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Performance of the FMF First-Trimester Preeclampsia Screening Model and Aspirin Prophylaxis Outcomes in Vietnam: A Prospective Cohort Study

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Abstract

Early identification of women at high risk of preeclampsia enables timely preventive interventions, particularly low-dose aspirin prophylaxis. This prospective cohort study evaluated the performance of the Fetal Medicine Foundation (FMF) first-trimester screening model and assessed pregnancy outcomes following aspirin prophylaxis among singleton pregnancies between 11 weeks 3 days and 13 weeks 6 days of gestation at a tertiary center in Vietnam from November 2023 to November 2025. Screening integrated maternal characteristics, mean arterial pressure, uterine artery pulsatility index, and placental growth factor, with high-risk women receiving targeted aspirin prophylaxis (150 mg daily). Among 1187 analyzed pregnancies, 84 women (7.1%) were classified as high risk. The overall incidence of preeclampsia was 0.9%, with no cases occurring before 34 weeks of gestation. Preeclampsia was significantly associated with a lower gestational age at delivery, reduced birth weight, and higher rates of neonatal intensive care unit admission. Overall, the integration of the FMF first-trimester screening model with targeted aspirin prophylaxis demonstrated high feasibility and effectiveness, yielding favorable maternal and neonatal outcomes and supporting its broader implementation in clinical practice in Vietnam.

Keywords

Preeclampsia, First-Trimester Screening, FMF Model, Aspirin Prophylaxis

1. Introduction

Preeclampsia is a multisystem disorder of pregnancy characterized by new-onset

hypertension and organ dysfunction after 20 weeks of gestation. It affects approximately 2% - 8% of pregnancies worldwide and remains a major cause of maternal and perinatal morbidity and mortality, particularly in low- and middle-income countries [1]. Hypertensive disorders of pregnancy are responsible for a substantial proportion of maternal deaths globally and are also associated with adverse perinatal outcomes, including preterm birth, fetal growth restriction, and stillbirth [2].

The pathophysiology of preeclampsia is complex and is believed to involve abnormal placentation, impaired trophoblastic invasion of the spiral arteries, and endothelial dysfunction. These abnormalities result in reduced uteroplacental perfusion and an imbalance between angiogenic and anti-angiogenic factors, including decreased placental growth factor (PlGF) [3]. Because clinical manifestations usually appear in the second half of pregnancy, early identification of women at high risk has become an important strategy for prevention and management.

In recent years, several screening models have been developed to predict preeclampsia in early pregnancy. Among these, the screening algorithm proposed by the Fetal Medicine Foundation (FMF) has gained widespread attention. This model combines maternal demographic characteristics with biophysical and biochemical markers, including mean arterial pressure (MAP), uterine artery pulsatility index (UtA-PI), and maternal serum placental growth factor (PlGF) [4]. Previous studies have demonstrated that this combined screening approach can achieve high detection rates for early-onset preeclampsia with relatively low false-positive rates [5].

Early identification of high-risk pregnancies allows the implementation of preventive strategies such as low-dose aspirin. Evidence from the Aspirin for Evidence-Based Preeclampsia Prevention (ASPRE) trial demonstrated that administration of low-dose aspirin initiated before 16 weeks of gestation significantly reduced the incidence of preterm preeclampsia among women identified as high risk through first-trimester screening [6].

Despite the growing evidence supporting first-trimester screening for preeclampsia, most validation studies have been conducted in European populations. Data regarding the performance and feasibility of the FMF screening model in Southeast Asian populations, including Vietnam, remain limited. Differences in maternal characteristics and healthcare systems may influence the predictive performance of screening models.

Therefore, this study aimed to evaluate the performance of first-trimester preeclampsia screening using the FMF model and to assess the outcomes of aspirin prophylaxis among high-risk pregnant women at Quang Ninh Obstetrics and Pediatrics Hospital.

2. Materials and Methods

2.1. Study Design, Setting, and Timeline

This study was designed as a prospective observational cohort study with longitudinal follow-up and was conducted at Quang Ninh Obstetrics and Pediatrics Hospital, a tertiary maternity care center in Quang Ninh Province, Vietnam.

