

Prediction of Adverse Outcome in Preeclampsia Using fullPIERS Model

Dr. Indra Bhati¹, Dr. Manvika Chandel², Dr. Priyanka Choudhary³

Abstract: Introduction: Preeclampsia is a proteinuric state with gestational hypertension occurring in mid or late pregnancy leading to adverse maternal outcome which can be controlled by standardized assessment of pregnant women. The preeclampsia integrated estimate of risk model is a recently developed tool for prediction of adverse maternal outcomes up to 7 days after eligibility when predictor variables are collected following the diagnosis of preeclampsia within 48 hours after hospital admission. Aims and Objectives: To study the performance of full PIERS model in prediction of adverse maternal outcome in preeclampsia. Materials and Methods: A prospective observational study was carried out in the department of obstetrics and gynecology of Umaid hospital, Dr SN Medical College, Jodhpur. All women admitted for delivery in labor ward, having signs and symptoms of preeclampsia were included in the study. Discussion: A total of 410 women were studied, out of which 72 had adverse outcome. Eclampsia was the most common adverse outcome (in 27 women i.e., 37.5%) followed by abruptio. Mean gestational age of women with adverse outcome was 37 weeks. Out of 72 women presenting with adverse outcomes, 37 presented with symptoms. Swelling was the most common symptom of patients (69%). Out of 37 women who presented with symptoms, 21 (56%) had adverse outcomes. In women with adverse outcomes, mean systolic and diastolic BP on admission was 162 mm Hg and 102 mmHg, sPO₂ < 96% had significant association, platelet count was < 1.19 lacs/microliter, AST & ALT values more than 82 & 71 mg/dl respectively. Conclusion: The fullPIERS risk prediction model for preeclampsia which is supported by our study will help prevent severe maternal complications through early identification and if universally implemented could guide clinical decision making, improve understanding of the disease process and to define at risk groups based on prognosis, thus, reducing the global burden of deaths due to HDOP.

Keywords: hypertensive disorders of pregnancy, eclampsia, preeclampsia, fullPIERS

1. Introduction

The obstetric career of a female is of utmost importance in her life, which should culminate into healthy mother and healthy baby. Unfortunately, there are many obstacles to break these expectations, one of the most important being pre-eclampsia. About 10% of all pregnant women around the world are affected by HDOP resulting into maternal and peri natal morbidity and mortality.¹⁻³

In Asia, estimates of around one tenth of maternal deaths are associated with hypertensive disorders of pregnancy.³

Preeclampsia along with being a proteinuric state is also a state of exaggerated inflammation.² It typically occurs after 20 weeks of gestation. The outcome is dangerous when the onset is early i.e. onset at <34 weeks of gestation compared with late onset preeclampsia.⁴⁻⁷ Early onset preeclampsia maybe influenced by aberration in trophoblastic invasion of spiral uterine arteries.⁸ Later onset disease involves placental dysfunction, but most often occurs in women with pro-inflammatory maternal constitutional and environmental factors i.e. multiple gestation, high BMI, co morbid conditions and chronic hypertension.⁹

The only treatment of choice for preeclampsia is delivery of the fetus and placenta, though, it is not always the best choice specially if remote from term because of complications attributable to iatrogenic prematurity.¹⁰⁻¹² The risk benefit ratio should be calculated but how this risk can be predicted to assure maximum fetomaternal benefit, remains a questionable decision.

Numerous studies examining the role of maternal symptoms and biochemical markers in predicting the outcome of preeclampsia complicated pregnancies have been put forth,

but without much success.¹³⁻¹⁵ Efforts by Canadian hypertension society, national high blood pressure education program, ACOG, for evaluating the severity of preeclampsia are not uniform and have not been proven effective.

