ORIGINAL ARTICLE

Prediction by Full Preeclampsia Integrated Estimate of Risk Model in Preeclampsia Patients for Adverse Maternal and Neonatal Outcomes

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Abstract

Introduction: Hypertensive disorders of pregnancy are one of the leading causes of maternal and perinatal mortality worldwide. Preeclampsia complicates 2–8% of pregnancies globally. Despite the serious clinical consequences, there is currently no effective preventive measure for preeclampsia hence the focus has shifted to identifying good predictors for diagnosing the severity of preeclampsia.

Materials and methods: This was a prospective cohort hospital-based study done in our department. A total of 400 women were found to be eligible for the study after meeting the inclusion criteria. All the patients underwent detailed evaluation and investigation and the risk was calculated using the full preeclampsia integrated estimate of risk (PIERS) calculator. All patients were followed weekly till delivery. The adverse maternal and fetal outcomes were assessed. If the predicted probability of the adverse outcome came out to be >30%, that case was considered as high risk.

T-test and Chi-square tests were used for statistical analysis as appropriate.

Results: Considering our cut-off value of >30% in our study, out of 384 patients, 82 were categorized into a high-risk group, among them 54 (65.85%) patients had the adverse maternal outcome. ($X^2 = 96.413$, *p*-value = < 0.0001).

Among 377 patients, excluding seven women who expired in antenatal period, 75 patients (19.89%) were categorized into high-risk group (>30% predicted probability), among them 59 (78.67%) patients had the adverse fetal outcomes. ($X^2 = 96.413$, *p*-value = < 0.0001).

Conclusion: The fullPIERS model successfully stratifies the population into clinically relevant high-risk categories by using a few important clinical and biochemical parameters and does not require extensive laboratory testing. It is economically feasible and quick to use and predict the probability of an adverse outcome.

Thus timely referral to the higher centers will help in having a significant impact in reducing maternal morbidity and mortality and perinatal morbidity and mortality associated with preeclampsia in low-resource settings.

Keywords: Full preeclampsia integrated estimate of risk model, Gestational hypertension, Maternal and perinatal outcome, Pre-eclampsia, Prediction of severity of preeclampsia, Prospective cohort study, Risk calculation by full preeclampsia integrated estimate of risk calculator.

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Introduction

Preeclampsia characterized by gestational hypertension and proteinuria, is a state of exaggerated systemic inflammation that remains a leading direct cause of maternal and perinatal morbidity and mortality worldwide.

Numerous studies have tried to evaluate the predictability of various tests including clinical characteristics (mean arterial pressure), biochemical markers, and ultrasound markers (uterine artery pulsatility index, Doppler analysis), individually or in combination, in order to predict early/late/ and any onset preeclampsia. Biochemical markers are expensive, therefore not cost-effective, and are not available at low resource settings.

To predict preeclampsia, many trials using a combination of the first-trimester uterine artery pulsatility index and various biochemical serum markers have been tried. However, facilities to assess these parameters are available only at tertiary levels and higher centers.

The preeclampsia integrated estimate of risk (fullPIERS) model is a tool developed for predicting adverse maternal outcomes following the diagnosis of preeclampsia within 48-hours after admission to the hospital. The fullPIERS model is based on biochemical and clinical parameters that do not require extensive laboratory testing.[1]

The goal of the PIERS model was to develop and validate a tool that identifies women with preeclampsia who are prone to developing adverse maternal or perinatal outcomes and so to plan the time and place of delivery.

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The likelihood ratio associated with the higher risk group (predicted probability of the outcome >30%) showed an excellent correlation with fullPIERS model.[2]

It will be helpful for health workers at primary and secondary health care centers to identify high-risk women with preeclampsia so that they are referred timely to higher centers for appropriate care.

Materials and Methods

This was a prospective hospital-based cohort study done in our Department of Obstetrics and Gynaecology, ethical clearance was taken for the same. A total of 400 women were found to be eligible for the study after meeting the inclusion criteria. Among these 16 patients were lost to follow-up, so 384 women fulfilling the study criteria were included in the study after informed consent.

