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RESEARCH ARTICLE

Is mid-gestational uterine artery Doppler still useful in a setting with routine first-trimester pre-eclampsia screening? A cohort study

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Abstract

Objective: To evaluate whether routine mid-gestational uterine artery Doppler (UtAD) modifies the risk for preterm pre-eclampsia after first-trimester combined pre-eclampsia screening.

Design: Retrospective cohort study.

Setting: London Tertiary Hospital.

Population: A cohort of 7793 women with singleton pregnancies, first-trimester pre-eclampsia screening using the Fetal Medicine Foundation (FMF) algorithm and UtAD pulsatility index (PI) assessment at the mid-gestation ultrasound.

Methods: Pregnancies were divided into four groups: high risk in both trimesters (H^1H^2), high risk in the first but not in the second trimester (H^1L^2), low risk in the first but high risk in the second trimester (L^1H^2) and low risk in both trimesters (L^1L^2).

Main outcome measures: Small for gestational age (SGA), hypertensive disorders of pregnancy (HDP) and stillbirth.

Results: In this cohort, 600 (7.7%) and 620 (7.9%) women were designated as being at high risk in the first and second trimesters, respectively. Preterm pre-eclampsia was more prevalent in the H^1L^2 group (4.5%) than in women considered at low risk in the first trimester (0.4%, $p < 0.0001$). The prevalence of preterm pre-eclampsia in the L^1H^2 group (3.3%) was significantly lower than that in women considered at high risk in the first trimester (7.0%, $p = 0.0076$), and was higher than that observed in the L^1L^2 group (0.2%, $p < 0.0001$). The prevalence of SGA and term HDP followed similar trends.

Conclusions: Pre-eclampsia risk after first-trimester FMF pre-eclampsia screening may be stratified through mid-gestational routine UtAD assessment. Pregnancy care should not be de-escalated for low mid-gestational UtAD resistance in women classified as being at high risk in the first trimester. The escalation of care may be justified in women at low risk but with high mid-gestational UtAD resistance.

KEYWORDS
First-trimester pre-eclampsia screening, hypertensive disorders of pregnancy, placenta-related adverse outcomes, small for gestational age, stillbirth, uterine artery Doppler

1 | INTRODUCTION

Pre-eclampsia (PE) is associated with adverse perinatal outcomes, such as fetal growth restriction, iatrogenic preterm birth and perinatal death.[1] In the UK, the screening recommendations from the National Institute for Health and Clinical Excellence (NICE) for pregnancies at high risk of placentally mediated disorders are based on a checklist structured approach. This approach considers medical, social and obstetric characteristics as independent risk factors, irrespective of their prevalence or strength of association with adverse pregnancy outcomes.[2–4] Despite the widespread use of this approach in many countries, this method has limited screening performance, achieving a 30.2% detection rate for term pre-eclampsia and a 41.5% detection rate for preterm pre-eclampsia, for a 10% overall screen-positive rate.[5,6] As a consequence of this limitation, the Royal College of Obstetricians and Gynaecologists (RCOG) recommend the re-evaluation of PE risk at the mid-gestation anatomy scan using uterine artery Doppler (UtAD) assessment in women considered to be at high risk.[7] The rationale for this recommendation is based on robust data showing a strong association between increased mid-gestation UtAD vascular resistance and increased risk of hypertensive disorders of pregnancy (HDP), fetal growth restriction and stillbirth.[8–11]

Effective early pregnancy screening for PE using the Fetal Medicine Foundation (FMF) algorithm,[12] with targeted interventions in the high-risk group, has been shown to reduce the incidence of preterm PE and associated pregnancy adverse outcomes.[6,13–16] However, there is a paucity of data on the clinical role for mid-gestation UtAD assessment in a population that has already undergone such early pregnancy screening. The aim of this study is to evaluate whether mid-gestational UtAD assessment significantly further modifies the risk of placentally mediated adverse pregnancy outcomes in a population who has undergone routine first-trimester multi-parameter combined pre-eclampsia screening.

Contribution

What are the novel findings of this work?

Routine uterine artery (UtAD) Doppler assessment in the second trimester may be used to further stratify pre-eclampsia risk in women who have had first-trimester pre-eclampsia screening using the Fetal Medicine Foundation (FMF) combined screening algorithm.

What are the clinical implications of this work?

