# FMF vs NICE screening for preeclampsia in first trimester

Malligiannis Ntalianis K, Daher L, Sowah J, Saji B, Harrington A, Reddings K, Whale E, Gatley P, Abdul I, Raajkumar S

Southend University Hospital, Southend, United Kingdom

## Objective

The aim of the study was to compare first trimester screening for preeclampsia in our unit using the NICE guidelines (based on maternal characteristics and medical history) vs the Mini-combined test using the Fetal Medicine Foundation algorithm (combining maternal characteristics and medical history with the combined uterine artery mean PI and PAPPA results), as part of a Quality Improvement Project to suggest which method is superior, more feasible and should be adopted in our unit taking into account the COVID-19 restrictions.

## Methods

Participants were women who attended the Fetal Medicine Unit at Southend University Hospital for a routine antenatal visit at $11^{+0}$–14 weeks' gestation, between 1st of May 2021 and 1st of September 2021. Inclusion criteria were maternal age ≥18 years and singleton live pregnancy with no major fetal abnormality, and an NT < 3.5mm at the 11–14-week scan. The sample size included was 646 women. The following data were obtained and stored on the digital system Astraia/Maternal Notes, and then saved in Excel Sheet: Maternal Characteristics, Medical History, the Uterine Artery-mean Pulsatility Index, and the biochemical marker PAPP-A results. All data were anonymized. The first trimester risk for Preeclampsia was then calculated using the NICE guidelines as well as the newly proposed Mini-combined test as per the Fetal Medicine Foundation algorithm.

## Results

The risk for PET calculated using the mini-combined method had a 50% sensitivity when using a 1 in 100 cut-off, with a 89.9% specificity for all cases of preeclampsia. The NICE screening method had 22.7% sensitivity with a similar specificity of 90.9%. A secondary analysis for small for gestational age (SGA) babies, showed that the mini-combined method had a 30% sensitivity when using a 1 in 100 cut-off, with a 89.1% specificity for all cases of SGA, whereas the NICE screening method had 6% sensitivity and 89.7% specificity.

## Conclusion

Screening for PET with the Mini-combined method using FMF algorithm is superior to NICE's method, even in its more simplified form. Therefore, we are proposing to adopt the Fetal Medicine Foundation screening for PET method, ideally in its complete form including maternal characteristics, medical history, uterine artery mean PI, the Mean Arterial Pressure (MAP) plus the biochemical - placental growth factor (PLFG). A secondary analysis of the data showed that the Mini-Combined method is also superior to NICE for screening for SGA.

| Table 1. Maternal demographic data and characteristics | | N | % |
|---|---|---|---|
| Maternal age, mean (SD) | | 30.4 (5.1) | |
| Race | White/Caucasian | 602 | 93.2 |
| | Black/African | 13 | 2.0 |
| | East Asian | 10 | 1.5 |
| | South Asian | 16 | 2.5 |
| | Mixed | 5 | 0.8 |
| BMI (kg/m2), mean (SD) | | 27.6 (6.2) | |
| BMI levels | Underweight <18.5 | 14 | 2.2 |
| | Normal 18.5-25 | 243 | 37.7 |
| | Overweight >25 | 202 | 31.3 |
| | Obese >30 | 186 | 28.8 |
| Smoking | No | 593 | 91.8 |
| | Yes | 44 | 6.8 |
| | In the past | 9 | 1.4 |
| Alcohol | No | 646 | 100.0 |
| | Yes | 0 | 0.0 |
| Diabetes I / II | No | 642 | 99.4 |
| | Yes | 4 | 0.6 |
| Chronic hypertension | No | 646 | 100.0 |
| | Yes | 0 | 0.0 |
| Nephropathy | No | 646 | 100.0 |
| | Yes | 0 | 0.0 |
| Antiphospholipid syndrome (APS)/ Systemic Lupus Erythematosus (SLE) | No | 646 | 100.0 |
| | Yes | 0 | 0.0 |
| Conception | Spontaneous | 626 | 96.9 |
| | ART/IVF | 20 | 3.1 |
| Parity | Nulliparous | 297 | 46 |
| | Multiparous | 349 | 54 |

| Table 2. Obstetric outcomes | | N | % |
|---|---|---|---|
| Birth weight, mean (SD) | | 3388.7 (535.3) | |
| Low birth weight newborn (SGA) | No | 585 | 90.7 |
| | Yes | 60 | 9.3 |
| Low birth weight newborn with PE | | 12 | 20% |
| Gender of newborn | Female | 325 | 50.3 |
| | Male | 321 | 49.7 |
| Apgar 1', mean (SD) | | 8.8 (1.1) | |
| Apgar 5', mean (SD) | | 9.8 (0.8) | |
| Arterial pH, mean (SD) | | 7.2 (0.5) | |
| Venous pH, mean (SD) | | 7.2 (0.7) | |
| NNU admission | | 23 | 3.6 |
| Intrauterine/Neonatal death | | 2 | 0.3 |