Inclusion Criteria

Patient with Preeclampsia attending OPD after 32 weeks of gestation and patient with Preeclampsia being admitted to labor room after 32 weeks of gestation diagnosed by ACOG 2020 diagnostic criteria for preeclampsia.[3]

Exclusion Criteria

Women were excluded if any adverse outcome occurred before their meeting the eligibility criteria or before calculation by using predictor variables was possible.

Also patient of following diseases were excluded:

- Eclampsia
- Severe anemia (<7 gm/dL),
- Congestive heart failure,
- Chronic renal disease,
- Known case of liver disease,
- Idiopathic thrombocytopenia.

In the fullPIERS calculator, the following parameters were used for risk calculation: (Fig. 1)

- Gestation age
- Presence of dyspnea/chest pain
- SpO_2
- Platelet count
- Serum Creatinine
- AST/ SGOT (U/L)

All patients underwent detailed evaluation and investigation and risk was calculated (Table 1). All patients were followed weekly till delivery.[4] Adverse maternal and fetal outcomes were assessed. If the predicted probability of the adverse outcome came out to be >/= 30%, that case was considered as high risk.

Adverse Maternal Outcomes

- Eclampsia
- Abruptio placentae
- Thrombocytopenia
- Acute renal failure
- Hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome
- Pulmonary edema
- Postpartum hemorrhage
- Thromboembolic episodes
- Cortical blindness
- Admission to intensive care unit (ICU)
- Maternal death

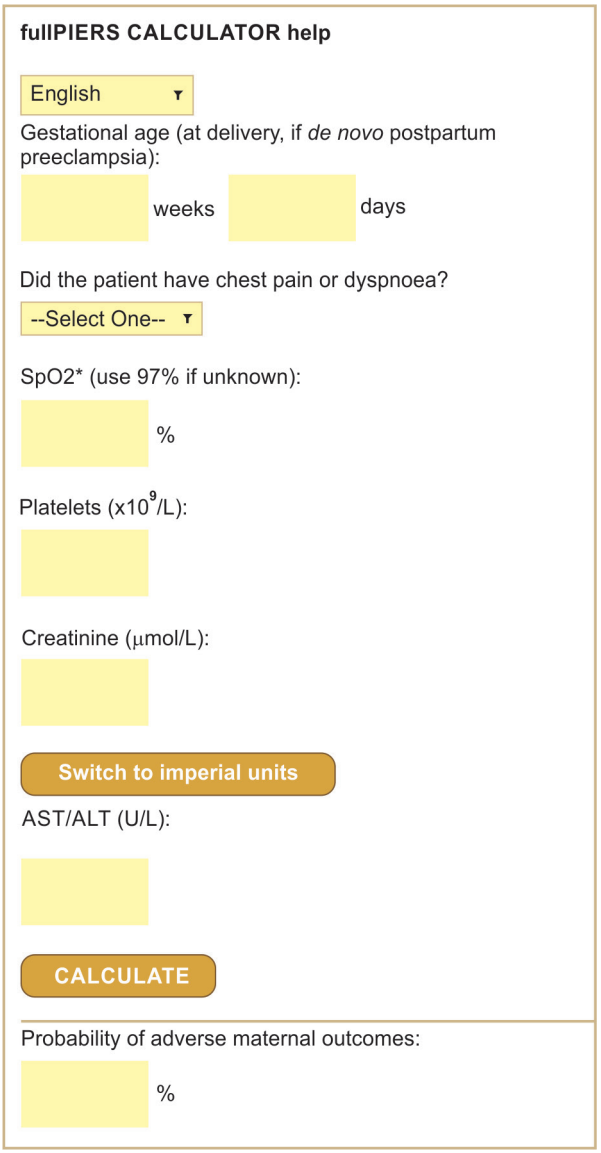

Fig. 1: Shows the fullPIERS calculator which was used for risk calculation

Adverse Fetal Outcomes

- Prematurity
- APGAR score <4 at the time of birth
- Meconium stained liquor
- Neonatal intensive care unit (NICU) admission
- Neonatal death
- Intrauterine death

For statistical analysis, *T*-test and Chi-square test were used.

Results

Among 384 subjects, most patients (45.83%) were in the age-group from 23 to 27 years. However, the mean + SD values for maternal age at presentation was 26.98 + 4.775.

