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Original Research Article

Correlation of FMF criteria scores with severe preeclampsia - prediction of preeclampsia in first trimester

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ABSTRACT

Background: For the prediction of Preeclampsia, a combination of tests and risk factors are superior to single predictors, some multivariable screening algorithms have been developed for predicting PE, one of which is developed by the Fetal Medicine Foundation (FMF) which uses maternal history and a combination of biophysical and biochemical measurements between 11+0 to 13+6 weeks gestation. To apply the FMF algorithm for prediction of preeclampsia in the first trimester, on antenatal women admitted with severe preeclampsia by retrospectively using information from their first trimester visits and to determine the sensitivity in the study subjects.
Methods: This is a retrospective study performed using medical records of antenatal women admitted in Cheluvamba Hospital, OBG Department, MMCRI, Mysuru over 12 months period (January 2023 to December 2023) admitted for severe preeclampsia.
Results: A total of 7719 deliveries were recorded in Cheluvamba hospital over the 12 months period. 176 antenatal women were diagnosed with Severe Preeclampsia who delivered during this period and were selected for the study. The FMF Algorithm applied using the information obtained from first trimester records (11+0 to 13+6 weeks) correctly predicted: 85% of early onset preterm Severe PE, 93% of late onset preterm Severe PE, 68% of term Severe PE, 81% of all Severe PE
Conclusion: The availability of this algorithm as a simple, free to use, online website calculator allows primary care physicians at primary care centers to recognise the potential high-risk pregnancy and to start aspirin prophylaxis, refer her to a tertiary care center for further evaluation and adequate follow up care.

Keywords: Preeclampsia prediction algorithm, Fetal medicine foundation algorithm, First trimester preeclampsia prediction

INTRODUCTION

Hypertension in pregnancy and its complications is responsible for a significant proportion of maternal and neonatal morbidity and mortality worldwide. Preeclampsia continues to be a major global cause of maternal and neonatal morbidity and mortality, especially in developing nations. When proteinuria with edema coexists with hypertension in late pregnancy, the disease is typically identified. Any disease process must be prevented by having an understanding of its etiology, pathophysiology and prevalence. It also helps to have techniques for identifying those who are at a high risk of developing the disease. Preeclampsia can be predicted or detected early with a variety of clinical, biophysical and biochemical tests that have been proposed. The frequency of maternal and fetal problems varies greatly across research, even when the diagnostic standards, the clinical presentation of the illness, the treatment and the prognosis are all distinct and uniform.[1] Preeclampsia is a pregnancy-related illness that affects almost every organ system. Although preeclampsia encompasses more than just gestational hypertension with proteinuria, the presence of protein remains a key diagnostic requirement. It is an objective

measure that depicts the system-wide endothelial leak that defines the preeclampsia condition. Preeclampsia is classified as early onset (<34 weeks), late onset (≥34 weeks), preterm onset (<37 weeks) or term onset (≥37 weeks).[2]

Low-dose aspirin is commonly used during pregnancy to prevent or delay the onset of preeclampsia. The American College of Obstetricians and Gynecologists recommend daily low-dose aspirin use for women with a history of early-onset preeclampsia and preterm delivery at less than 34 0/7 weeks of gestation or for women with multiple pregnancies complicated by preeclampsia. The U.S. Preventive Services Task Force also published a similar guideline. Daily low-dose aspirin use is considered safe and associated with a low likelihood of serious maternal or fetal complications. Prophylaxis is recommended for women at high risk of preeclampsia, starting between 12 and 28 weeks of gestation and continuing daily until delivery. In the absence of high-risk factors, current evidence does not support the use of prophylactic low-dose aspirin for preventing early pregnancy loss, fetal growth restriction, stillbirth or preterm birth.[3,4]

There are numerous practical clinical risk indicators that, alone or in combination, may identify women in early pregnancy who are at "high risk" for pre-eclampsia. These findings can help develop a clinical prediction model for pre-eclampsia and guide the use of aspirin prophylaxis throughout pregnancy.[4]

Preeclampsia/eclampsia is one of the top three causes of maternal morbidity and death globally. Recent studies also confirmed that hypertension is the most common reason for obstetrical referral to an intensive care unit.[5]

It is critical to identify pregnant women at risk of developing preeclampsia within the first trimester of pregnancy, allowing for prompt therapeutic intervention. Several professional organizations, including the American College of Obstetricians and Gynecologists (ACOG) and the National Institute for Health and Care Excellence (NICE), have suggested screening for preeclampsia based on maternal risk factors. ACOG and NICE's methodology effectively considers each risk factor as a distinct screening test, with an additive detection rate and screen-positive rate.