The Pre-eclampsia Integrated Estimate of Risk (fullPIERS) model is a recently developed tool for predicting adverse maternal outcomes following diagnosis of preeclampsia within 48 hours after admission to the hospital.¹⁶ This model was developed and internally validated by tertiary care centres of obstetrics in Canada, new Zealand, Australia and UK. This model is an outcome prediction tool to identify the adverse fetomaternal outcome in hospitalized women with preeclampsia.

Need to study: Being a tertiary care centre of western Rajasthan, with approximately 2000 vaginal and operative deliveries in a month and a significant prevalence of preeclampsia, we wanted to evaluate how accurately fullPIERS model performs in our settings to predict adverse maternal outcome when all the predictor variables are all obtained within 24 hr of admission.

2. Aims and Objectives

- 1) To study the performance of fullPIERS model in prediction of adverse maternal outcome in preeclampsia.
- 2) To study the prevalence of adverse maternal outcome in preeclampsia.

3. Results

This study included 410 women

Table 1: Distribution of Cases According to Age, Booking Status and Gestational Age and their Correlation with Maternal Outcome

Age (in years)	With adverse outcome (N=72)	Without outcome (N=338)	P value
18-20 (16, 3.90%)	4 (25%)	12	0.498
20-25 (275, 67.07%)	45 (16%)	230	0.440
25-30 (91, 22.20%)	18 (19%)	63	0.285
30-35 (20, 4.87%)	02 (10%)	18	0.548
35-40 (8, 1.95%)	03 (37%)	05	0.150
Total (410)	72 (17%)	338	
Mean±SD	24.43±3.93	24.39±3.48	P=0.936
Bookingstatus			
Booked (198, 48.30%)	23 (11%)	175	0.002
Unbooked (212, 51.70%)	49 (23%)	163	
Total (410, 100%)	72	338	
Gestational age (in weeks)			
<30 (19)	13	06	<0.0001
30-34 (64)	24	40	<0.0001
34-37 (200)	23	177	0.091
>37 (127)	12	115	0.003
Total	72	338	
Mean ± SD	34.00±3.40	36.64±2.13	P=<0.0001

In our study population, out of 410 women, maximum i.e. 275 (67.07%) were in age group of 20-25 yrs. Minimum i.e. 8 (1.95%) women in 35-40 yrs. of age

A total of 72 out of 410 had adverse outcome. Maximum adverse outcome was seen in age group of 20-25 yrs. (45 women) but it is related to their overall incidence (67%) in the study population. In the age group of 35-40 yrs., 3 out of 8 had adverse outcome which is significant.

About 212 women out of 410 were unbooked who were either referred from peripheral center or it was their first antenatal visit. In these 212 women, 49 (23%) had adverse outcome and only 11 % booked patients had adverse outcome.

Out of 410 women, 83 (19%) women, were at <34 weeks of gestational age. Out of 72 women with adverse outcome, 37 (about 50%) were <34 weeks. There were 200 (48.73%) women between gestational age of 34-37 weeks, out of them only 23 (12%) got adverse outcome whereas 12 (9%) out of 127 who were in group of <37 weeks had adverse outcome.

Although many women had multiple complaints, swelling i. e. pedal edema and/ or facial puffiness was the most common complaint of patients (69%) either isolated or associated with other symptoms. Headache was the second most common symptom (21.70%) followed by others, as mentioned in the table.

Table 6: Distribution of Cases According to Symptoms and the Association of Symptoms with Maternal Outcome

Symptoms (N=410)	With adverse effect (N=72)	Without outcome (N=338)	OR (95% CI)	P value
Swelling (251) (61.21%)	38 (15%)	213	0.655 (0.39-1.09)	0.137
Headache (89) (21.70%)	23 (25%)	56	2.36 (1.33-4.19)	0.004
Pain abdomen (87) (21.21%)	11 (13%)	76	0.621 (0.31-1.24)	0.230
Nausea, vomiting, epigastric pain (47) (11.46%)	21 (44%)	26	4.94 (2.58-9.43)	<0.0001
High blood pressure (39) (9.51%)	12 (30%)	27	2.30 (1.10-4.80)	0.043
Chest pain, dyspnea (37) (9.02%)	21 (56%)	16	8.28 (4.05-16.93)	<0.0001
Visual disturbance (32) (7.80%)	15 (46%)	17	4.96 (2.34-10.51)	<0.0001
Loss of fetal movement (11) (2.68%)	03 (27%)	08	1.79 (0.46-6.93)	0.417