Out of 384 subjects, 182 (47.40%) were primigravida, and 202 (52.6%) subjects were multigravida, among which 120 patients (59.41 %) were second gravida.

Mostly, patients presented with headache, which was present in 129 (33.59%) patients, chest pain was present in 76 (19.79%)

Table 1: Shows parameters of fullPIERS calculator used for risk estimation of adverse events in patients of preeclampsia with their statistical correlation

	Parameters of fullPIERS calculator		*No. (%) (n = 384)*	*Adverse maternal outcomes*		
				Present	*Absent*	
Variables (for risk calculation)	Gestational age (in weeks)	<34	42 (10.94%)	15	27	$X^2 = 18.816$ *p*-value = 0.0003
		34–36	125 (32.55%)	51	74	
		37–39	181 (47.135%)	38	143	
		> 40	36 (9.375%)	00	36	
	Chest pain	Present	76 (19.79%)	53	23	$X^2 = 84.620$
		Absent	308 (80.21%)	51	257	*p*-value = < 0.0001 odd ratio = 11.612
	SpO_2 (%)	<94.9	97 (25.26%)	62	35	$X^2 = 97.456$
		>95	287 (74.74%)	42	245	*p*-value = < 0.0001
	Platelet count(/cumm)	<100,000	86 (22.40%)	35	51	$X^2 = 9.532$
		>100,000	298 (77.60%)	69	229	*p*-value = < 0.0020 odd ratio = 2.278
	Serum creatinine (mg/dL)	<1.4	328 (85.42%)	83	245	$X^2 = 3.011$
		>1.4	56 (14.58%)	21	35	*p*-value = 0.0827 odd ratio = 0.5646
	Serum SGOT levels (IU/L)	<40	80 (20.83%)	06	74	$X^2 = 18.392$
		>40	304 (79.17%)	98	206	*p*-value = < 0.0001 odd ratio = 0.1704

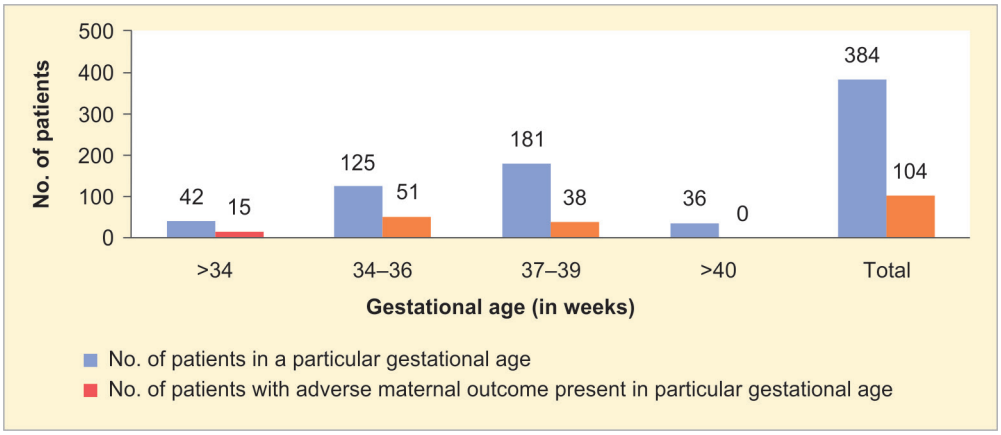

Fig. 2: Depicts distribution of women according to gestational age along with incidence of adverse maternal outcome in that gestational age

patients, excessive weight gain was present in 79 (20.57%) patients, whereas visual disturbances, severe nausea, and epigastric pain were present in 30 (7.81%), 28 (7.29%) and 24 (6.25%) patients respectively.

As shown in Figure 2, amongst the 384 patients, 42 (10.94%) patients were having gestation age <34 weeks, and among these 15 patients had adverse maternal outcomes, whereas 125 patients (32.55%) were of 34 to 36 gestation age, from which 51 patients had adverse maternal outcomes and out of 217 (56.51%) patients who were of gestation age >37 weeks, 38 patients had adverse maternal outcomes. Our study significantly shows an association between early disease onset and disease severity ($X^2 = 18.816$, *p*-value 0.0003).