Care should not be de-escalated in patients classified as high risk for pre-eclampsia by the FMF algorithm in the first trimester upon measurement of low mid-gestational UtAD resistance. Conversely, the escalation of care may be justified in women at low risk but with high mid-gestational UtAD Doppler resistance.

2 | METHODS

2.1 | Population

This was a single-centre study conducted at St George's University Hospital NHS Trust. A retrospective analysis was performed on information routinely collected between May 2019 and January 2022. Data were extracted from the ultrasound databases (ViewPoint 5.6.26.148; ViewPoint Bildverarbeitung GmbH, Weßling, Germany) and the maternity registry (EuroKing; Wellbeing Software, Mansfield, UK). These databases are subject to regular clinical governance review. The identifiable information of the patients was removed from the data sets. Details collected involved maternal demographics, pregnancy characteristics and previous medical history. Only women who had first- and second-trimester routine scans in our unit and delivered in this hospital were included. Patients with missing outcome data, multiple pregnancy, major fetal defects or miscarriage <24 weeks of gestation were excluded from the analysis. The local ethics committee advised that formal ethical approval was not required for this retrospective study.

2.2 | Study variables and outcomes

At the first-trimester routine ultrasound scan, the risk of developing pre-eclampsia was calculated for each woman according to the FMF algorithm,[17] using maternal characteristics, mean arterial blood pressure (MAP), UtAD and pregnancy-associated plasma protein A (PAPP-A). Maternal serum PAPP-A was used in the algorithm instead of placental growth factor (PlGF), because of its routine use in screening for fetal trisomies.[18] Women with a result of >1:50 were classified as high risk and prescribed prophylactic low-dose aspirin (150 mg), in accordance with the recommendations from the Aspirin for evidence-based preeclampsia prevention (ASPRE) study,[19,20] serial growth scans at 28 and 36 weeks of gestation, and induction of labour at 40 weeks of gestation.[6] The suggested management of patients with different screening results is schematised in (Figure 1).

All women underwent mid-gestation UtAD assessment at the time of the mid-gestational routine anomaly scan.[21] Women with a high mean UtAD PI (>1.25), corresponding to the 90th centile, were classified as being at high risk.[22] Patients screened as high risk at the mid-gestation assessment were scheduled for additional fetal growth assessments at 28 and 36 weeks of gestation and induction of labour at 40 weeks of gestation. Women were divided into four distinct groups: patients at high risk in both trimesters (H^1H^2); patients at high risk in the first but not the second trimester

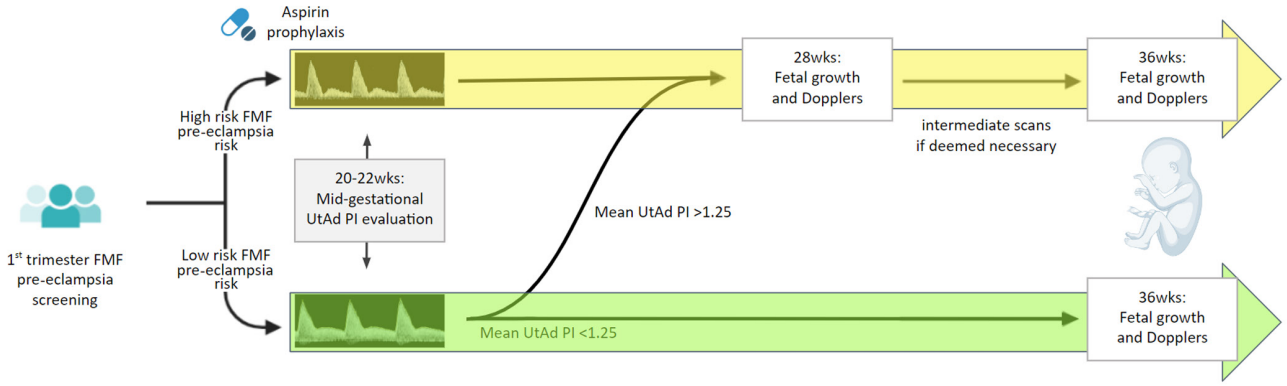

FIGURE 1 Suggested management of patients with different screening results. Women with a screening result of >1:50 after first-trimester Fetal Medicine Foundation (FMF) pre-eclampsia screening are classified as being at high risk and are prescribed prophylactic low-dose aspirin. Mid-gestational uterine artery Doppler (UtAD) pulsatility index (PI) is then measured and recorded. Serial growth scans at 28 and 36 weeks of gestation are scheduled, with intermediate scans when deemed necessary. Women classified as low risk at the first trimester FMF screening do not receive any prophylaxis. Uterine arteries are sampled at the routine scan at 20–22 weeks of gestation; depending on the mean UtAd PI, fetal growth and Dopplers are checked at 36 weeks of gestation or anticipated at 28 weeks of gestation, when the mean UtAd PI is (>1.25).