Preeclampsia screening based on the NICE and ACOG approaches has unsatisfactory performance, since the NICE prescription only achieves detection rates of 41% and 34%, with a 10% false-positive rate, for preterm and term preeclampsia, respectively. Screening according to the 2013 ACOG guideline can only detect 5% and 2% of preterm and term preeclampsia, respectively, with a 0.2% false-positive rate.[6,7]

Several first-trimester prediction models have been created. The majority of them have either not received external validation or failed it. However, it is worth noting that the fetal medicine foundation (FMF) first trimester prediction model (specifically the triple test), which combines maternal factors with measurements of mean arterial pressure, uterine artery pulsatility index and serum placental growth factor, has undergone successful internal and external validation. The FMF triple test has 90% and 75% accuracy in predicting early and preterm preeclampsia, respectively, with a 10% false-positive rate. Such screening performance outperforms that of older methods based only on maternal risk factors.[6,7]

The international federation of gynecology and obstetrics (FIGO) recommends that all pregnant women be screened for pre-eclampsia, which can lead to preterm delivery. Screening should occur during early pregnancy, employing a one-step first-trimester combination test with maternal risk factors and biomarkers, as well as the fetal medicine foundation's (FMF) criteria.[8]

Maternal risk factors

Maternal risk factors include demographics, medical history and current pregnancy.

Demographics

Age, race or ethnicity, height, weight, smoking while pregnant.

Medical history

Chronic hypertension, type 1 diabetes, type 2 diabetes, systemic lupus erythematosus, antiphospholipid syndrome, the patient's mother had pre-eclampsia.

Current pregnancy

Pregnancy type (twin vs. singleton pregnancy), fetal crown-rump length, conception technique, nulliparous or parous

Mean arterial pressure

It is determined using automated blood pressure monitoring equipment and computed from systolic and diastolic blood pressure values obtained twice from each arm.

Mean uterine artery pulsatility

The UtA-PI is assessed by transabdominal ultrasonography performed by a qualified radiologist. The mean is derived by averaging the measures of the left and right uterine arteries.

Biochemical markers

PAPP-A, are interpreted as having a level less than a 0.5 multiple of the median (MOM), which suggests an increased risk of pre-eclampsia. PLGF, is interpreted as

having a level lesser than 0.4 MOM, indicating an increased risk of pre-eclampsia.9

The majority of studies employed the FMF variant that combines maternal variables with three biomarkers: MAP, UtA-P index and PLGF (also known as the triple test). However, access to all three biomarkers may not always be accessible, particularly in rural places, necessitating a further investigation into whether employing any combination of biomarkers specified in the FMF algorithm is still superior to standard therapy.One such approach is the mini combination test, which includes maternal variables as well as two biomarkers: MAP and PAPP-A. It was utilized by Poon et al, and was shown to perform better than the NICE algorithm. Guy et al, substituted PLGF with PAPP-A in the triple test and found FMF to be superior to NICE. Rocha et al, utilized the FMF model that solely included maternal variables and MAP.[8,10]

This simplified model outperformed NICE; however, a comparison with the ACOG algorithm revealed mixed results, with ACOG having a higher detection rate but a significantly larger false-positive rate (73.3% for ACOG vs. 10% for FMF).[11] Given the well-known positive link between detection rate and false-positive rate, these findings are more likely to represent a high false-positive rate than improved ACOG algorithm performance.[12,13] Whereas another popular prediction model, the Gestosis HDP score has good sensitivity of upto 80%, but has a higher screen positive rate and hence higher false positive screens.[14,15]

Definition of problem

Despite the high number of mothers seeking hospital-based delivery care, there is a significant gap in the quality of care provided (WHO 2014). The National Eclampsia Registry (NER) FOGSI - ICOG interim statistics show a high incidence of hypertensive diseases during pregnancy, including eclampsia. The incidence of preeclampsia was determined to be 10.3% (NER 2013). The incidence of eclampsia is 1.9%, with more than half of cases occurring antepartum and around 13% postpartum. Maternal mortality due to eclampsia is 4-6%.[14]

The aim of the study was to determine the sensitivity of the FMF Criteria or prediction of preeclampsia in the first trimester. To apply the FMF algorithm for prediction of Preeclampsia in the first trimester, on antenatal women admitted with severe preeclampsia by retrospectively using information from their first trimester visits and to determine the sensitivity in the study subjects.

