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Original Research Article

An observational study on use of maternal risk factors, mean arterial pressure, mean uterine artery pulsatility index and serum placenta like growth factor for screening of preeclampsia in first trimester

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ABSTRACT

Background: Preeclampsia (PE) affects 2-3% of all pregnancies and is a major cause of maternal and perinatal morbidity and mortality. In the last decade extensive research has been devoted to screening for PE with the aim of reducing the prevalence of the disease through pharmacological intervention in the high-risk group. In our study we used the combined screening method to evaluate the risk of developing preeclampsia in pregnant women. Our primary objective was to estimate the screen positivity rate for preeclampsia using the first trimester combined screening method (maternal risk factors and biophysical methods) in our population in a tertiary care hospital setting.
Methods: Risk of preeclampsia was calculated using fetal medicine foundation algorithm accessed at https://fetalmedicine.org/research/assess/preeclampsia.
Results: Using the combined screening method, 10 out of 75 women (13.33%) were found to be screen positive for risk of developing preterm preeclampsia (at <37 weeks) with a risk cut off of 1:100. Using the maternal risk factors approach only (as per NICE guidelines) again 10 out of 75 women (13.3%) were found to be screen positive. However, the subset of women who were screen positive by each method were not the same. There were only 4 out of 10 women who were screen positive by both methods. The screen positivity rate for preterm preeclampsia (<37 weeks) in our population using combined screening approach was 13%, which means aspirin would be advisable to 13/100 pregnant women to reduce the risk of preterm preeclampsia.
Conclusions: Basis on our study we concluded that one cost effective method of screening could be, to offer aspirin to all women who are screen positive by the maternal risk factor approach (NICE guidelines approach). This approach does not require any extra blood test or skill to measure uterine artery pulsatility index.

Keywords: Biochemical screening, First trimester screening, Preeclampsia screening, Screening in early pregnancy

INTRODUCTION

Preeclampsia is a global maternal health issue responsible for maternal and neonatal severe morbidity and mortality.[1] International Society for the Study of Hypertension in Pregnancy (ISSHP) which is predominantly used globally defines preeclampsia as the presence of new-onset hypertension and proteinuria or other end-organ damage occurring after 20 weeks of gestation, with eclampsia defined as the development of grand seizures in a woman with preeclampsia.[2-4] Preeclampsia affects an estimated 4.6% of pregnancies worldwide.[5] In India it is one of the most common complications of pregnancy with an incidence of 10%.[6] In Asia and Africa nearly one tenth of maternal deaths are related to hypertensive disorders of pregnancy.[7]

Preeclampsia (PE) affects 2-3% of all pregnancies and is a major cause of maternal and perinatal morbidity and mortality. In the last decade extensive research has been

devoted to screening for PE with the aim of reducing the prevalence of the disease through pharmacological intervention in the high-risk group.

The traditional approach to screening for PE is to identify risk factors from maternal demographic characteristics and medical history, but such approach can identify only 30% of all-PE and about 41% of preterm-PE.[8]

Lately, first trimester combined screening prediction models have been developed. These consist of assessment of a combination of maternal risk factors and maternal biophysical markers (i.e., measurements of mean arterial pressure, uterine artery pulsatility index and serum placental growth factor). This method has been shown to detect 100% for early preeclampsia, 75% for preterm preeclampsia.[9]

In our study we used the combined screening method to evaluate the risk of developing preeclampsia in pregnant women.

Aim and objective

Our primary objective was to estimate the screen positivity rate for preeclampsia using the first trimester combined screening method (maternal risk factors and biophysical methods) in our population in a tertiary care hospital setting.

Our secondary objective was to estimate the screen positivity rate for preeclampsia using maternal risk factors only (as per NICE guidelines) in the same population.

We also wanted to check if there was any strong correlation of a specific maternal risk factor with screen positivity derived by biomarker screening.