(H^1L^2); patients at low risk in the first trimester but at high risk in the second trimester (L^1H^2); and patients at low risk in both trimesters (L^1L^2). The primary maternal and neonatal outcomes were ascertained and defined as the rates of HDP, small for gestational age (SGA) and stillbirth delivering at term (≥37 weeks of gestation) or preterm (<37 weeks of gestation).

2.3 | Statistical analysis

Descriptive data were presented as medians and interquartile ranges for continuous variables and as numbers and percentages for categorical variables. Comparisons between groups were performed using the chi-square test or Fisher's exact test for categorical variables, with Yates' correction where appropriate. R 4.2.1 (https://www.r-project.org/) was used for data analyses.

3 | RESULTS

Between May 2019 and January 2022, a total of 16 160 women booked for pregnancy care, and 7793 of these women, with both screening assessments recorder as well as birth outcomes, constituted the study population. The maternal demographic and pregnancy characteristics are described in Table 1. A total of 600 women (7.7%) were designated as being at high risk in the first trimester and 620 women (7.9%) were classified as being at high risk at mid-gestation (Figure 2). The risk groups were assigned as follows: 161 H^1H^2 (2.1%), 439 H^1L^2 (5.6%), 459 L^1H^2 (5.9%) and 6734 L^1L^2 (86.4%).

The prevalence of preterm pre-eclampsia decreased consistently through the risk groups, from 13.7% in the H^1H^2 group, to 4.5% in the H^1L^2 group, to 3.3% in the L^1H^2 group and to 0.2% in the L^1L^2 group (Figure 3; Table 2). This was also the case for the other adverse pregnancy outcomes ascertained. The prevalence of preterm pre-eclampsia in women at high risk with normal mid-gestational UtAD PI (H^1L^2, 4.5%) was significantly higher than in women classified as being at low risk in the first trimester (L^1H^2 + L^1L^2, 0.4%, $p < 0.0001$; Table 3). Similarly, the prevalence of preterm pre-eclampsia in women at low risk with high mid-gestational

TABLE 1 Maternal and pregnancy characteristics of the study population of 7793 women.

	Total population (n = 7793)
Weight (kg)	66.4 (59.0–76.2)
Height (cm)	164 (160–169)
Age (years)	32.0 (29.0–35.0)
Nulliparous	4016 (51.5%)
Ethnicity	
White	4928 (63.2%)
Black	944 (12.1%)
South Asian	1414 (18.1%)
East Asian	238 (3.1%)
Mixed	269 (3.5%)
Smoker	318 (4.1%)
Previous pre-eclampsia	221 (2.8%)
ART (IVF/ICSI/other)	330 (4.2%)
Renal disease	9 (0.1%)
Autoimmune disease (SLE/APLS)	95 (1.2%)
Pre-pregnancy diabetes	88 (1.1%)
Chronic hypertension	68 (0.9%)
Gestation at birth	39.6 (39.0–40.6)
Birthweight (g)	3300 (3035–3700)
Preterm births	412 (5.3%)

Note: Data showed as median (interquartile range) or number (%).
Abbreviations: ART, assisted reproductive technology; ICSI, intracytoplasmic sperm injection; IVF, in vitro fertilisation; SLE/APLS, systemic lupus erythematosus/Antiphospholipid syndrome.