To address the temporal constraints of recruitment and outcome tracking, participant enrollment took place from November 2023 to August 2025. All eligible pregnant women presenting for routine first-trimester antenatal care between 11 weeks 3 days and 13 weeks 6 days of gestation were invited to participate. Longitudinal follow-up and outcome assessment for the final enrolled cohort were completed by November 2025, ensuring that all participants had reached delivery and final postpartum endpoints before database closure. Follow-up assessments were conducted at 12, 20, 28, 34, and 37 weeks of gestation, as well as at delivery. At each visit, maternal blood pressure, proteinuria status, body weight, uterine artery Doppler indices, and biochemical test results were recorded. Pregnancy outcomes were systematically collected at delivery.

To maintain methodological rigor and minimize potential detection bias, the clinical management team and the outcome assessors (including obstetricians and pediatricians evaluating pregnancy and neonatal outcomes) were entirely blinded to the first-trimester FMF risk classification and biochemical assay results. Risk calculation and aspirin allocation were handled via automated software by an independent study coordinator, and screening results were concealed from medical staff providing routine clinical care.

2.2. Study Population and Participant Selection Flow

Pregnant women were eligible for inclusion if they met the following criteria: singleton pregnancy, gestational age between 11 weeks 3 days and 13 weeks 6 days confirmed by crown-rump length (CRL) measurement, live fetus with no detectable structural anomalies at screening, willingness to participate with written informed consent, availability for follow-up until delivery, and no contraindications to low-dose aspirin.

Participants were excluded from the final analysis if they met any of the following pre-specified criteria: miscarriage, pregnancy termination, spontaneous preterm birth, or stillbirth unrelated to preeclampsia or its complications; eclampsia or complications of preeclampsia occurring prior to evaluation; non-compliance with low-dose aspirin prophylaxis after classification as high risk; or incomplete clinical records resulting in loss to follow-up.

While the initial study protocol defined eligibility and potential exclusion parameters prior to enrollment, a total of 1335 women agreed to participate and were initially enrolled. During prospective follow-up, 148 participants were subsequently excluded from the final analysis due to the following post-enrollment reasons: 41 cases experienced stillbirth, pregnancy termination, miscarriage, or preterm birth unrelated to preeclampsia, and 107 cases were lost to follow-up. Consequently, a final cohort of 1187 participants with complete data sets was included in the statistical analysis.

2.3. Sample Size Calculation

The required sample size was calculated using the formula for estimating a single population proportion. The significance level was set at $\alpha = 0.05$. The expected

prevalence of preeclampsia was assumed to be $p = 0.038$, based on the study by Tran Manh Linh (2020) [7], and the desired absolute precision was $d = 0.011$. Based on these parameters, the minimum required sample size was determined to be 1160 pregnant women. Accounting for potential attrition, the final analyzed sample of 1187 participants adequately powered the study.

2.4. Screening Procedure and Risk Assessment

Eligible pregnant women underwent first-trimester screening during routine antenatal visits. Maternal demographic, clinical information, height, and weight were recorded to calculate body mass index (BMI). Blood pressure measurements were obtained from both arms using a validated automated device after at least 5 minutes of rest in a seated position, and the mean arterial pressure (MAP) was calculated.

Ultrasound examinations were performed to determine CRL and bilateral uterine artery Doppler measurements to obtain the uterine artery pulsatility index (UtA-PI). Venous blood samples were collected to measure placental growth factor (PlGF) concentrations. Individual risks of developing preeclampsia were calculated using the Fetal Medicine Foundation (FMF) first-trimester competing-risks model via official risk assessment software, integrating maternal characteristics, MAP, UtA-PI, and PlGF levels. Pregnant women with a calculated risk of ≥1 in 100 for preterm preeclampsia were classified as high risk.

2.5. Aspirin Prophylaxis Protocol

Participants identified as high risk (≥1 in 100 predicted risk) were prescribed a standardized low-dose aspirin prophylaxis protocol:

Dose: Oral aspirin at a daily dose of 150 mg, taken at bedtime.

Start criteria: Prophylaxis was initiated immediately following screening disclosure, within the first-trimester "golden window" (between 11 weeks 3 days and 14 weeks of gestation).

Stop criteria: Aspirin was routinely discontinued at 36 weeks of gestation, or earlier if preeclampsia was diagnosed, or in the event of severe adverse effects.

Adherence assessment: Patient adherence was evaluated prospectively at each follow-up visit using pill counts and interview questionnaires. High adherence was defined as taking ≥ 80% of the prescribed doses.