METHODS

This was an observational study conducted on 75 women attending routine antenatal clinic at Artemis Hospital, Gurugram and our study period was November 2020 to June 2021. Full detailed history was taken from all patients and looked for the risk factors according to NICE guideline. Woman who had one major risk factor or any two moderate risk factors she was classified as screen positive. The major risk factors include history of preeclampsia in previous pregnancy, chronic renal disease, chronic hypertension, diabetes mellitus and SLE or APS. Moderate risk factors include first pregnancy, age >40 years, BMI 35 kg/m^2, interpregnancy interval >10 years, multifetal gestation and family history of preeclampsia. A transabdominal ultrasound (TAS) was performed for all cases at 11-13+5 weeks to confirm the gestational age and measure the uterine artery pulsatility index (PI). Maternal serum levels of PLGF were analyzed and mean arterial pressure (MAP) was recorded. Risk of preeclampsia was calculated using fetal medicine foundation algorithm accessed at https://fetalmedicine.org/research/assess/preeclampsia for the combined method screening method approach.

Screen positivity rate was worked out by using both methods.

Screen positivity rate = number of screen positive women/total number of screened women × 100.

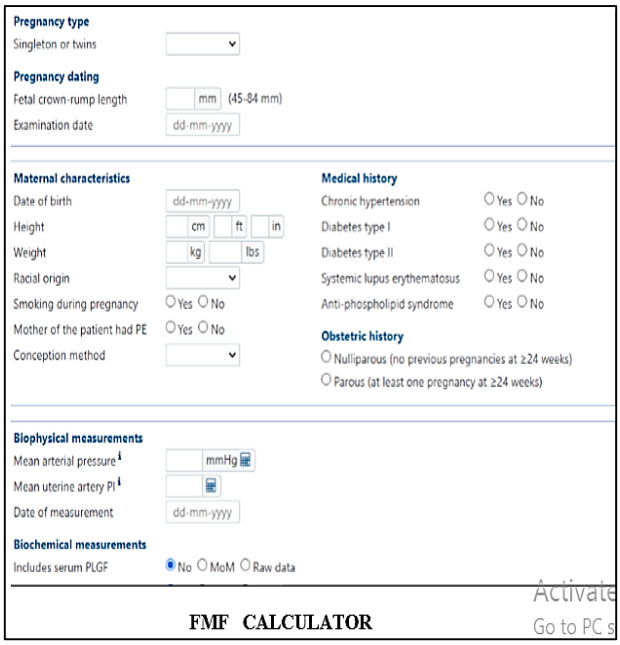

Figure 1: FMF calculator.

RESULTS

Using the combined screening method, 10 out of 75 women (13.33%) were found to be screen positive for risk of developing preterm preeclampsia (at <37 weeks) with a risk cut off of 1:100.

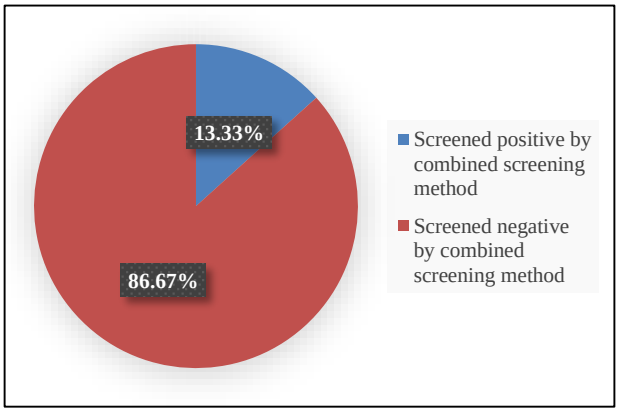

Figure 2: Screen positive rate by combined screening method.

Using the maternal risk factors approach only (as per NICE guidelines) again 10 out of 75 women (13.3%) were found to be screen positive.