METHODS

Study design

This is a retrospective study performed using medical records of antenatal women admitted in Cheluvamba Hospital, OBG Department, MMCRI, Mysuru.

Study duration

The durationof the study over 12 months period (January 2023 to December 2023) admitted for Severe Preeclampsia. Information obtained from the records was used to calculate the scores according to FMF algorithm to calculate the sensitivity across various groups of Severe Preeclampsia women such as early onset preterm severe preeclampsia, late onset preterm preeclampsia and term preeclampsia.

Statistical analysis

MS Excel was used to capture the data and STATISTICA version 9 was used for data analysis.

Study population and sampling procedures

The study population was all pregnant women admitted into Cheluvamba hospital, MMCRI, Mysore, OBG department for Severe Preeclamspia. It is an apex referral centre nearby peripheral centers, with availability of Obstetrical HDU and ICU. All patients admitted with Severe Preeclampsia in pregnancy and its complications during study period were enrolled for the study. The diagnosis of Severe Preeclampsia was made as described in the inclusion criteria.

Admission and delivery records were used to determine the total number of deliveries and the number of women with hypertensive complications of pregnancy. Information was retrieved from her first trimester OPD visits regarding her history, MAP and body weight measurements, 1st trimester NT scan reports which gave information about Mean Uterine artery PI and investigation reports of S. PLGF or S. PAPP-A reports if any.

Inclusion criteria

Antenatal women admitted for Severe Preeclamspia in Cheluvamba Hospital, over 12 months period (January 2023 to December 2023) were included or the study.

Severe preeclampsia was defined as BP>=140/90 mmHg after 20 weeks gestation in previously normotensive women. Chronic hypertension, women with BP ≥140/90 mm Hg before pregnancy or before 20 weeks' gestation: Chronic Hypertension with Superimposed PE. With any one like, BP>=160/110 mmHg.

Proteinuria of dipstick 1+ or more. Thrombocytopenia of <1,00,000/cc. S Creatinine>1.1 mg/dl or doubling of baseline. Serum transaminase levels more than twice of normal. Cerebral symptoms of headache or visual disturbances, convulsions (Eclampsia), fetal growth restriction, pulmonary edema. All pregnant women with identifiable risk factors and/or complications of pregnancy based on the criteria already mentioned were included

Exclusion criteria

Those without such complications either in terms of the blood pressure or features of end organ damage were excluded.

Data collection

Files of patients who are admitted with Severe Preeclamspia were retrieved and data was obtained from their first trimester records, including OPD visits, Ultrasonography reports and blood investigations. Data collected included variables pertaining to the parameters of the FMF calculator.

RESULTS

Sociodemographic and clinical characteristic of the study population

The age of the subjects ranged between 19 and 45 years with a median of 25.00 and a mean of 29.82 years. Those below the age of 30 formed 71.5% of the preeclampsia women while those above 30 years accounted for 28.5%.

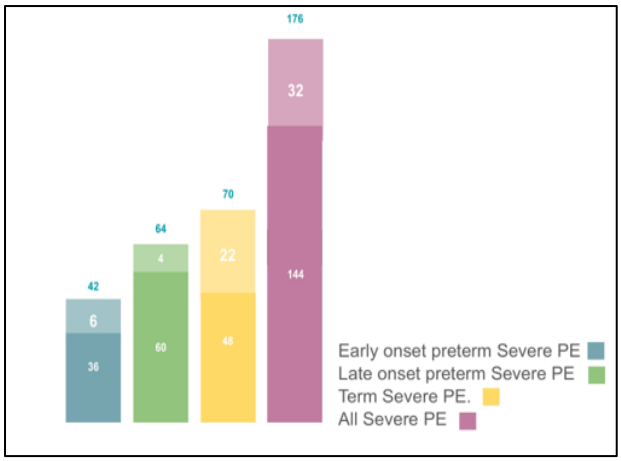

Figure 1: Results of the study.

5.6% are booked cases under our hospital of the Severe PE mothers, booked for antenatal care, 94.3% cases were booked elsewhere and referred to our hospital. Gravidity ranged from 1 to 5, with primigravida accounting for 72 cases (41.1%) while 104 cases (59%) were multigravida with gravidity ranging from 2 to 5.

