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Research Article

A PROGRAM ON OBSTETRIC POPULATION FOR PREDICTING PREECLAMPSIA DURING FIRST TRIMESTER

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ABSTRACT
Prediction of preeclampsia (PE) in obstetric patients under standard clinical conditions is examined by testing an aneuploidy screening program during the first trimester. Over the period, 567 pregnant women at a tertiary hospital received aneuploidy screenings in their first trimester. The logistic regression model was developed based on maternal characteristics, the lengths of the crown and rump, the thickness of the nuchal translucency, pregnancy-associated plasma protein-A (PAPP-A) and free human chorionic gonadotropin beta subunits (free-hCG) and pregnancy-associated plasma protein-A (free-hCG), a logistic regression model was developed for PE. PE detection rates were 31.4%/34.57% for early onset (EO) and 29.5%/35.25% for late onset (LO), respectively, with a false-positive rate of 5/10%. However, free-hCG, CRL, and NT contributed significantly to decreased PAPP-A regardless of the type of PE. Both EO-PE and LO-PE clinical manifestations can be predicted based on maternal history and biomarkers found during the first trimester. Due to the lack of new markers currently used in aneuploidy screening programs, it is necessary to improve the models.

Keywords: - Obstetric Population, Prediction preeclampsia, PAPP-A, CRL

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INTRODUCTION

There is considerable maternal and fetal morbidity and mortality associated with preeclampsia (PE) during pregnancy [1]. If PE can be predicted prenatally, interventions may be possible to prevent unfavorable outcomes for the mother and newborn. National Institute for Health and Clinical Excellence (NICE) guidelines recommend prenatal evaluation of maternal risk factors for PE in all pregnant women in the United Kingdom [2,3]. A materno-paternal history-based screening for PE, however, has been proven insufficient. Precursors to PE development during pregnancy have been suggested by several markers associated with PE pathophysiology [4]. We also screened for aneuploidy and evaluated the kidney, endothelial, and fetal-derived products. The onset of an illness as heterogeneous as PE cannot be predicted with just one biomarker, Ultrasonography and serum indicators are being tested in addition to history-based and physical screening [5]. PE prediction models are currently not accurate enough to be able to use biomarkers or maternal history as a predictor. We therefore aim to assess whether an aneuploidy screening program in the first trimester can accurately predict preeclampsia in an obstetric population [6].

Methodology

Participants, Setting, and Design

Aneuploidy screening was conducted at southern area of tertiary hospital in Chennai. Aneuploidy screening during the first trimester was conducted on 567 pregnant women.

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This study included singleton pregnancies with gestational ages of 9 weeks, 0 days, and 13 weeks, 6 days. Several factors were excluded from participating in the study, including multiple pregnancies, severe structural or chromosomal abnormalities, miscarriages, and death of the foetus before 24 weeks of pregnancy. At the end of the first trimester, we screened for aneuploidy and monitored the birth process. Regional ethics committees and institutional review boards have approved the study protocol.

Maternal Assessment

We performed an aneuploidy screening during the ninth and thirteenth weeks of pregnancy. The team collected data on participants' age, ethnicity, method of conception, weight, smoking status, chronic illnesses, parity, and previous pregnancy difficulties [7]. We analyzed maternal serum samples using customary automated analyzers after taking blood samples. These biochemical markers were measured with DELFIA XPRESS instead of IMMULITE 2000 due to this change. During eleven weeks and six days and thirteen weeks and six days of pregnancy, ultrasound examinations were performed. The nuchal translucency thickness and crown-rump length were used to estimate gestational age [8]. A combined risk assessment for the first trimester was completed by integrating these clinical data into an integrated electronic form.

Measures of Results

During the pregnancy, information was gathered from maternal and paediatric records. A woman with previously normal blood pressure who suddenly develops hypertension (>140/90 mmHg) after 20 weeks of gestation, accompanied by substantial proteinuria, is classified as having PE cases. A chronic hypertensive patient has high blood pressure that was developed before or during pregnancy. A substantial amount of proteinuria developed after 20 weeks of pregnancy in women with chronic hypertension and PE. Pregnant women with gestational hypertension would experience new-onset hypertension without associated proteinuria after 20 weeks of pregnancy. These outcome diagnoses were recorded in the mother's maternity records when she was discharged from the hospital. It is recommended that patients with preeclampsia begin to experience symptoms before or after 34 weeks of gestation, based on their onset date. Furthermore, we considered birth weight, stillbirth frequency, and gestational age at delivery as well as other obstetric and neonatal outcomes. In this study, low birth weight (LBW) refers to a birth weight less than 2500 grams as a rule of thumb.