Chest pain was present in 76 (19.79%) patients, 53 (69.74%) patients had adverse maternal outcomes, while 308 (80.21%) patients who were not having either chest pain or dyspnea, and out of these non-symptomatic patients, 51 (16.56%) had adverse maternal outcomes. (*p*-value < 0.001, and odd ratio = 11.612). Out of 30 patients with SpO_2 <88%, 25 patients (83.33%) had adverse maternal outcomes, while out of 287 patients with SpO_2 >95%, 42 (16.67%) had the adverse maternal outcomes. Hence, SpO_2 levels were used with success to predict an adverse maternal outcomes. The adverse maternal outcomes showed an increase with the decreased SpO_2 value. (The *p*-value is < 0.0001).

In the study, 86 patients had platelet count <1 lakh/cumm, and 35 patients (40.70%) had an adverse outcomes. Out of 298 (77.40%) patients having >1 lakh/cumm, 69 (23.15%) patients had adverse outcomes, while 229 (76.85%) patients didn't have any adverse outcomes. (*p*-value < 0.0020, odd ratio = 2.278)

Majority of participants of the study, 328 (85.42%) patients were having serum creatinine value <1.4 mg/dL, out of which 83 had adverse outcomes, and 56 (14.58%) patients having serum creatinine >1.4 mg/dL, 21 (37.5%) patients had an adverse outcome. (*p*-value = 0.0827, odd ratio = 0.5646). Among the biochemical markers, serum creatinine did not show any significant association.

In our study, 98 (32.24%) women out of 304 with AST >40U/L had adverse maternal outcome, whereas 06 (7.5%) out of 80 with

Table 2: Shows distribution of patients according to predicted probability (%) calculated by fullPIERS calculator in predicting maternal adverse outcomes

Predicted probability (%)	*No. n = 384*	*Adverse maternal outcomes*	
		Present (in %)	*Absent (in %)*
0.00–0.99	48	5 (10.42%)	43 (89.58%)
1.0–2.4	73	11 (16.07%)	62 (84.93%)
2.5–4.9	95	08 (8.42%)	87 (91.58%)
5.0–9.9	48	11 (22.92%)	37 (77.08%)
10.0–19.9	27	09 (33.33%)	18 (66.67%)
20.0–29.9	11	06 (54.55%)	05 (45.45%)
>30	82	54 (65.85%)	28 (34.15%)
Total	384	104 (27.08%)	280 (72.92%)

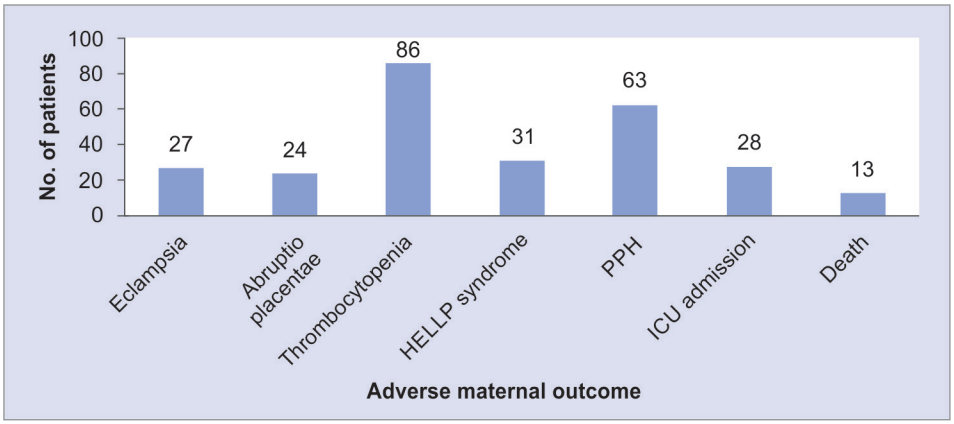

Fig. 3: Depicts distribution of women according to adverse maternal outcomes

Table 3: Shows distribution of women according to predicted probability (%) calculated by fullPIERS calculator in predicting adverse fetal outcomes