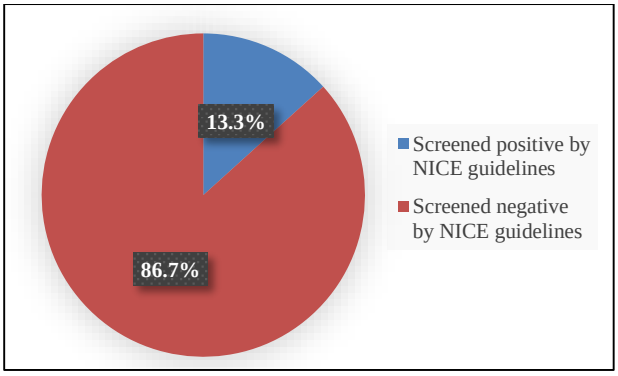

Figure 3: Screen positive rate by NICE guideline.

However, women screened positive by combined screening method were not the same as women screened positive by the NICE criteria. There were only 4 out of 10 women who were commonly screen positive in the two groups.

There was no significant difference with regards to maternal age in screened positive and screened negative women for development of preeclampsia in both the screening method (screening by NICE criteria and screening by combined screening method).

In screened positive women 60% were primiparous and 40% were multipara by either of the methods.

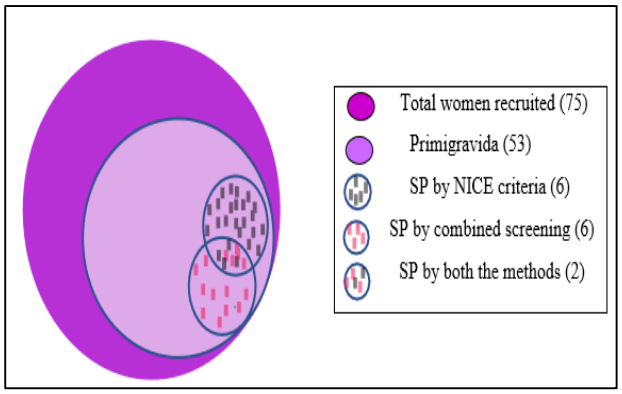

Figure 4: Correlation of first pregnancy with screen positivity (SP).

Mean uterine artery PI was higher in screened positive women (1.86) compared to screened negative women (1.50). Serum PLGF levels were significantly reduced in screened positive women lower (0.74 MoM) compared to screened negative women (1.17 MoM).

We found correlation of some maternal risk factors i.e., history of PE in previous pregnancy, diabetes mellitus, BMI>35 kg/m^2 with screen positivity derived by biomarker screening

2 out of 3 patients with BMI>35 kg/m^2 were screen positive by both NICE and combined screening method. 1 out of 3 patients with diabetes were screened positive by both NICE and combined screening method. Only 1 patient had history of preeclampsia in previous pregnancy who was screened positive by both methods. Risk of term preeclampsia (at >37 weeks) with a risk cut off of 1:35 was observed in 44 out of 75 women (58%). All women screen positive by NICE guidelines method were also screen positive for either preterm or term preeclampsia.

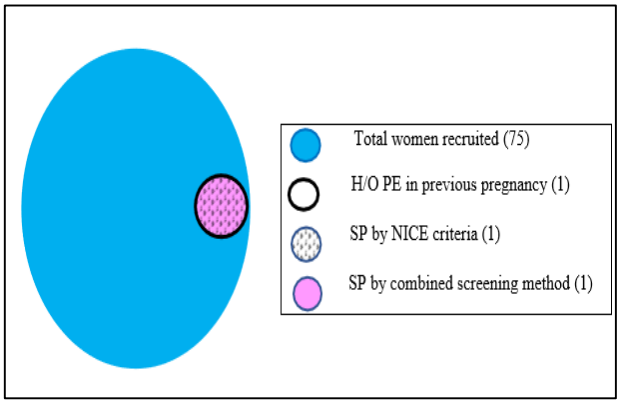

Figure 5: Correlation of history of previous preeclampsia with screen positivity (SP).