Management of interruptions: For participants experiencing mild gastric discomfort, proton pump inhibitors were co-prescribed. In cases of minor vaginal bleeding, aspirin was temporarily interrupted until bleeding subsided and safely resumed under clinical supervision. Participants who permanently discontinued aspirin due to non-compliance or adverse effects were tracked and categorized according to protocol deviation guidelines.

2.6. Study Variables and Outcome Definitions

Primary outcomes: Estimated FMF preeclampsia risk score and the development

of preeclampsia during pregnancy. Preeclampsia was diagnosed in accordance with international obstetric guidelines (such as ISSHP/ACOG criteria) defined as new-onset hypertension (systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg on two occasions at least 4 hours apart) arising after 20 weeks of gestation, accompanied by either: 1) proteinuria (≥300 mg per 24-hour urine collection, or protein/creatinine ratio ≥ 0.3, or a dipstick reading of ≥2+), or 2) in the absence of proteinuria, new-onset systemic organ dysfunction involving renal insufficiency (serum creatinine > 1.1 mg/dL or doubling of serum creatinine), liver involvement (elevation of transaminases to twice normal concentration), neurological complications (visual disturbances, severe persistent headache, stroke), hematological complications (platelet count < 100,000/μL, DIC, hemolysis), or uteroplacental dysfunction (such as fetal growth restriction).

Secondary outcomes: Gestational age at delivery, neonatal birth weight, mode of delivery, and neonatal intensive care unit (NICU) admission.

2.7. Statistical Analysis

Data were analyzed using SPSS software. Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR), and categorical variables as frequencies and percentages. Group comparisons utilized chi-square tests, Fisher's exact tests, independent t-tests, or Mann-Whitney U tests. Logistic regression models were used to identify predictors of aspirin prophylaxis failure, and receiver operating characteristic (ROC) curves evaluated screening performance, with statistical significance set at $p < 0.05$.

2.8. Ethical Considerations

The study protocol was approved by the Biomedical Research Ethics Committee of Quang Ninh Obstetrics and Pediatrics Hospital (No. 03/BVSN-HDDD). Written informed consent was obtained from all participants prior to enrollment in compliance with the Declaration of Helsinki.

3. Results

3.1. Participant Recruitment and Baseline Characteristics

From November 2023 to November 2025, a total of 2283 pregnant women underwent preeclampsia screening at 11 to 13^{+6} weeks of gestation at Quang Ninh Obstetrics and Pediatrics Hospital. Among them, 1335 women agreed to participate in the study. Participants were prospectively followed from enrollment until delivery. After excluding 41 cases due to stillbirth, pregnancy termination, miscarriage, or preterm birth unrelated to preeclampsia, and 107 cases lost to follow-up, a total of 1187 pregnant women met the eligibility criteria and were included in the final analysis (**Figure 1**).

Among the 1187 analyzed pregnancies, 84 women (7.1%) were classified as high risk (predicted risk ≥ 1 in 100) and 1103 women (92.9%) as low risk. The baseline

demographic, clinical, and screening characteristics of the study population are summarized in Table 1.