Predicted probability (%)	*No. (n = 377)*	*Adverse fetal outcomes*	
		Present (%)	*Absent (%)*
0.00–0.99	48	4 (8.3%)	44 (91.7%)
1.0–2.4	73	21 (28.77%)	52 (71.23%)
2.5–4.9	95	25 (26.31%)	70 (73.69%)
5.0–9.9	48	30 (62.5%)	18 (37.5%)
10.0–19.9	27	15 (55.5%)	12 (44.5%)
20.0–29.9	11	10 (90.9%)	1 (9.1%)
>30	75	59 (78.67%)	16 (21.33%)
Total	377	164 (43.50%)	213 (56.50%)

AST ≤40 U/L had adverse outcome (*p*-value = < 0.0001, odd ratio = 0.1704).

Among 384 patients, 133 patients (35.28%) delivered via vaginal delivery while 244 patients (64.72%) had caesarean section.

According to Table 2, among 384 patients, using the fullPIERS calculator, 82 patients were categorized into high-risk group (>30% predicted probability), among them 54 (65.85%) patients had the adverse maternal outcomes (X^2 = 96.413, *p*-value = <0.0001).

As shown in Figure 3, out of 384 patients, 27 (7.03%) had eclampsia, 24 (6.25%) had abruptio placentae, 86 (22.40%) had thrombocytopenia, 31 (8.07%) developed HELLP syndrome, 63 (16.41%) had postpartum hemorrhage, 28 (7.29%) required intubation and ICU admission and there were 13 (3.38%) maternal deaths, out of whom seven died in the antenatal period.

As 7 women died in the antenatal period, the calculation for adverse fetal outcomes was possible in 377 patients. As shown in Table 3, using the fullPIERS calculator, 75 patients were categorized into high-risk groups (>30% predicted probability), among them 59 (78.67%) patients had the adverse fetal outcomes (X^2 = 96.413, *p* value = <0.0001).

In Figure 4, out of 377 neonates, 167 (44.30%) were premature, 203 (53.85%) had fetal growth restriction, 64 (16.97%) had APGAR score <4 at the time of birth, 67 (17.77%) had meconium-stained liquor (MSL), 90 (25.50%) neonates were admitted to NICU, 24 (6.37%) died intrauterine and 06 (1.59%) died in the neonatal period.

Discussion

Our study shows a significant association between the early disease onset and disease severity (X^2 = 18.816, *p*-value 0.0003). A study by Ni Y and Cheng W on early and late-onset preeclampsia, concluded that early onset preeclampsia is a distinct and more severe clinical entity with earlier gestational age onset and delivery.[5]

In our study, a significant association was found between decreased SpO_2 levels and adverse maternal outcomes (The *p*-value is <0.0001). Srivastava S et al., in their study, found that SpO_2 successfully predicted adverse maternal outcomes (Table 4).[6]

In our study, a platelet count of <1 lakh/cumm was significantly associated with adverse maternal outcomes. In studies by Agrawal et al.[2] and Srivastava S et al.[6] low platelet count was significantly associated with adverse maternal outcomes.

In our study, among the biochemical markers, serum creatinine did not show any significant association. In the study by Srivastava S et al., no correlation was found between Serum creatinine levels and adverse outcomes.[6] In a study on fullPIERS by Agrawal and Maitra, serum creatinine was found to be an independent predictor of adverse maternal outcomes.[2]

In our study, 98 (32.24%) women out of 304 with AST >40U/L had adverse maternal outcomes (*p*-value < 0.0001, odd ratio = 0.1704). In a systematic review of PIERS data, Thangaratinam et al. found that the presence of increased liver enzymes was associated with an increased probability of maternal and fetal complications, but normal liver enzyme levels did not rule out disease, as specificity was often higher than sensitivity.[7] In a similar study by Srivastava S