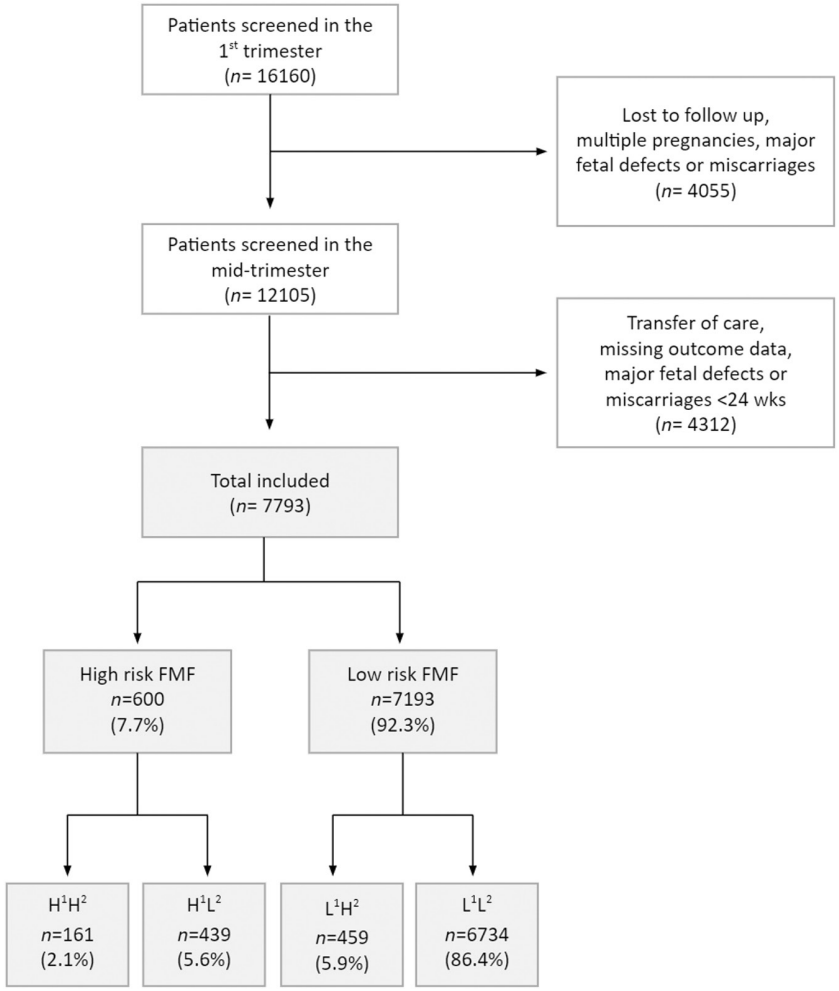

FIGURE 2 Flow chart summarizing the process of patient selection and the final distribution of the patients in the four study groups. A total of 7793 patients were included and then grouped by results from the first-trimester Fetal Medicine Foundation (FMF) pre-eclampsia screening and uterine artery Doppler (UtAD) pulsatility index (PI) at the mid-gestational scan: H^1H^2, patients at high risk in both trimesters; H^1L^2, patients at high risk in the first but not the second trimester; L^1H^2, patients at low risk in the first trimester but at high risk in the second trimester; and L^1L^2, patients at low risk in both trimesters.

UtAD PI (L^1H^2, 3.3%) was significantly lower than in women classified as high risk in the first trimester (H^1H^2 + H^1L^2, 7.0%, p = 0.0076). The prevalence for term HDP, SGA birth and stillbirth followed the same trends as for preterm pre-eclampsia (Table 3).

4 | DISCUSSION

The findings of this study suggest that routine UtAD assessment in the second trimester may be used to further stratify pre-eclampsia risk in women who have had first-trimester combined pre-eclampsia screening using the FMF algorithm. When considering composite adverse perinatal outcomes, the level of care should not be de-escalated for low second-trimester UtAD resistance in patients that were classified as being at high risk for pre-eclampsia in the first trimester. In contrast, an escalation of care may be justified in women judged to be at low risk in the first trimester on the basis of high mid-gestational UtAD resistance.