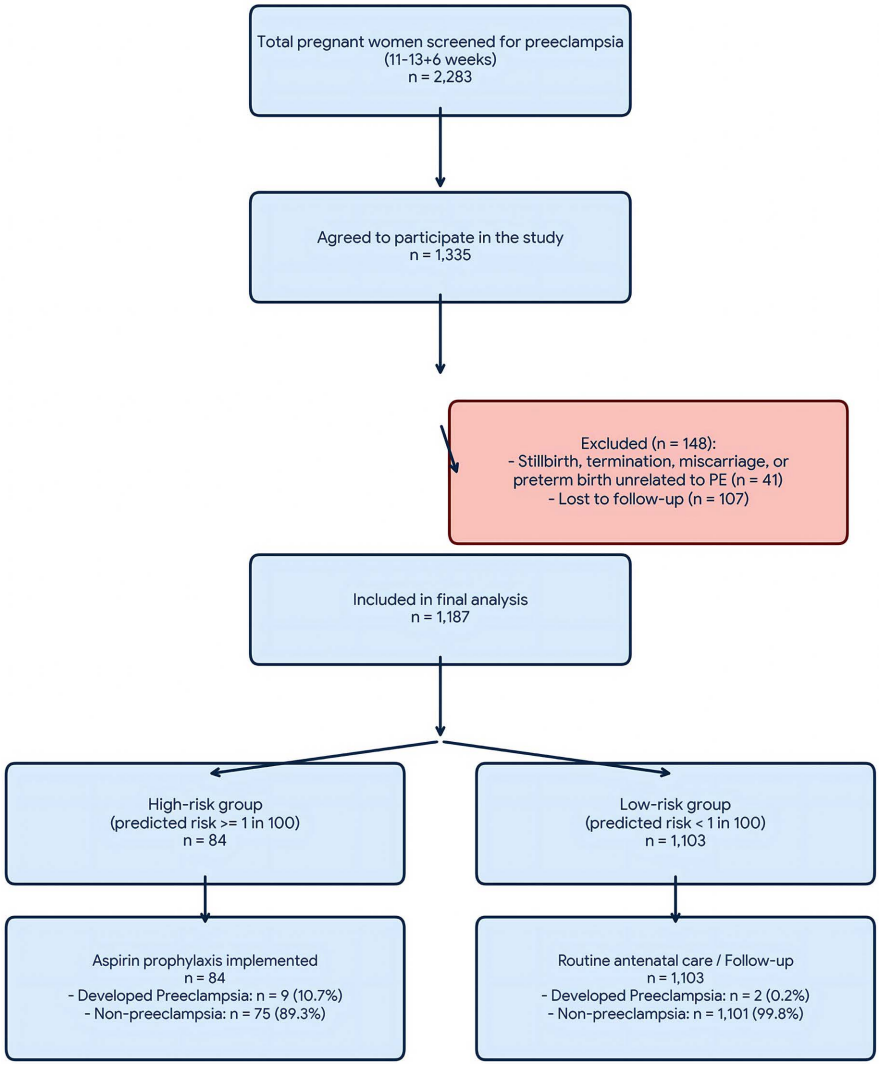

Figure 1. Flow diagram of participant selection and risk stratification for preeclampsia screening.

Table 1. Baseline characteristics and screening parameters of the study population.

	High rick (N = 84)	Low rick (N = 1103)	Overall (N = 1187)
Maternal_age			
Mean (SD)	30.3 (6.19)	29.7 (5.70)	29.8 (5.74)
Median [Min, Max]	30.0 [19.0, 43.0]	30.0 [16.0, 49.0]	30.0 [16.0, 49.0]
History_PE			
No	82 (97.6%)	1101 (99.8%)	1183 (99.7%)
Yes	2 (2.4%)	2 (0.2%)	4 (0.3%)

Continued

Family_history_PE			
No	84 (100%)	1103 (100%)	1187 (100%)
Medical_conditions			
Lupus	2 (2.4%)	0 (0%)	2 (0.2%)
No	78 (92.9%)	1102 (99.9%)	1180 (99.4%)
MHT	4 (4.8%)	1 (0.1%)	5 (0.4%)
Parity			
Mean (SD)	0.571 (0.796)	0.830 (0.819)	0.812 (0.820)
Median [Min, Max]	0 [0, 3.00]	1.00 [0, 5.00]	1.00 [0, 5.00]
History_stillbirth			
Mean (SD)	0.226 (0.567)	0.257 (0.630)	0.255 (0.625)
Median [Min, Max]	0 [0, 3.00]	0 [0, 5.00]	0 [0, 5.00]
Conception_method			
IVF	7 (8.3%)	55 (5.0%)	62 (5.2%)
Nomal	77 (91.7%)	1048 (95.0%)	1125 (94.8%)
Bmi_cat			
Normal	66 (78.6%)	830 (75.2%)	896 (75.5%)
Obese	3 (3.6%)	17 (1.5%)	20 (1.7%)
Overweight	4 (4.8%)	123 (11.2%)	127 (10.7%)
Underweight	11 (13.1%)	133 (12.1%)	144 (12.1%)
MAP_mmHg			
Mean (SD)	80.6 (7.53)	80.4 (7.61)	80.4 (7.60)
Median [Min, Max]	79.2 [67.5, 112]	79.6 [60.6, 117]	79.6 [60.6, 117]
MAP_MoM			
Mean (SD)	0.982 (0.0845)	0.981 (0.0872)	0.981 (0.0869)
Median [Min, Max]	0.970 [0.830, 1.32]	0.970 [0.730, 1.43]	0.970 [0.730, 1.43]
UtA_PI			
Mean (SD)	1.76 (0.451)	1.74 (0.469)	1.75 (0.467)
Median [Min, Max]	1.70 [0.860, 3.56]	1.72 [0.520, 3.63]	1.72 [0.520, 3.63]
UtA_PI_MoM			
Mean (SD)	1.05 (0.263)	1.04 (0.279)	1.04 (0.278)
Median [Min, Max]	1.01 [0.500, 2.03]	1.03 [0.330, 2.34]	1.03 [0.330, 2.34]
PlGF_pg_mL			
Mean (SD)	67.9 (29.0)	67.6 (30.4)	67.6 (30.3)
Median [Min, Max]	60.8 [26.8, 213]	62.3 [15.7, 547]	62.3 [15.7, 547]
PlGF_MoM			
Mean (SD)	1.05 (0.386)	1.05 (0.428)	1.05 (0.425)
Median [Min, Max]	0.970 [0.431, 2.61]	0.988 [0.292, 7.08]	0.986 [0.292, 7.08]