Statistical analysis

Both impacted and unaffected groups had their maternal characteristics analyzed based on their PE status. For the logistic regression analysis, we used multiples of the medians (MoM), log transformed maternal weight, PAPP-A, and hCG. Considering the different platforms used for measuring PAPP-A and hCG, median values for each assay were transformed using the MoM method [9]. Statistically, no statistically significant differences are observed between the distribution of MoM values generated by this method and those generated by other methods. Discrete categorical and quantitative variables were analysed using Mann-Whitney tests and Pearson correlations. Using paired analysis following the Kruskal-Wallis test, we also compared quantitative variables across several groups. Predictive values were estimated using ROC analysis (receiver operating characteristic analysis).

Results

Results were expressed as estimated detection rates (DR) based on false-positive rates of 5% and 10%. Based on stepwise backward estimation, all binomial logistic models were estimated using a 0.05 -value cut-off. We used SPSS 21.0, a statistical software program, to analyze the data. There were 465 pregnancies without PE and 140 (0.9% new incidences) with PE among the remaining 479. There were 35 people suffering from early-onset PE in the PE group (or 25%) and 105 people suffering from late-onset PE (or 75%). Combined first trimester aneuploidy screening used biomarkers that were accessible in every case. The following table provides descriptive information about maternal traits, aneuploidy screening biomarker results, and pregnancy outcomes.

Pregnant women with PE were older, heavier, and more likely to be nulliparous, as well as have a Hypertension history and type 2 diabetes. Across groups, there were no significant differences in maternal smoking behaviour, conception type, or new-born gender. Pregnancies with EO-PE and LO-PE had lower levels of PAPP-A than those without, but free hCG, CRL, or NT were not affected. PE pregnancies had lower median gestational ages that the EO-PE group and LO-PE group, when compared with unaffected pregnancies. Seventy-five percent of pregnancies with PE resulted in a caesarean delivery, compared to 34.1% without. In the EO-PE group as opposed to the LO-PE group, the prevalence of LBW and median birth weight were higher than those in the PE group.

As evident from logistic regression analysis of the maternal variables, there was a decrease in PAPP-A levels in EO-PE and LO-PE (0.93 MoM and 0.85 MoM, respectively), but no decrease in PAPP-A in LO-PE (Table 2). According to our results, PE, EO-PE, and LO-PE each achieved 10.0%, 9.4%, and 10.3%. Diabetes did not significantly affect PE's early manifestations, but it was

associated with diabetes mellitus, chronic hypertension, and family history. Old age, obesity, and nulliparity are also risk factors for PE. In the Free hCG and PAPP-A in univariate analyses, LBW women had lower median PAPP-A, while free hCG levels were not significantly different (Figure 3).

Table.1: Population demographics

Adaptable	Pregnancies without complications	(PE)	EO-PE	The LO-PE test
Median (IQR) of maternal age, years	29.9 (25.8–34.0)	31.0 (27.7–32.6)	30.0 (25.0–35.9)	31.0 (28.0–34.0)
Weight of mothers, median (IQR)				
Kg*a	43.6 (57.0–75.0)	80.1 (60.9–92)	82.0 (64.5–83.0)	78.3 (67.6–88.4)
MoM*a	0.88 (0.89–1.23)	1.22 (0.95–1.28)	1.23(1.01–1.28)	1.18 (0.94–1.30)
Number of ethnicities (%)				
The color white	235 (98.2)	112 (97.6)	42 (98.1)	115 (98.0)
the color Black	83 (1.7)	1 (0.8)	1 (2.8)	0 (0.1)
Other	47 (1.1)	1 (0.6)	0 (0.0)	1 (1.0)
N (%)b Nulliparous	232 (61.1)	87 (70.2)	32 (77.2)	32 (67.5)
N (%) of patients with a medical history				
Chronic hypertension	132 (2.3)	15 (8.5)	5 (32.4)	7 (6.5)
Kidney diseases	2 (0.2)	1 (0.4)	1 (2.2)	0 (0.1)
Medications to treat diabetes	32 (1.0)	8 (6.4)	1 (2.2)	8 (7.4)
Smoking rate among pregnant women, n (%)	92 (20.4)	32 (15.0)	5 (17.1)	13 (14.3)
% of spontaneous conceptions	432(96.8)	132 (92.6)	32 (94.4)	96 (92.6)
Indicators of ultrasound (IQR), median				
CRL, mm	63.9 (56–71)	74.5 (58–71)	64.2 (56–67.8)	65.0 (59–70.8)
NT, mm	2.5 (1.2–1.7)	1.3 (1.2–1.9)	1.5 (1.2–1.9)	1.5 (1.1–1.4)
Serum content of pregnant women, median (IQR)				
PAPP-A, MoM*a	1.12 (0.64–1.61)	0.95 (0.56–1.34)	0.98 (0.32–1.39)	0.85 (0.58–1.34)
Free -hCG, MoM	1.00 (0.66–1.54)	1.10 (0.66–1.65)	0.43 (0.53–1.35)	1.17 (0.70–1.77)
Outcomes of pregnancy				
N (%) of pregnant women with hypertension	58 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
N (%) of C-sections	158 (34.2)	98 (70.6)	21 (88.67)	67 (64.5)
Median gestational week (IQR)	39 (38–41)	37 (35–37)	23 (29–35)	37 (36–39)
A birth's outcomes				