Women having complaints of chest pain, dyspnoea, nausea, vomiting, epigastric pain, and visual disturbance had a strong association with adverse outcome. Most significant association of adverse outcome was with chest pain and

dyspnoeai. e.21 out of 37 (56%). Although, swelling and pain abdomen were among the most common causes for which women sought medical help, these were least commonly associated with adverse outcome.

Table 7: Correlation of Investigations with Maternal Outcome

Parameters (Mean ± SD)	With outcome (N=72)	Without outcome (N=338)	P value
Systolic blood pressure (mm Hg)	162.36±9.83	152.50±8.21	<0.0001
Diastolic blood pressure (mm Hg)	102.83±5.03	96.59±4.89	<0.0001
Respiratory rate	15.56±1.09	15.15±0.78	0.0002
sPO ₂ (%)	96.94±1.38	98.00±0.93	<0.0001
Hb (gm%)	9.84±2.17	11.09±1.59	<0.0001

Platelet (per microliter)	1.19±0.66	2.06±0.66	<0.0001
LDH (U/L)	1501.08±683.62	842.42±439.29	<0.0001
S. creatinine (mg/dl)	1.06±0.23	0.87±0.15	<0.0001
Blood urea (mg/dl)	33.29±11.16	25.32±4.94	<0.0001
Uric acid (mg/dl)	5.59±0.82	4.19±0.95	<0.0001
Alkaline phosphatase (IU/L)	237.73±85.44	205.20±83.55	0.003
Bilirubin total (mg/dl)	0.89±0.20	0.85±0.59	0.556
Bilirubin direct (mg/dl)	0.25±0.08	0.23±0.07	0.075
AST (U/L)	82.41±67.16	40.30±32.59	<0.0001
ALT (U/L)	71.98±57.03	33.92±28.0	<0.0001
Dipstick Urine albumin	1.90±0.80	1.20±0.48	<0.0001

The investigation reports obtained within 24 hours of admission had very important correlation and appear to be beneficial tool for prediction of maternal outcomes.

Table 13: Adverse Maternal Outcomes

Maternal Outcome (%)	No. of Women (N=72)
Abruption (29.1%)	23
Eclampsia	27
PPH	8
DIC	4
Mortality	3
Transfusion	21
Pulmonary Edema	2
Renal Failure	2
PRESS	2

The adverse maternal outcome in our study population is depicted in the table. 72 out of 410 women had adverse outcome. Although most women had combined adverse outcome, eclampsia was the most common adverse. Eclampsia was ante partum in 23 women and post partum in 4 women also 4 out of these needed transfusion and 2 developed PRESS. Among 23 who had developed abruption, 6 needed multiple transfusion of blood and blood products and 8 were associated with eclampsia.

Third most common adverse outcome was transfusion of either blood or blood products (platelets, fresh frozen plasma)-done in 21 women. transfusion, as an isolated adverse outcome was done in 6 patients while rest 15 also

had another adverse outcome in association with anemia and thrombocytopenia. Out of these 72 women, 8 women had massive PPH, one required hysterectomy, 7 others were managed by uterotonics, balloon tamponade or intrauterine packing, 3 developed DIC and all of them needed transfusion. 4 women developed DIC requiring transfusion. Renal failure occurred in 2 patients, one was associated with DIC and one with PPH. Pulmonary edema was seen in 2 patients. We had three mortalities in the study population- one antenatal death due to pulmonary embolism and 2 postnatal deaths, of which one was due to acute hepatic rupture of pregnancy and another due to embolism and multi organ failure. Ventilator support was given in total of 12 women.