4.1 | Interpretation of study findings and comparison with published literature

Hypertensive disorders of pregnancy, SGA and stillbirth are a major cause of maternal and neonatal morbidity and mortality.[23] Previous work has highlighted the role of second-trimester UtAD in an unscreened population for the identification of pregnancies at increased risk of both preterm pre-eclampsia and placentally mediated complications.[24] Most studies looked at the use of UtAD in isolation, but others showed improved screening performance when combined with other biomarkers.[23] Combining UtAD, MAP and PlGF together with the maternal demographic factors allowed 85% of preterm pre-eclampsia cases to be detected for a 10% false-positive rate.[25] FMF first-trimester screening identifies women at risk of pre-eclampsia and allows the modification of disease course and outcomes through the offer of aspirin prophylaxis and additional monitoring and intervention.[19,26] Nevertheless, this screening test may not account for progressive maternal cardiovascular

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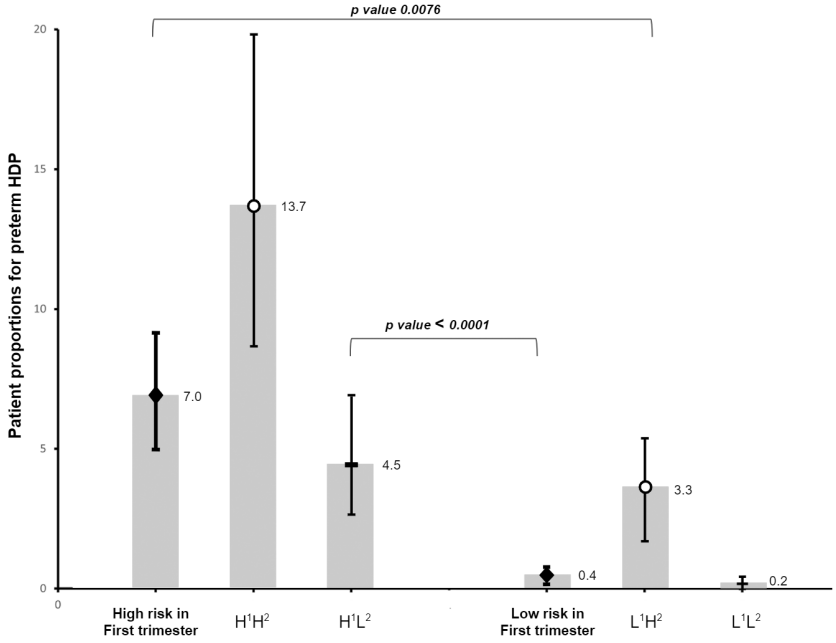

FIGURE 3 Distributions and proportions of patients with preterm hypertensive disorders of pregnancy (HDP) for the four groups of risk: H^1H^2, high risk in first-trimester screening and high UtAD PI at mid-gestational scan; H^1L^2, high risk in first-trimester screening and low UtAD PI at mid-gestational scan; L^1H^2, low risk in first-trimester screening and high UtAD PI at mid-gestational scan; and L^1L^2, low risk in first-trimester screening and low UtAD PI at mid-gestational scan. UtAD PI, uterine artery Doppler pulsatility index.

TABLE 2 Prevalence of the various placentally mediated adverse outcomes in the study population.

Prevalence	SGA < 10th centile	SGA < 5th centile	Stillbirth	All HDP	Preterm HDP
H^1H^2 (n = 161)	68 (42.2%)	52 (32.3%)	5 (3.1%)	53 (32.9%)	22 (13.7%)
H^1L^2 (n = 439)	87 (19.8%)	51 (11.6%)	1 (0.2%)	109 (24.8%)	20 (4.5%)
L^1H^2 (n = 459)	146 (31.8%)	101 (22.0%)	4 (0.9%)	47 (10.2%)	15 (3.3%)
L^1L^2 (n = 6734)	833 (12.4%)	472 (7.0%)	21 (0.3%)	229 (3.4%)	11 (0.2%)
Total (n = 7793)	1134 (14.6%)	676 (8.7%)	31 (0.4%)	438 (5.6%)	68 (0.9%)

Note: Women were divided into four distinct groups: patients at high risk in both trimesters (H^1H^2); patients at high risk in the first but not the second trimester (H^1L^2); patients at low risk in the first but high risk in the second trimester (L^1H^2); and patients at low risk in both trimesters (L^1L^2). The outcomes include hypertensive disorders of pregnancy (HDP) and small for gestational age (SGA).

TABLE 3 Statistical analysis of the prevalence of placentally mediated adverse outcomes in the study population.

