image of vaginal stones. A and B: Vaginal stones overlying the site of sacrocolpopexy vaginal mesh exposure visualized during vaginoscopy.

The most common composition of kidney stones is calcium oxalate with a frequency of 67%, followed by hydroxyapatite stones with a frequency of 16%. Struvite kidney stones are relatively uncommon with a frequency of 3%[10].

The predominantly hydroxyapatite composition of our patient's vaginal stones is unusual since most published cases of vaginal stones report a struvite composition. Hydroxyapatite is more common for kidney stones. Our patient has no history of nephrolithiasis; but she does have hyperaldosteronism. We propose that this patient's history of hyperaldosteronism is responsible for the atypical composition of the secondary vaginal stones. Hyperaldosteronism causes hypercalciuria, phosphaturia, and hypocitraturia. These urinary changes are risk factors associated with kidney stone formation and recurrence [11]. In our patient's case, these urinary changes secondary to hyperaldosteronism likely contributed to the atypical composition of her vaginal stones, which more closely resemble that of the most common types of kidney stones rather than the typical struvite composition of vaginal stones. Therefore, it is prudent for clinicians to be aware of medical conditions that increase the risk of kidney stones because patients with such conditions may be at increased risk for forming vaginal stones.

In addition to the unusual hydroaxyapatite composition of this patient's vaginal stones, this patient's rapid reaccumulation of stone material overlying the mesh exposure after the initial stone removal is unique to this case. The reaccumulation suggests that patients with vaginal mesh exposure who are at increased risk of kidney stones may not be optimal candidates for expectant management, even if they have asymptomatic mesh exposure. This is particularly pertinent for individuals with risk factors for persistent contact of the mesh exposure to urine, such as significant urinary incontinence as with our patient. In addition, the short-interval reaccumulation of stones in this patient favors recommending excision of exposed mesh rather than temporizing measures, such as removal of the stone material only. Leaving exposed mesh is likely to result in reaccumulation of the vaginal stones.

Our patient's case highlights an example of vaginal stone formation overlying a vaginal mesh exposure in the setting of a medical condition that increases the risk of kidney stones. The stone analyses from this case suggest that individuals with underlying conditions that predispose them to kidney stones may be at increased risk of forming secondary vaginal stones with compositions that more closely resemble kidney stones rather than vaginal stones. This patient's case was also compounded by severe urgency urinary incontinence, which resulted in significant exposure of the mesh foreign body to urine. Individuals with a vaginal nidus, such as exposed mesh, that is in persistent contact with urine may be at higher risk of stone reaccumulation without definitive management. This case illustrates the importance of clinician awareness of conditions that increase the risk of kidney stones, as well as individualized patient counseling about the risk of developing stones overlying a mesh exposure. These patients are not optimal candidates for expectant management, and definitive surgical management with excision of the entire area of mesh exposure should be recommended.

CONCLUSION

Patients with vaginal mesh exposure and underlying conditions that predispose them to urinary calculi formation may not be ideal candidates for expectant management, especially if they have coexisting urinary incontinence. These individuals should be counseled about the possibility of stone accumulation, and surgical management should be considered. This unusual case adds to the current limited literature on vaginal stones. This case additionally helps to guide counseling of patients with vaginal mesh exposure that have concomitant risk factors for kidney stones and persistent contact of exposed mesh with urine.

FOOTNOTES

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REFERENCES

1 **Griffiths KM**, Towers GD, Yaklic JL. Vaginal Urinary Calculi Formation Secondary to Vaginal Mesh Exposure with Urinary Incontinence. *Case Rep Obstet Gynecol* 2017; **2017**: 8710315 [PMID: 28912989 DOI: 10.1155/2017/8710315]
2 **Nygaard I**, Brubaker L, Zyczynski HM, Cundiff G, Richter H, Gantz M, Fine P, Menefee S, Ridgeway B, Visco A, Warren LK, Zhang M, Meikle S. Long-term outcomes following abdominal sacrocolpopexy for pelvic organ prolapse. *JAMA* 2013; **309**: 2016-2024 [PMID: 23677313 DOI: 10.1001/jama.2013.4919]
3 **Crosby EC**, Abernethy M, Berger MB, DeLancey JO, Fenner DE, Morgan DM. Symptom resolution after operative management of complications from transvaginal mesh. *Obstet Gynecol* 2014; **123**: 134-139 [PMID: 24463673 DOI: 10.1097/AOG.0000000000000042]
4 **Jo JY**, Lee SM, Shin JK, Choi WJ, Cho IA. Huge vaginal stone: Case report and review of the literature. *Front Surg* 2022; **9**: 937371 [PMID: 35846952 DOI: 10.3389/fsurg.2022.937371]
5 **Aronson SL**, Hovius MC, Janszen EWM. Large primary vaginal stone in a woman with multiple sclerosis. *BMJ Case Rep* 2020; **13** [PMID: 33127724 DOI: 10.1136/bcr-2020-235103]
6 **Avsar AF**, Keskin HL, Catma T, Kaya B, Sivaslioglu AA. A large primary vaginal calculus in a woman with paraplegia. *J Low Genit Tract Dis* 2013; **17**: 61-65 [PMID: 22885639 DOI: 10.1097/LGT.0b013e31824d6f9c]
7 **Wei D**, Xie Y, Niu X. Vaginal stones caused by urethrovaginal fistula: A case report. *Medicine (Baltimore)* 2019; **98**: e18003 [PMID: 31764813 DOI: 10.1097/MD.0000000000018003]
8 **Raghavaiah NV**, Devi AI. Primary vaginal stones. *J Urol* 1980; **123**: 771-772 [PMID: 7420576 DOI: 10.1016/s0022-5347(17)56126-1]
9 **Malhotra N**, Kumar S, Roy KK, Agarwal R, Verma V. Vaginal calculus secondary to vaginal outlet obstruction. *J Clin Ultrasound* 2004; **32**: 204-206 [PMID: 15101082 DOI: 10.1002/jcu.20015]
10 **Levy FL**, Adams-Huet B, Pak CY. Ambulatory evaluation of nephrolithiasis: an update of a 1980 protocol. *Am J Med* 1995; **98**: 50-59 [PMID: 7825619 DOI: 10.1016/S0002-9343(99)80080-1]
11 **Lieske JC**, Rule AD, Krambeck AE, Williams JC, Bergstralh EJ, Mehta RA, Moyer TP. Stone composition as a function of age and sex. *Clin J Am Soc Nephrol* 2014; **9**: 2141-2146 [PMID: 25278549 DOI: 10.2215/CJN.05660614]

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