N (%) of males	232 (50.7)	78 (48.4)	28 (54.2)	57 (46.3)
Stillbirth rate (%)	25 (0.1)	2 (1.3)	2 (5.7)	0 (0.0)
Weight at birth (g) as a median (IQR)	429 (287–344)	267 (215–305)	191 (105–244)	283 (248–315)
LBW, n (%)b	35 (7.5)	55 (39.5)	27 (77.2)	28 (26.8)

Table.2: Modelling of PE, EO-PE, and LO-PE with logistic regression models.

	PE		EO-PE		LO-PE	
	The b	Value of p	The b	Value of p	The b	Value of p
Hypertension chronic (if true)	1.971	0.013	2.518	0.004	0.051	0.012
If it is true, diabetes mellitus	2.529	0.000			2.648	0.000
A multiparous couple's parity	−1.788	0.000	−2.202	0.008	−2.622	0.008
A brief history of PE, if true	2.853	0.000	4.202	0.001	3.665	0.000
Age of the mother	1.022	0.027				
MoM weight (logarithm)	6.158	0.000	6.109	0.000	5.734	0.000
RRC	1.032	0.011			0.138	0.003
New Testament	−1.582	0.037			−0.693	0.026
(MoM, log) -hCG free	0.658	0.019			1.145	0.007
Invariable	−6.822	0.000	−5.952	0.000	−9.349	0.000

EO-PE, LO-PE, and PE are modelled using a logistic regression model.

Table.3: ROC curves for logistic regression models were determined using maternal characteristics and aneuploidy screening biomarkers.

Adaptable	Accreditation of ROC	FPR = 5% for DR	ADR (10% FPR)
PE	0.743	28.8	35.5
EO-PE	0.763	32.5	46.8
LO-PE	0.743	28.6	36.3

Figure 2: Aneuploidy screening biomarkers and logistic regression curves for predicting PE, EO-PE, and LO-PE. There are three types of preeclampsia: PE, EO-PE, and LO-PE.

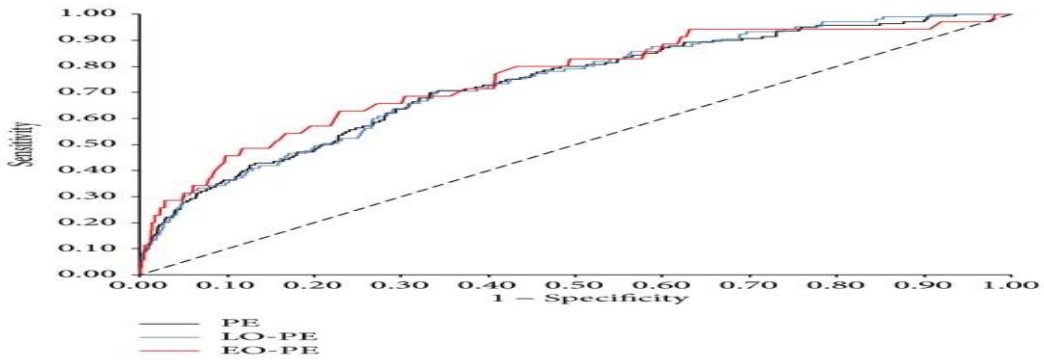
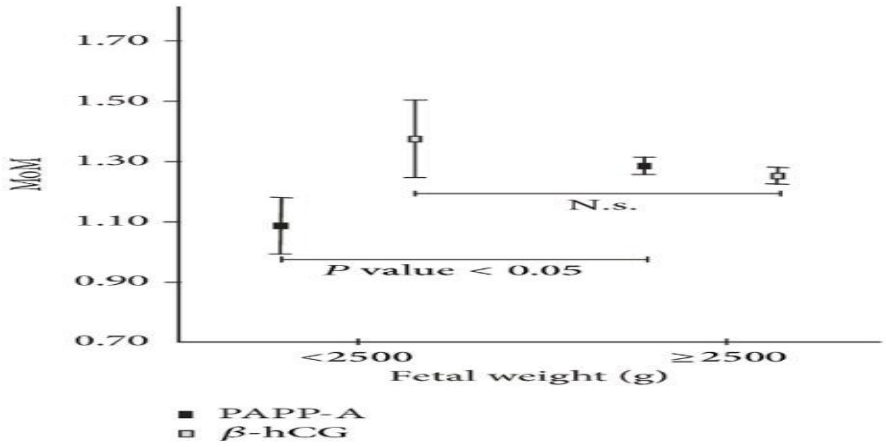


Figure 3: A comparison of PAPP-A and +-hCG following delivery of a fetal of the different weights.