Prevalence	SGA < 10th centile	SGA < 5th centile	Stillbirth	All HDP	Preterm HDP
H^1L^2 vs H^1H^2	**<0.0001**	**<0.0001**	**0.0062**	**0.0479**	**0.0001**
H^1L^2 vs ($L^1H^2 + L^1L^2$)	**0.0003**	**0.0067**	1	**<0.0001**	**<0.0001**
L^1H^2 vs L^1L^2	**<0.0001**	**<0.0001**	0.0714	**<0.0001**	**<0.0001**
L^1H^2 vs ($H^1H^2 + H^1L^2$)	**0.0326**	**0.0479**	1	**<0.0001**	**0.0076**

Note: Comparisons are shown for H^1L^2 versus either H^1H^2 or all women designated as being at high risk ($H^1H^2 + H^1L^2$) and also for L^1H^2 versus L^1L^2 and all women designated as being at low risk ($L^1L^2 + L^1H^2$). Statistically significant values are reported in bold.

and uteroplacental system changes occurring later in pregnancy.[27,28] There is a paucity of data on how the UtAD in the mid-trimester scan modifies the FMF pre-eclampsia risk. The findings of this study suggest that after first-trimester FMF screening, mid-trimester UtAD assessment may have a role in further stratifying the risk of pre-eclampsia and other placentally mediated adverse outcomes.

4.2 | Clinical and research implications

Women with a high first- and low second-trimester risk for pre-eclampsia (H^1L^2) still had a significantly higher prevalence of preterm pre-eclampsia than the low-risk group from the first trimester (4.5% vs 0.4%, $p < 0.0001$). Similarly, women with a low first- and high second-trimester risk

(L^1H^2) still had a significantly lower prevalence of preterm pre-eclampsia than the first-trimester high-risk group (3.3% vs 7.0%, $p < 0.0001$). These findings indicate that for preterm pre-eclampsia it would be inappropriate to de-escalate care in women deemed at high risk in the first trimester after screening using second-trimester UtAD assessment. However, women with a low first- and high second-trimester risk (L^1H^2) had a significantly lower but similar risk of preterm pre-eclampsia as women with a high first- and low second-trimester (H^1L^2) risk: 3.3% and 4.5%, respectively. This finding would support escalating care after mid-gestational UtAD assessment under these circumstances.

A strategy of escalating care in the low-risk group by second-trimester UtAD will require all women to have mid-gestational UtAD assessment and will result in a doubling of the high-risk group from 7.7% to 13.6%. For this increase in screen-positive rate there will be only a modest improvement in the detection of adverse pregnancy outcomes. For example, the detection of all HDP would rise from 37.0% (162/438) to 47.7% (209/438). A notable finding in this study is that, overall, 53.8% of pregnancies from the first trimester high-risk group ($H^1H^2 + H^1L^2$) resulted in HDP, SGA and/or stillbirth. The high prevalence of adverse pregnancy outcomes justifies very close fetal and maternal monitoring in women assigned as high risk after first-trimester FMF screening. As aspirin use in the late second trimester has poor efficacy,[29] an escalation of care after mid-gestational UtAD would only involve serial fetal well-being and maternal blood pressure assessments.[30]

4.3 | Strengths and limitations of the study

This is a large pragmatic population-based study investigating how mid-gestational UtAD assessment influences the risk of placentally mediated adverse pregnancy outcomes in a population that has already been screened in the first trimester using the FMF combined screening algorithm for pre-eclampsia. Unfortunately, the study was underpowered to evaluate the impact on stillbirth prevention. There are inherent limitations to a single-centre retrospective study that lacks a control population and cannot account for the impact of intervention bias (treatment paradox). For example, the use of aspirin prophylaxis in women at high-risk of preterm pre-eclampsia has been shown to have significantly reduced the prevalence of this disorder in the population.[6] The use of aspirin may have also had an effect on the mid-gestational UtAD results, by decreasing the number of patients that would have been assigned to the H^1H^2 group. Furthermore, first-trimester and mid-gestation risks were considered in a dichotomous way (high versus low risk), where the use of UtAD PI as a continuous variable may have led to improvements and the personalisation of risk for the women – as with first-trimester screening.

5 | CONCLUSION

Routine UtAD assessment in the second trimester may be used to further stratify the pre-eclampsia risk in women who have had first trimester pre-eclampsia screening using the FMF combined screening algorithm. Care should not be de-escalated in patients that were classified as being at high risk for pre-eclampsia in the first trimester by the FMF algorithm on the basis of low mid-gestational UtAD resistance. In contrast, an escalation of care may be justified in women at low risk but with high mid-gestational UtAD resistance.