Risk profile pattern of the study population. None of them were smokers. 97.7% were singleton pregnancies whereas 2.27% pregnancies were twin gestations. 7.9 % had a family history of PE in the mother. 13.6% of them had a history of GHTN/preeclampsia / antepartum eclampsia in previous pregnancies. 20% had predisposing comorbidities like HTN/ DM/ SLE /APLA syndrome. 10.2% had BMI of more than 30. 1st trimester mean MAP of the study subjects was 94.6 mmHg and mean Uterine artery PI was 1.75.

Only 8 women had their first trimester S. PAPP-A reports available as a part of Downs screening and none of them had gotten S. PLGF done.

A total of 7719 deliveries were recorded in Cheluvamba hospital over the 12 months period. 176 antenatal women were diagnosed with severe preeclampsia who delivered during this period and were selected for the study.

The FMF algorithm applied using the information obtained from first trimester records (11+0 to 13+6 weeks) correctly predicted: 85% of early onset preterm severe PE, 93% of late onset preterm severe PE, 68% of term Severe PE, 81% of all severe PE

Merits of the algorithm

Maternal history reveals most of the risk factors and can be easily elicited by the primary care physicians. Routine examination includes measurement of blood pressure and first trimester body weight.

Widespread availability of USG facilities has made it possible to screen Uterine artery PI and integrate it into the NT scan. Previous studies have proven the algorithm to perform better than most predictor models even in the absence of serum markers.

Limitations of the algorithm

Only 8 women had PAPP-A reports as part of Downs screening in the first trimester and none of the women had PLGF done in antenatal period. Blood investigations PAPP-A and PLGF are expensive and are not affordable and easily accessible to the majority of Indian rural population (83 out 88 women were from rural background).

Table 1: Sociodemographic characteristics of the study population.

Variable	No. of observation	Mean age
Age (in years)		
<20	18	19
20-29	108	23.5
30-39	38	34.6
>40	12	42.2
Marital status		
Single	0	
Married	176	
Divorced	0	
Employment status		
Employed	12	
Unemployed	164	
Booking status		
In hospital booked	10	
Referred case	166	

Table 2: Complication profile of the study population.

Risk factor	Number	N
Racial origin		
Indian	176	100
Others	0	0
Smoking during pregnancy	0	0
Obesity	18	10.2
Mother had PE	14	7.95
Methods of conception		
Spontaneous	164	93.1
Ovulation induction	12	6.8
Medical history		
Chronic Hypertension	28	15.9
Overt DM	8	4.5
APLA/SLE	0	0
History of PE in previous pregnancy	24	13.6

DISCUSSION

All studies are prospectively looking at the preeclampsia detection rates with either adjustment being accommodated or not for the study subjects who have been started on Apirin prophylaxis. In the present study, since it is retrospectively conducted on women with severe preeclampsia not on any aspirin prophylaxis.

Table 3: Comparison of sensitivity of algorithm across various studies.

Study	FMF parameters used	Sensitivity
Chaemsaithong et al[12]	Maternal + MAP, UtA-PI, PlGF	75.8
O'Gorman et al[16]	Maternal + MAP, UtA-PI, PlGF	75
Poon et al[8]	Maternal + MAP, UtA-PI, PlGF	79.6
Present study	Maternal + MAP, UtA-PI, PAPP-A (in 8 subjects)	81

The table compares the sensitivity rates of different studies using FMF parameters for maternal, MAP (mean arterial pressure), UtA-PI (uterine artery pulsatility index) and PlGF (placental growth factor). The studies by Chaemsaithong et al, O'Gorman et al and Poon et al, all used these parameters, with sensitivities of 75.8%, 75% and 79.6%, respectively.[8,12,16] The present study, however, included PAPP-A (pregnancy-associated plasma protein-A) for eight subjects in addition to the aforementioned parameters, achieving the sensitivity rate of 81%.

Dubon Garcia et al, study from Belgium was one of the few that took into consideration screening using maternal risk variables alone and the screening accuracy of the FMF algorithm. Its findings were rather dubious, nevertheless, because it based the sensitivity and specificity of these screening techniques on research that did not account for the therapeutic effects of low-dose ASA prophylaxis.[17]

CONCLUSION

First-trimester screening for preeclampsia (PE) is helpful because prophylactic administration of the high-risk group with low dose aspirin reduces the rate of early-PE with delivery at <34 weeks' gestation by about 80% and preterm-PE with delivery at <37 weeks by 60%. The availability of this algorithm as a simple, free to use, online website calculator allows primary care physicians at primary care centres to recognise the potential high risk pregnancy and to start aspirin prophylaxis, refer her to a tertiary care centre for further evaluation and adequate follow up care.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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