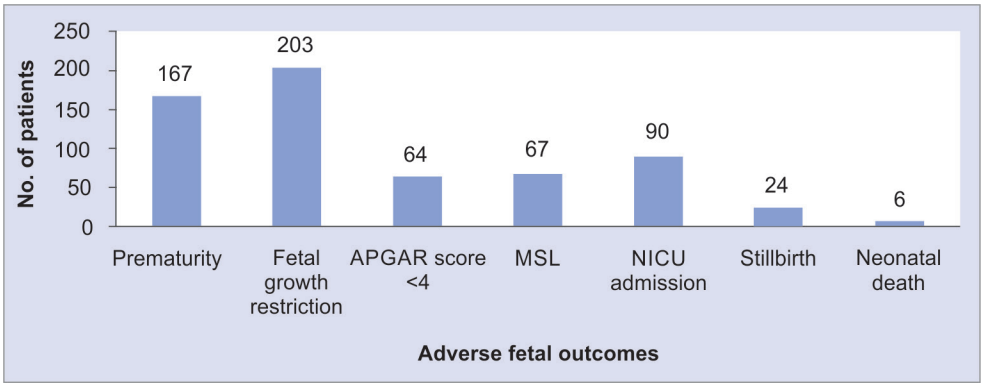

Fig. 4: Shows distribution of women according to adverse fetal outcome

Table 4: Shows comparison between different studies on assessment of variable of fullPIERS model in predictability of adverse maternal outcome

	Gestational age	*Chest pain*	*Oxygen saturation*	*Platelet count (>1.5 lacs/cu mm)*	*Serum creatinine level (>1 mg/dL)*	*AST level (>40 IU/L)*	*Predictability of fullPIERS model*
In our study	Significant *p*-value = 0.0003	Significant OR = 11.612 *p*-value < 0.0001	Significant *p*-value < 0.0001	Significant OR = 2.278 *p*-value < 0.002	Not significant OR = 0.5646 *p*-value = 0.0827	Significant OR = 0.1704 *p*-value < 0.0001	Significant *p*-value < 0.0001
In Srivastava et al. 2017 study	Significant *p*-value < 0.05	Significant *p*-value < 0.05	Significant *p*-value < 0.0001	Significant *p*-value < 0.05	Not significant *p*-value > 0.05	Not significant *p*-value > 0.05	Significant *p*-value < 0.0001
In Agarwal et al. 2016 study	Significant *p*-value = 0.01	Significant OR = 4.69 *p*-value < 0.0001	Significant *p*-value < 0.05	Significant OR = 1.89 *p*-value = 0.014	Significant OR = 8.9 *p*-value < 0.0001	Not significant *p*-value = 0.21	Significant positive likelihood ratio = 17.53 for predicted probability >30

Table 5: Shows comparison of different studies in stratifying cases according to fullPIERS score and assessing predictability of adverse maternal and fetal outcomes

	Distribution of cases according to fullPIERS score	*No. of women in high risk group*	*No. of women with adverse outcome*	*% of women with adverse outcome*
In our study	High risk (>30)	82	54	65.85%
In Srivastava et al. 2017 study	High risk (>30)	06	05	83.33%
In Agarwal et al. 2016 study	High risk (>30)	27	15	55.55%

et al., Serum AST levels of >40U/L were not significantly associated with adverse maternal outcomes.[6]

As shown in Table 5, in the study by Agrawal et al., the risk prediction model used showed that the likelihood ratio associated with the highest risk group (predicted probability of the outcome >30 %) showed excellent performance (i.e., 17.5) of fullPIERS model as a rule in test.[2] Srivastava S et al. in their study found that 21 patients in all had the adverse maternal outcome. Six patients who belonged to the high-risk group according to the fullPIERS calculator and 5 women had adverse outcomes (*p*-value < 0.00001). The result was statistically significant in identifying high-risk cases in their study.[6]

Conclusion

In our study, the fullPIERS model performed well in the prediction of adverse maternal and fetal outcomes in women with preeclampsia. The fullPIERS model successfully stratifies the population into clinically relevant high-risk categories by using a few important clinical and biochemical parameters and does not require extensive laboratory testing. It is economically feasible and quick to use and predicts the probability of an adverse outcome.

Hence, it will be of great help to health workers at primary and secondary healthcare centers to identify women with preeclampsia who are at high risk of developing complications and will need specialist care by timely referral to higher-center for appropriate care. This will go a long way in having a significant impact in reducing maternal morbidity and mortality and perinatal morbidity and mortality associated with preeclampsia in countries with low resource settings of healthcare belonging to South East Asia.

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