AUTHOR CONTRIBUTIONS

Conceptualisation: BT and AF. Methodology: BT. Data collection: AM, BL, MM, MM and RE. Statistical analysis: AM and RE. Data interpretation: AM and BT. Drafting of article: AM and BT. Article review and editing: AM, MM, MM, BL, AF and BT.

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CONFLICT OF INTEREST STATEMENT

None declared. Completed disclosure of interests form available to view online as supporting information.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS APPROVAL

This retrospective study of routinely collected clinical data was collated from a continuing audit and was deemed not to require ethics approval or signed patient consent, in accordance with the Health Regional Authority (HRA) decision tool.

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REFERENCES

1. Duhig KE, Myers J, Seed PT, Sparkes J, Lowe J, Hunter RM, et al. Placental growth factor testing to assess women with suspected pre-eclampsia: a multicentre, pragmatic, stepped-wedge cluster-randomised controlled trial. Lancet. 2019;393:1807–18.
2. NICE. Overview | Hypertension in pregnancy: diagnosis and management | Guidance | NICE. NICE.org.uk. [cited 2022 Aug 18]. Available from: www.nice.org.uk/guidance/ng133
3. Overview | Antenatal care | Guidance | NICE. [cited 2022 Aug 18]; Available from: https://www.nice.org.uk/guidance/ng201
4. Elawad T, Scott G, Bone JN, Elwell H, Lopez CE, Filippi V, et al. Risk factors for pre-eclampsia in clinical practice guidelines: comparison with the evidence. BJOG. 2022;00:1–17. https://doi.org/10.1111/1471-0528.17320