DISCUSSION

Since the sensitivity and specificity of the methods using maternal risk factors for prediction of PE is low, considerable efforts have been made to identify biomarkers (biophysical and biochemical) which can be used in addition to maternal risk factors, that can predict preeclampsia in the first trimester of pregnancy.

An approach by combining maternal risk factors, measurement of mean arterial pressure uterine artery pulsatility index and serum placental growth factor has been proposed by Fetal medicine foundation. The additional cost for carrying out these tests is Rs 1500 approximately in Indian scenario. It could be argued that if aspirin is inexpensive and safe then it could be potentially prescribed to all pregnant women as a blanket, avoiding the burden of performing a screening test which is never going to be 100% accurate anyway. There are two issues with this approach. First, that even though low dose aspirin is considered safe, there may be an occasional case maternal cerebral haemorrhage or of fetal premature closure of PDA. The second issue is that of compliance. If prescribed to everyone, there is a greater likelihood of non-compliance amongst women, than when prescribed to only limited number of screen positive women. Literature shows that Aspirin needs to have adherence of >90% for reduction in incidence of preterm-PE about 75% and adherence of <90% for reduction in incidence of preterm PE of about 40%.[10] So compliance plays an important role when it comes to efficacy of aspirin.

The "maternal risk factors only" approach to screening does not differentiate between risk of preterm and term

preeclampsia whereas "combined screening" approach using maternal risk factors and biomarkers can work out gestational age specific risk (early, preterm and term PE)

In Caucasian population, on screening by a combination of maternal factors, MAP, UtA-PI and PlGF and using a risk cut-off of 1 in 100 for preeclampsia at <37 weeks, the detection rates for early, preterm and term PE were 88%, 69% and 40%, respectively with the screen-positive rate of 10%.[11]

In women of Afro-Caribbean racial origin, with the same method of screening and risk cut-off, the detection rates for early, preterm and term PE were 100%, 92% and 75%, respectively with the screen-positive rate of 34%.[11]

We did not find any studies on screen positivity rate using a combination of maternal risk factors, maternal biochemical and biophysical markers in Indian population.

We recruited 75 women to undergo screening by the combined screening method as well as criteria laid by the NICE guidelines. In our population, out of 75 women, 10 women (13.3%) were screen positive for preterm pre-eclampsia by combined screening method using FMF algorithm. This would mean that 14/100 pregnant women would need to take aspirin daily in pregnancy if this approach is used for screening.

Using the NICE guideline approach also, 10 out 75 women (13.3%) were found to be screen positive. So again 14/100 pregnant women would need to take aspirin daily if screening is done by NICE method.

However, the subset of women who were screen positive by each method were not the same. There were only 4 out of 10 women who were screen positive by both methods.

In that case, one could use a contingency screening plan i.e., screen for PE by NICE method first and those who are screen negative be screened again by combined method so as to not miss those who would have been missed by first method.

The screen positivity rate for preterm preeclampsia (<37 weeks) in our population using combined screening approach was 13%, which means aspirin would be advisable to 13/100 pregnant women to reduce the risk of preterm preeclampsia

The screen positivity rate for term preeclampsia using the same approach was 58% which would mean aspirin would be recommended to 58/100 women to reduce the risk of term preeclampsia.

The screen positivity rate using NICE guidelines (which does not differentiate between risk of preterm and term preeclampsia) was again 13%, meaning 13/100 women would need to be advised aspirin for prevention of preeclampsia. All these women were picked up by the combined screening method too (40% for preterm preeclampsia, 60% for term preeclampsia).

Limitation of our observation study was more prone to bias and confounding, cannot be used to demonstrate causality.

CONCLUSION

Basis on our study we concluded that one cost effective method of screening could be, to offer aspirin to all women who are screen positive by the maternal risk factor approach (NICE guidelines approach). This approach does not require any extra blood test or skill to measure uterine artery pulsatility index. Then further screen the initial screen negative women by the combined screening approach to pick up the remaining "at risk" women who may have been missed by "risk factors only" approach.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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