3.2. Preeclampsia Screening Performance and Incidence

Based on the FMF-predicted risk threshold of ≥1 in 100, the overall incidence of preeclampsia in the cohort was 0.9% (11/1187). Among the 84 high-risk women,

9 developed preeclampsia (10.7%), whereas only 2 out of 1103 low-risk women developed preeclampsia (0.2%) (Table 2).

Table 2. Preeclampsia outcomes according to the FMF-predicted risk threshold of 1 in 100.

FMF-predicted risk of preeclampsia	Total screened (n)	Proportion of cohort (%)	Preeclampsia (n, %)	Severe preeclampsia (n, %)
≥1 in 100 (high-risk group)	84	7.1	9 (10.7)	Not specified
<1 in 100 (low-risk group)	1,103	92.9	2 (0.2)	1 (0.1)
Total	**1,187**	**100.0**	**11 (0.9)**	**1 (0.1)**

3.3. Pregnancy and Neonatal Outcomes

The comparison of pregnancy and neonatal outcomes between the high-risk and low-risk groups is detailed in Table 3. The mean gestational age at screening was comparable across groups. Gestational age at delivery was slightly lower in the high-risk group compared to the low-risk group. Regarding the mode of delivery, cesarean section rates were 65.5% in the high-risk group and 56.2% in the low-risk group. Neonatal intensive care unit (NICU) admission rates were 6.0% in the high-risk group versus 0.8% in the low-risk group. Mean birth weight was 2940 ± 398 g in the high-risk group and 3190 ± 358 g in the low-risk group.

Table 3. Pregnancy and neonatal outcomes.

	High rick (N = 84)	Low rick (N = 1103)	Overall (N = 1187)
GA_screening			
Mean (SD)	12.5 (0.586)	12.4 (0.537)	12.5 (0.541)
Median [Min, Max]	12.4 [11.6, 13.9]	12.4 [11.0, 13.9]	12.4 [11.0, 13.9]
GA_delivery			
Mean (SD)	38.5 (1.06)	38.9 (0.873)	38.8 (0.891)
Median [Min, Max]	38.7 [35.0, 40.1]	39.0 [33.0, 41.0]	39.0 [33.0, 41.0]
GA_PE_onset			
Mean (SD)	36.4 (2.06)	35.1 (2.64)	35.7 (2.41)
Median [Min, Max]	36.0 [34.0, 39.1]	35.5 [29.0, 37.0]	35.5 [29.0, 39.1]
Mode_delivery			
CS	55 (65.5%)	620 (56.2%)	675 (56.9%)
NVD	29 (34.5%)	483 (43.8%)	512 (43.1%)
Neonatal_status			
NICU	5 (6.0%)	9 (0.8%)	14 (1.2%)
Room- in	79 (94.0%)	1094 (99.2%)	1173 (98.8%)
Birth_weight_g			
Mean (SD)	2940 (398)	3190 (358)	3180 (366)
Median [Min, Max]	3000 [1500, 4200]	3200 [1600, 4400]	3200 [1500, 4400]

3.4. Aspirin Prophylaxis Compliance, Safety, and Associated Risk Factors

All 84 women identified as high risk were prescribed aspirin prophylaxis. Table 4 outlines the compliance and safety profile of aspirin therapy in this cohort, as well as the univariate regression analysis evaluating factors associated with aspirin prophylaxis failure.