Table 14: Predictor Range of PIERS Score

PIERS score	With adverse outcome (N=72)	Without outcome (N=338)	P Value
0.001-0.99 (268)	16 (5%)	252	<0.0001
1.0-2.4 (36)	08 (22%)	28	0.490
2.5-4.9 (26)	09 (34%)	17	0.029
5.0-9.9 (21)	07 (33%)	14	0.071
10-19.9 (17)	08 (47%)	09	0.004
20.0-29.9 (8)	04 (50%)	04	0.02
≥30 (34)	20 (58%)	14	<0.0001
TOTAL (410)	72	338	

The above table showing that 410 women in our study population, maximum 268 women were in the low risk group of PIERS score i. e. 0.001-0.99%, in which only 16 women met with adverse outcome and 252 delivered uneventfully with a significant p value. In the group with score 1-2.4%, only 8 out of 36 i. e. 22% and in group of 2.5-4.9%, 9 out of 26 i. e. 34% had adverse outcome. In both these groups maternal outcome did not have any significant association. In 21 women PIERS score was 5.00-9.9%. Out of these 7 (33%) women had adverse outcomes. 17 women

had probability score between 10-19.9%, 8 of them had adverse outcome (47%) while in group of probability of 20-20.9%, 4 (50%) out of 8 had adverse outcome. Probability score of 30% or more was the highest risk group. Out of 34 women in this group, 20 (58%) had adverse outcomes showing a significant association with increasing score.

4. Discussion

Sajith et al 2014¹⁷ reported that highest incidence of hypertension in pregnant women was seen in age group of 18-22 years. Similar findings were also present in our study where 67% women affected with preeclampsia were in the age group of 20-25 years. But in respect to adverse outcomes, elderly age group was more important with adverse maternal outcome than younger women.

The value of ANC visits exhibit a crucial role. Only 11% of booked women met with adverse outcome as compared to almost double (23%) in unbooked women. Various risk factors can be addressed at ANC visits like age, parity, previous pre eclampsia, family h/o preeclampsia, multiple pregnancy, preexisting medical conditions, IDDM, chronic hypertension, renal disease, autoimmune disease, antiphospholipid syndrome, interpregnancy interval and BMI. BP and proteinuria can be measured for early diagnosis and initiating preventive measures of preeclampsia.

According to Pauli JM, Repke JT 2015¹⁸ & A Aziz, JC Mose 2016¹⁹, incidence of early on set preeclampsia is lower (27.5%) than late onset preeclampsia (72.5%). Early onset preeclampsia group experienced more maternal complications. Our study supported the same findings.

According to Ukah UV, De Silva DA 2017²⁰, the most promising prediction was with multivariable models, especially when oxygen saturation, or chest pain/ dyspnea were included. A mean oxygen saturation of $96.94 \pm 1.38\%$ was associated with adverse outcomes and women with mean saturation of $98.00 \pm 0.93\%$ delivered uneventfully.

In our study we found that although symptoms were overlapping each other, most common presenting symptom was swelling either pedal edema or puffiness in face in 61.21% similar to study by Srivastava S et al 2017¹¹³.

In our study, platelet count < 1.5 lacs (mean 1.19 ± 0.66) and LDH > 1500 (1501.08 ± 683.62) positively correlated with adverse outcomes. Increased values of serum creatinine (1.06 ± 0.23), uric acid (5.59 ± 0.82) and alkaline phosphatase (237.73 ± 85.44) had p value < 0.001 suggesting a significant correlation with adverse outcome. Blood levels of AST (82.41) and ALT (71.90) had a significant association with adverse maternal outcomes. Similar results were seen by Agarwal and Mitra 2016.