**Table 3. Comparison of screening performance between NICE vs FMF methods for all-PET, <37 and >37 weeks.**

| | AUC [+] | 95% DE | P | Cut-off | Sensitivity (%) | Specialty (%) | PPV ‡ (%) | NPV‡ ‡ (%) | Accuracy (%) |
|---|---|---|---|---|---|---|---|---|---|
| **Sample total** | | | | | | | | | |
| NICE Risk | 0.57 | 0.47 – 0.66 | 0.132 | - | 22.7 | 90.9 | 15.4 | 94.1 | 86.2 |
| FMF Risk | 0.75 | 0.66 - 0.84 _ | **<0.001** | < 165.5 | 70.5 | 80.9 | 21.2 | 97.4 | 80.2 |
| **FMF Risk** | | | | **100** | **50** | **89 . 9** | | | |
| **<37 weeks** | | | | | | | | | |
| NICE Risk | 0.59 | 0.26 – 0.92 | 0.576 | - | 25.0 | 92.6 | 33.3 | 89.3 | 83.9 |
| FMF Risk | 0.88 | 0.68 – 1.00 | **0.014** | < 74 | 75 | 100 | - [1] | 87.1 | 87.1 |
| **≥37 weeks** | | | | | | | | | |
| NICE Risk | 0.57 | 0.47 – 0.67 | 0.160 | - | 22.5 | 90.8 | 14.5 | 94.4 | 86.3 |
| FMF Risk | 0.74 | 0.64 -0.84 | **<0.001** | < 165.5 | 70 | 80.9 | 20.3 | 97.5 | 80.2 |

+Area under the curve ‡Positive predictive value ‡‡Negative predictive value 1 could not be calculated due to zero values

**Table 3. Rates of preeclampsia and logarithmic regression**

| | | | Pre-eclampsia | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | No | | Yes | | | |
| | | | N | % | N | % | OR (95% CI)+ | P |
| **Sample total** | **NICE** | Low risk | 547 | 94.1 | 34 | 5.9 | | |
| | **Risk** | High risk | 55 | 84.6 | 10 | 15.4 | 2.93 (1.37 – 6.24) | **0.005** |
| | **FMF** | >165.5 | 487 | 97.4 | 13 | 2.6 | | |
| | **Risk** | <165.5 | 115 | 78.8 | 31 | 21.2 | 10.1 (5.1 – 19.9) | **<0.001** |
| **<37 weeks** | **NICE** | Low risk | 25 | 89.3 | 3 | 10.7 | | |
| | **Risk** | High risk | 2 | 66.7 | 1 | 33.3 | 4.17 (0 .29 – 60 . 9) | 0.297 |
| | **FMF** | >74 | 27 | 87.1 | 4 | 12.9 | | |
| | **Risk** | <74 | 0 | 0.0 | 0 | 0.0 | | - |
| **>= 37 weeks** | **NICE** | Low risk | 522 | 94.4 | 31 | 5,6 | | |
| | **Risk** | High risk | 53 | 85.5 | 9 | 14.5 | 2.86 (1.29 – 6.33) | **0.010** |
| | **FMF** | >165.5 | 465 | 97.5 | 12 | 2.5 | | |
| | **Risk** | <165.5 | 110 | 79.7 | 28 | 20.3 | 9.86 (4.86 – 20.0) | **<0.001** |

+relative ratio (95% Confidence Interval) could not be calculated in all cases due to zero values

**Table 5. Comparison of prognostic value of the two methods for SGA overall, <37 and >37 weeks**

| | AUC [+] | 95% DE | P | Cut-off | Sensitivity (%) | Specialty (%) | PPV ‡ (%) | NPV‡ ‡ (%) | Accuracy (%) |
|---|---|---|---|---|---|---|---|---|---|
| **Sample total** | | | | | | | | | |
| NICE Risk | 0.48 | 0.41 – 0.56 | 0.647 | - | 6,7 | 89.7 | 6.3 | 90.4 | 82.0 |
| FMF Risk | 0.63 | 0.55 – 0.71 | **0.001** | < 318 | 60 | 61.9 | 13.9 | 93.8 | 61.7 |
| **FMF Risk** | | | | **100** | **30** | **89.1** | | | |
| **FMF Risk** | | | | **210.5** | **50** | **72.5** | | | |
| **<37 weeks** | | | | | | | | | |
| NICE Risk | 0.54 | 0.30 – 0.78 | 0.743 | - | 12.5 | 95.5 | 50.0 | 75.0 | 73.3 |
| FMF Risk | 0.54 | 0.28 – 0.79 | 0.760 | - | - | - | - | - | - |
| **≥37 weeks** | | | | | | | | | |
| NICE Risk | 0.48 | 0.40 – 0.56 | 0.574 | - | 5.8 | 89.5 | 4.8 | 91.1 | 82.4 |
| FMF Risk | 0.64 | 0.55 -0.72 | **0.001** | < 318 | 63.5 | 62.0 | 13.4 | 94.8 | 62.1 |

**Table 6. SGA rates and logarithmic regression**

| | | | SGA | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | No | | Yes | | | |
| | | | N | % | N | % | OR (95% CI)+ | P |
| **Sample total** | **NICE** | Low risk | 525 | 90.4 | 56 | 9.6 | | |
| | **Risk** | High risk | 60 | 93.8 | 4 | 6.3 | 0 , 63 ( 0.22 – 1.78 ) | 0 , 380 |
| | **FMF** | > 318 | 362 | 93.8 | 24 | 6.2 | | |
| | **Risk** | < 318 | 223 | 86.1 | 36 | 13.9 | 2.44 (1.42 – 4.19) | **0.001** |
| **<37 weeks** | **NICE** | Low risk | 21 | 75.0 | 7 | 25.0 | | |
| | **Risk** | High risk | 1 | 50.0 | 1 | 50.0 | 3.00 ( 0.17 – 54.6) | 0 , 458 |
| **>= 37 weeks** | **NICE** | Low risk | 504 | 91.1 | 49 | 8,9 | | |
| | **Risk** | High risk | 59 | 95.2 | 3 | 4.8 | 0.52 ( 0.16 – 1.73 ) | 0 , 288 |
| | **FMF** | > 318 | 349 | 94.8 | 19 | 5.2 | | |
| | **Risk** | < 318 | 214 | 86.6 | 33 | 13.4 | 2.83 (1.57 – 5.11) | **0.001** |