The mean gestational age at aspirin initiation was 12.83 ± 0.59 weeks, and the mean gestational age at discontinuation was 35.95 ± 0.26 weeks. High adherence (≥80%) was achieved in 95.2% (n = 80) of the high-risk participants. Regarding safety, early discontinuation due to gastric pain occurred in 1 case (1.2%), temporary interruption due to vaginal bleeding (followed by successful resumption) occurred in 3 cases (3.6%), and discontinuation before 36 weeks due to the onset of preeclampsia occurred in 2 cases (2.4%). No severe bleeding adverse effects or placental abruption events were reported.

Table 4. Aspirin prophylaxis compliance and safety characteristics in the high-risk group (n = 84).

Compliance and safety characteristic	Value/ count	Percentage (%)
Gestational age at aspirin initiation (weeks), mean ± SD	12.8 ± 0.59	—
Gestational age at aspirin discontinuation (weeks), mean ± SD	5.95 ± 0.26	—
Adherence level (≥80%)	80	95.2%
- Early discontinuation due to gastric pain	1	1.2%
- Temporary interruption due to vaginal bleeding (subsequently resumed)	3	3.6%
- Discontinuation before 36 weeks due to preeclampsia onset	2	2.4%
Bleeding adverse effects (severe hemorrhage / placental abruption)	0	0%

4. Discussion

4.1. The Role of Maternal Demographic and Clinical Factors in Preeclampsia Prediction

In this prospective cohort study, we examined the performance of the Fetal Medicine Foundation (FMF) first-trimester screening model in a Vietnamese obstetric population. Our findings indicate that while advanced maternal age (≥35 years) is a well-established risk factor for hypertensive disorders of pregnancy due to age-related vascular stiffening and increased prevalence of comorbidities, its independent predictive contribution is diminished when integrated into comprehensive, multifactorial algorithms [8]. This observation is consistent with the findings of Wright et al., who emphasized that the strength of the competing-risks model lies in the synergetic interaction between biophysical and biochemical markers, rather than reliance on individual clinical variables [8].

In contrast, maternal BMI ≥ 25 kg/m^2 demonstrated a significant association

with a high-risk classification. Overweight and obesity are increasingly recognized as primary drivers of preeclampsia, largely mediated by chronic low-grade systemic inflammation, oxidative stress, and insulin resistance, which collectively impair early trophoblastic invasion [9] [10]. Furthermore, our data underscore that prior medical history, including chronic hypertension and autoimmune conditions, remains a foundational pillar in risk assessment. These clinical conditions serve as markers for pre-existing endothelial vulnerability, necessitating the early intervention strategies facilitated by the FMF model [11] [12].

4.2. Pathophysiological Insights from Biophysical and Biochemical Markers

The significant association between Mean Arterial Pressure (MAP), Uterine Artery Pulsatility Index (UtA-PI), and Placental Growth Factor (PlGF) with preeclampsia risk in our study reinforces the central role of placental dysfunction in the pathophysiology of the disease. Our findings regarding MAP (AUC 0.70) align with established evidence that early elevations in blood pressure reflect increased systemic vascular resistance and an initial failure in maternal cardiovascular adaptation during the first trimester [13] [14].

Among the biomarkers tested, UtA-PI provided the highest predictive discrimination (AUC 0.78, OR 8.08). This metric directly mirrors the resistance to blood flow within the spiral arteries, serving as a surrogate for failed physiological remodeling—a hallmark of early-onset preeclampsia [4] [15]. Moreover, our observation that reduced PlGF levels were associated with a >7-fold increased risk highlights the importance of the angiogenic-antiangiogenic balance. As PlGF is essential for healthy placental angiogenesis, its deficiency is a potent precursor to ischemic placental changes [16] [17]. By integrating these parameters, our screening strategy moves beyond traditional clinical observation toward a precise, mechanism-based prediction model that is highly suitable for clinical practice [18] [19].

4.3. Efficacy of the FMF Algorithm and Targeted Aspirin Prophylaxis

The identification of 7.1% of our cohort as "high-risk" falls perfectly within the 5% - 10% screening-positive rate recommended by the International Federation of Gynecology and Obstetrics (FIGO) [20]. This suggests that the FMF model is not only applicable but also highly efficient in a Vietnamese setting, balancing the need for broad detection with the imperative to avoid the over-prescription of aspirin [20].