In an analysis of the PIERS dataset, Beth Payne et al 2011²¹ concluded that dipstick proteinuria performs equally well as other methods in assessing proteinuria for prediction of adverse outcomes. In our study, proteinuria measured by dipstick appears a good predictor, but quantifying value would be more promising for prediction of adverse outcome.

In our study, out of 72 women developing adverse outcomes, eclampsia (23 antepartum and 4 postpartum) was the most common adverse outcome (in 27 women i. e. 37.5%) with 2 patients also developing PRESS, followed by abruption in 23 women (29.1%). Among 23 women developing abruption, 6 needed multiple transfusion of

blood and blood products and 8 were associated with eclampsia. In a study by Malik, Naushaba 2017.1²⁰ 37.73% women with preeclampsia developed abruptio placenta, while 20.75% developed eclampsia.

The association of PIERS score with adverse outcome is well correlated in our study. We found that as probability score increases from 0.001% to $> 30\%$ probability of adverse outcomes increases. Out of 410 women in our study population, maximum 268 women were in the low risk group of PIERS score i. e. 0.001%-0.99%, in this group only 16 (5%) women met with adverse outcome and 252 delivered uneventfully with a significant p value. In group of probability score 1-2.4%, only 8 out of 36 i. e. 22% and in group of 2.5-4.9%, 9 out of 26 i. e. 34% had adverse outcome. In both these group maternal outcome did not have any significant association. In 21 women, PIERS score was 5.00-9.9%. out of these 21, 7 (33%) women had adverse outcomes. 17 women had a probability score between 10-10.9%, 8 (47%) had adverse outcome while in group of probability score 20-29.9%, 4 (50%) out of 8 had adverse outcome. Probability score of 30% or more was the highest risk. Out of 34 women of this group, 20 (58%) had adverse outcomes showing a significant association of increasing PIERS score with increasing risk. The risk prediction model used in our study found that probability score $> 30\%$ i. e. the highest risk has shown excellent correlation with adverse outcome (approx. -58%)

According to the fullPIERS study, among the 1935 women for whom complete data were available, 65% of women were stratified as low-risk, with a predicted probability of adverse outcome below 0.025, and at the other end of the risk spectrum were the 4% at highest risk, with a predicted probability of 30% or more. Only 1% of women in the low risk category experienced an adverse outcome, compared with 59% of those in the high risk category. They divided all women in only two groups. In our study, the incidence of adverse outcome continuously increased with increasing probability score but in group of 10-19.9% probability score, the incidence of adverse outcomes increases significantly as compared to lower probability scores. If we hypothesized the score of 10% as cut off high risk group, 32 (54%) women would have adverse outcome out of 59 women in this group. So the PIERS score of $> 10\%$, can predict adverse maternal outcome more efficiently and it can be used as a predictive test for as adverse outcome for pre eclampsia.

5. Conclusion

Our study supports the fullPIERS risk prediction model for preeclampsia. The model will help prevent severe maternal complications through early identification. This model if universally implemented could aid in reducing the global burden of deaths due to HDOP. It can be used to predict maternal outcome in preeclampsia more accurately and to guide clinical decision making, improve understanding of the disease process and to define at-risk groups based on prognosis. The other predictor variables which can be proposed for prediction of maternal and fetal outcome other than those used in fullPIERS calculator are symptoms of nausea, vomiting, epigastric pain and visual disturbances, levels of LDH, serum uric acid and serum alkaline

phosphatase as they were significantly associated with adverse outcome in our study. Although the fullPIERS model accurately performed in our study, yet it needs to be validated at large scale in different demographic areas. This will allow us to determine the generalizability, sensitivity, specificity, predictive values and accuracy of the model in numerous jurisdiction and across all conditions. Once revalidation is complete and a PIERS scoring system has been created, the PIERS models must be methodologically introduced into routine clinical use at all levels of care. Since the positive results of our study we have started incorporating the fullPIERS model at our centre for better maternal-fetal care and outcome. We strongly recommend its routine clinical at all levels of care.

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