5. Tan MY, Wright D, Syngelaki A, Akolekar R, Cicero S, Janga D, et al. Comparison of diagnostic accuracy of early screening for pre-eclampsia by NICE guidelines and a method combining maternal factors and biomarkers: results of SPREE. Ultrasound Obstet Gynecol. 2018;51:743–50.
6. Guy GP, Leslie K, Diaz Gomez D, Forenc K, Buck E, Khalil A, et al. Implementation of routine first trimester combined screening for pre-eclampsia: a clinical effectiveness study. BJOG. 2021;128:149–56.
7. RCOG. RCOG.org.uk. [cited 2022 Aug 18]. Available from: https://www.rcog.org.uk/media/t3lmjhnl/gtg_31.pdf
8. Papageorghiou AT, Yu CKH, Nicolaides KH. The role of uterine artery Doppler in predicting adverse pregnancy outcome. Best Pract Res Clin Obstet Gynaecol. 2004;18:383–96.
9. Cnossen JS, Morris RK, ter Riet G, Mol BWJ, van der Post JAM, Coomarasamy A, et al. Use of uterine artery Doppler ultrasonography to predict pre-eclampsia and intrauterine growth restriction: a systematic review and bivariable meta-analysis. CMAJ. 2008;178:701–11.
10. Familiari A, Bhide A, Morlando M, Scala C, Khalil A, Thilaganathan B. Mid-pregnancy fetal biometry, uterine artery Doppler indices and maternal demographic characteristics: role in prediction of small-for-gestational-age birth. Acta Obstet Gynecol Scand. 2016;95:238–44.
11. Plasencia W, Maiz N, Poon L, Yu C, Nicolaides KH. Uterine artery Doppler at 11 + 0 to 13 + 6 weeks and 21 + 0 to 24 + 6 weeks in the prediction of pre-eclampsia. Ultrasound Obstet Gynecol. 2008;32:138–46.
12. Rolnik DL, Wright D, Poon LCY, Syngelaki A, O'Gorman N, de Paco Matallana C, et al. ASPRE trial: performance of screening for preterm pre-eclampsia. Ultrasound Obstet Gynecol. 2017;50:492–5.
13. Tan MY, Poon LC, Rolnik DL, Syngelaki A, de Paco Matallana C, Akolekar R, et al. Prediction and prevention of small-for-gestational-age neonates: evidence from SPREE and ASPRE. Ultrasound Obstet Gynecol. 2018;52:52–9.
14. Liu B, Frick A, Bhide A, Thilaganathan B. Placental dysfunction screening and perinatal loss. BJOG. 2022;129:1617–8.
15. Guy GP, Leslie K, Diaz Gomez D, Forenc K, Buck E, Bhide A, et al. Effect of routine first-trimester combined screening for pre-eclampsia on small-for-gestational-age birth: secondary interrupted time series analysis. Ultrasound Obstet Gynecol. 2022;59:55–60.
16. Papastefanou I, Nowacka U, Buerger O, Akolekar R, Wright D, Nicolaides KH. Evaluation of the RCOG guideline for the prediction of neonates that are small for gestational age and comparison with the competing risks model. BJOG. 2021;128:2110–5.
17. Tan MY, Syngelaki A, Poon LC, Rolnik DL, O'Gorman N, Delgado JL, et al. Screening for pre-eclampsia by maternal factors and biomarkers at 11–13 weeks' gestation. Ultrasound Obstet Gynecol. 2018;52:186–95.
18. Noël L, Guy GP, Jones S, Forenc K, Buck E, Papageorghiou AT, et al. Routine first-trimester combined screening for pre-eclampsia: pregnancy-associated plasma protein-a or placental growth factor? Ultrasound Obstet Gynecol. 2021;58:540–5.
19. Rolnik DL, Wright D, Poon LC, O'Gorman N, Syngelaki A, de Paco Matallana C, et al. Aspirin versus placebo in pregnancies at high risk for preterm preeclampsia. N Engl J Med. 2017;377:613–22.
20. Roberge S, Nicolaides K, Demers S, Hyett J, Chaillet N, Bujold E. The role of aspirin dose on the prevention of preeclampsia and fetal growth restriction: systematic review and meta-analysis. Am J Obstet Gynecol. 2017;216:110–20.e6.
21. Bhide A, Acharya G, Baschat A, Bilardo CM, Brezinka C, Cafici D, et al. ISUOG practice guidelines (updated): use of Doppler velocimetry in obstetrics. Ultrasound Obstet Gynecol. 2021;58:331–9.
22. Gómez O, Figueras F, Fernández S, Bennasar M, Martínez JM, Puerto B, et al. Reference ranges for uterine artery mean pulsatility index at 11–41 weeks of gestation. Ultrasound Obstet Gynecol. 2008;32:128–32.
23. Chaemsaithong P, Sahota DS, Poon LC. First trimester preeclampsia screening and prediction. Am J Obstet Gynecol. 2022;226:S1071–97.e2.
24. García B, Llurba E, Valle L, Gómez-Roig MD, Juan M, Pérez-Matos C, et al. Do knowledge of uterine artery resistance in the second trimester and targeted surveillance improve maternal and perinatal outcome? UTOPIA study: a randomized controlled trial. Ultrasound Obstet Gynecol. 2016;47:680–9.
25. Gallo DM, Wright D, Casanova C, Campanero M, Nicolaides KH. Competing risks model in screening for preeclampsia by maternal factors and biomarkers at 19–24 weeks' gestation. Am J Obstet Gynecol. 2016;214:619.e1–17.
26. Liu B, Nadeem U, Frick A, Alakaloko M, Bhide A, Thilaganathan B. Reducing health inequality in black, Asian and other minority ethnic pregnant women: impact of first trimester combined screening for placental dysfunction on perinatal mortality. BJOG. 2022;129:1750–6.
27. Ridder A, Giorgione V, Khalil A, Thilaganathan B. Preeclampsia: the relationship between uterine artery blood flow and trophoblast function. Int J Mol Sci. 2019;20:3263.
28. Melchiorre K, Giorgione V, Thilaganathan B. The placenta and preeclampsia: villain or victim? Am J Obstet Gynecol. 2022;226:S954–62.
29. Yu CKH, Papageorghiou AT, Parra M, Palma Dias R, Nicolaides KH, The Fetal Medicine Foundation Second Trimester Screening Group. Randomized controlled trial using low-dose aspirin in the prevention of pre-eclampsia in women with abnormal uterine artery Doppler at 23 weeks' gestation. Ultrasound Obstet Gynecol. 2003;22:233–9.
30. Poon LC, Magee LA, Verlohren S, Shennan A, Dadelszen P, Sheiner E, et al. A literature review and best practice advice for second and third trimester risk stratification, monitoring, and management of pre-eclampsia: compiled by the Pregnancy and Non-Communicable Diseases Committee of FIGO (the International Federation of Gynecology and Obstetrics). Int J Gynaecol Obstet. 2021;154(Suppl 1):3–31.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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