The most compelling finding of our study is the total absence of early-onset preeclampsia (before 34 weeks). This strongly validates the "golden window" hypothesis—that initiating low-dose aspirin before 14 weeks of gestation significantly disrupts the pathophysiological cascade leading to severe disease [1] [6]. Our high adherence rate of 95.2% (≥80% compliance) serves as a critical explanation for these positive results. As demonstrated by recent meta-analyses, the prophylactic

benefit of aspirin is highly dependent on both initiation timing and patient adherence; thus, our findings suggest that when implemented with rigorous patient counseling, this screening and prevention strategy can drastically reduce severe maternal and neonatal morbidity [21] [22]. The observed "shift" in the disease spectrum—whereby preeclampsia cases were confined to the late-onset, milder phenotype—parallels the outcomes of the landmark ASPRE trial [21] [22].

4.4. Clinical Impact on Perinatal Outcomes

Our study demonstrates that the FMF screening model acts as an effective gatekeeper for resource allocation. The concentration of adverse outcomes, including lower birth weight and increased NICU admissions, within the preeclampsia and high-risk groups suggests that the model is highly sensitive to the spectrum of placenta-mediated disorders [23].

While the overall preeclampsia rate was low (0.8%), the significantly lower gestational age at delivery in preeclampsia patients (36.86 ± 1.35 weeks) compared to their non-preeclamptic counterparts suggests that the model enables closer surveillance and timely management. Furthermore, the higher rate of fetal growth restriction (FGR) in the high-risk group confirms that this screening protocol identifies pregnancies at risk of broader placental insufficiency beyond preeclampsia alone [23]. Importantly, the lack of severe maternal complications, such as eclampsia or HELLP syndrome, provides strong evidence that this integrated approach—combining early screening, prophylactic aspirin, and structured follow-up—is a robust framework for improving maternal and neonatal safety in tertiary care settings in Vietnam [1].

5. Conclusions

In conclusion, our prospective cohort study demonstrates that the Fetal Medicine Foundation (FMF) first-trimester screening algorithm, integrating maternal characteristics, MAP, UtA-PI, and PlGF, is an effective and robust tool for preeclampsia risk stratification in a Vietnamese population. By accurately identifying high-risk pregnancies within the 11 - 13^{+6} weeks gestation window, this screening model facilitates the timely initiation of aspirin prophylaxis, which is critical for maximizing prophylactic efficacy.

Our findings provide strong evidence that this screening strategy is associated with favorable maternal and neonatal outcomes, specifically the significant reduction in severe early-onset preeclampsia. Although our study confirmed the role of clinical factors such as BMI and medical history, the superior predictive discrimination offered by the combined biophysical and biochemical markers suggests that a multifactorial screening approach should be considered the standard of care. Given the feasibility and clinical benefits observed, we recommend the broader implementation of the FMF first-trimester screening protocol in tertiary maternity care settings across Vietnam. Further long-term studies are warranted to assess the impact of this model on wider population-based perinatal mortality and

morbidity rates in low- and middle-income healthcare systems.

Declarations

Ethics Approval and Consent to Participate

This study was conducted in accordance with the principles of the Declaration of Helsinki. The study protocol was reviewed and approved by the Institutional Review Board of Quang Ninh Obstetrics and Pediatrics Hospital, Vietnam (No.03/BVSN-HDDD).

All pregnant women who participated in the study were informed about the study objectives, procedures, potential benefits, and risks. Written informed consent was obtained from all participants prior to enrollment in the study.

Participants were assured that their personal information would remain confidential and that they could withdraw from the study at any time without affecting their medical care.

Consent for Publication

Written informed consent for publication of anonymized clinical data was obtained from all participants included in the study. No identifiable personal information is presented in this manuscript.

Data Availability Statement

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

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Author Contributions

T.H.C. and B.M.C conceptualized and designed the study.

N.T.M. and N.T.H. collected the data and performed the clinical assessments.

T.H.C. and V.T.H. conducted the statistical analysis and drafted the manuscript.

N.V.K and D.D.L contributed to data interpretation and critically revised the manuscript.

All authors read and approved the final manuscript.

Conflicts of Interest

The authors declare that they have no competing interests.

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