The final model for LBW was calculated by including all the predetermined factors in a logistic regression model: 1.86 1.013 (for chronic hypertension) + 0.658 (for Caucasian), 0.570 (for smokers) + 0.196 (for multiparous women) + 1.155 PAPP-A (MoM, Log) + 3.381 Maternal Weight (MoM, Log). A logistic regression model, in contrast to PE prediction models, shows a positive correlation between PAPP-A and LBW.

Discussion

Screening for aneuploidy during the first trimester is associated with PE in pregnant women, according to epidemiologic findings reported in the literature [10]. Aneuploidy screening in the first trimester combined with maternal history and biomarkers confirmed earlier studies showing EO-PE and LO-PE could be predicted. In the regression models, variables were included differently and their performance was different for each clinical form of PE [11]. As a result, the model needs to be updated as the detection rate was low.

We found 31.4% and 45.7% detection rates of EO-PE, respectively, with 5% and 10% false-positive rates. Though EO-PE does not consider biochemical or ultrasound markers, LO-PE does, so it may be able to beat LO-PE prediction [12]. A significant contribution was made by maternal variables, free hCG, CRL, and NT to LO-PE and overall PE prediction in combination with PAPP-A

PAPP-A levels lower than 65 were associated with lower EO-PE and LO-PE in the univariate study, but no logistic model incorporating this biomarker was developed for PE prediction. According to this, the addition of PAPP-A to the models added no new, significant information to what had already been revealed by the other variables taken together, and PAPP-A measurement may therefore provide essentially no additional value when combined with other biomarkers [13]. A combination of free-hCG, NT, and CRL could be more effective for PE prediction than PAPP-A alone. Our findings are supported by research reports that also found a substantial correlation between PE and PAPP-A, but the correlation declined when the biomarker was paired with other biomarkers. Unlike free hCG, NT, and CRL, PAPP-A showed a highly significant correlation with LBW [14]. Although these biomarkers have previously been linked with birth weight, some studies have found a significant correlation while others didn't.

Several restrictions are imposed on our study due to its retrospective nature. During the study period, the clinical chemistry laboratory used a different analytical platform for measuring PAPP-A and -hCG serum levels, so all participants' measurements weren't conducted using the same assay method [15]. Statistical analysis of the data took this event into account, however. A number of studies have demonstrated that the maternal mean arterial pressure (MAP) before and after the first trimester of pregnancy is an important prognostic indicator for PE. Furthermore, PE patients' diagnoses were likely biased by their treating doctor. The study is the first of its kind among obstetricians to be conducted under standard clinical conditions and represents the reality of over five years of performing prenatal screening during the first trimester [16].

Research is underway to discover what combination of markers can enhance history-based PE screening, since conventional techniques based solely on maternal demographics and medical history have failed to produce effective results [17]. Prenatal screening should integrate simple PE markers into standard testing procedures so they can be easily measured and integrated into the existing testing procedures. Incorporating PE screening into the current analytical platforms would also save money, equipment, and labour [18]. Moreover, those markers could suggest the risk of preterm birth during the

first trimester of pregnancy, assisting in the development of healthy placentas through preventative and prophylactic treatment options. As a result, biomarkers that are measured during the testing of aneuploidies fulfil these requirements [19].

In a large unselected sample of obstetric patients under routine clinical care conditions, PE screening was demonstrated to be feasible in a low-a priori risk population. According to our findings, just using the biomarkers currently used for aneuploidy screening is not sufficient for achieving sufficient detection rates and predictive values. Adding additional biomarkers associated with PE's pathogenesis can improve the first trimester combined aneuploidy screening, however. A recent study found that uterine artery pulsatility index (UtA Doppler) and serum placental growth factor (P_lGF) may be useful in the prediction of preeclampsia. Since the designs, demographics, and statistical methods of the studies vary greatly, it is difficult to generalize and establish conventional cut-offs at particular gestational ages, even if those results are positive. PE screening effectiveness should therefore be assessed in prospective studies with a larger sample size. As a result of PE screening in routine prenatal care, the risk of PE can be assessed in a patient-specific way and intervention opportunities can be provided in early pregnancy, even though there is no definitive evidence to support its effectiveness in the society.

Conclusion

Based on our findings, maternal history and biomarkers used during first trimester aneuploidy screening can be used to predict both EO-PE and LO-PE clinical manifestations. In light of the low detection rates of aneuploidy, existing screening procedures should be upgraded with new markers.

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