RESEARCH ARTICLE

Prediction of Adverse Maternal and Fetal Outcome in Preeclampsia Using a Risk Prediction Model Prospective Cohort Study

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Abstract

Introduction: Preeclampsia (PE) is a syndrome unique to pregnancy that ranks second globally in terms of maternal mortality (14% in India and 29.54% globally). PE complicates 2–8% of pregnancies, while 10% of women experience hypertensive problems during pregnancy [hypertensive disorders in pregnancy (HDP)]. For women to have better maternal and perinatal outcomes, we must swiftly identify HDPs. The prognosis of these patients is contingent upon prompt identification, prompt referral to the tertiary care facility, patient accessibility to the facility, and careful management.

Materials and methods: Enrolled in the study were patients who met the inclusion and exclusion criteria and gave their consent for the current investigation. To get the risk of unfavorable outcomes for both mother and fetus, we employed the complete preeclampsia integrated estimate of risk score (PIERS) calculator.

All patients were intensively monitored and managed accordingly with antihypertensive and steroids for fetal lung maturation in patients needing preterm delivery.

Results and discussion: All patients requiring premature birth were closely observed and treated with antihypertensive medications and steroids to promote fetal lung maturation. About 33.33% of the patients in our study with hypertensive diseases of pregnancy experienced adverse maternal outcomes. The full-PIERS prediction model applied to the study population demonstrated a statistically significant *p*-value of <0.05 in the prediction of adverse maternal and fetal outcomes. The area under the curve (AUC) [receiver operating characteristic (ROC)] for the PIER score at various cutoffs is *C* = 0.903, with a 95% confidence interval (CI) of 0.855–0.951 and a standard error (SE) of 0.024. The optimal cutoff points are 2.85 for maternal outcomes and 0.95 for fetal outcomes, respectively, in order to maximize (sensitivity + specificity).

Conclusion: Our results may help with decision-making when it comes to scheduling the patient's delivery, maintaining conservative treatment, administering blood products, or moving the patient to an intensive care unit. PIER score is a highly reliable indicator ($p < 0.001$) for predicting the health of the mother and fetus.

Keywords: Full-preeclampsia integrated estimate of risk, Maternal Complications, Mini-preeclampsia integrated estimate of risk, Preeclampsia.

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Introduction

Preeclampsia (PE), a disease unique to pregnancy, is the second most common cause of maternal death (14% globally, 29.54% in India).[1,2] PE complicates 2–8% of pregnancies, while hypertensive disorders in pregnancy (HDP) affect 10% of pregnant women. From mild, asymptomatic hypertension to severe hypertension and convulsions, maternal disease can take many different forms. In extreme situations, there may also be compromise to the kidneys, heart, and nervous system. Globally, an estimated 50,000–60,000 people die from PE each year.[3,4]

When compared to PE that develops later (36–40 weeks gestation), early onset PE—that is, PE that begins before 32 weeks of gestation—is linked to a markedly higher risk of complications for both the mother and the fetus.[5]

For women to have better maternal and perinatal outcomes, we need to immediately recognize HDPs. The prognosis of these patients is predicated upon prompt identification, prompt referral to the tertiary care center, patient accessibility to the facility, and careful management. Delivery is the definitive and preferred course of therapy for the woman in this situation, but it is not necessarily the best course of action for the fetus, particularly if the gestation is far from term (<32–34 weeks). When PE and other HDPs are present, the decision to deliver the fetus prematurely is based on weighing the probable risk of an adverse outcome against the considerable advantages of the pregnancy being prolonged for the fetus.[6]

Randomized controlled trials (RCTs) have provided evidence that expectant treatment, which involves delaying delivery until a medical need arises from a problem affecting the mother or the fetus, can reduce severe perinatal morbidity without posing an increased danger to the mother.[7–9] However, due to the lack

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of power in these RCTs to discern differences in the incidence of severe maternal outcomes between groups, some physicians are reluctant to use expectant management because they are unsure of the extent of maternal risk involved.[10]

An algorithm for predicting maternal and perinatal outcomes in patients with PE is developed by the preeclampsia integrated estimate of risk score (PIERS), which analyzes maternal signs, symptoms, and test results.[11] The PIERS calculator includes gestational age, the symptom complex of chest pain and dyspnea, oxygen saturation by pulse oximeter, and laboratory estimation of platelet count, serum creatinine, and aspartate transaminase (Fig. 1).

The final preeclampsia integrated estimate of risk equation

$$\begin{aligned} logit(\pi) = {} & 2.8 + (-5.1\times10-2;\times gestational\ age\ at\ eligibility) \\ & +1.23\ (chest\ pain\ or\ dyspnea) \\ & +(-2.71\times10-2\times creatinine)+(2.07\times10-1\times platelets) \\ & +(4.0\times105\times platelets2) \\ & +(1.01\times10-2\times aspartate\ transaminases) \\ & +(-3.05\times10-6\times AST2) \\ & +(2.50\times10-4\times creatinine\times platelet) \\ & +(-6.99\times10-5\times platelet\times aspartate\ transaminases) \\ & +(-2.56\times10-3\times platelet\times SpO2) \end{aligned}$$

The goal of the whole PIERS model's development and validation was to identify adverse outcomes in preeclamptic women within 48 hours to 7 days. This allowed the patient's treatment plan to be modified to reduce the risk of morbidity and mortality in both the mother and the fetus.[11,-13] This study was conducted to evaluate how the PIERS model performs in the prediction of adverse maternal and fetal outcomes when the predictor variables are all obtained within 24 hours of admission for PE in a low- or middle-income country where health services are limited.

Materials and Methods

This was a prospective cohort study conducted in the Department of Obstetrics and Gynecology, All India Institute of Medical Sciences (AIIMS), Raipur, on 162 women who fulfilled the following inclusion and exclusion criteria.

Inclusion Criteria

Preeclampsia (PE) is defined as systolic blood pressure at ≥140 mm Hg and diastolic blood pressure at ≥90 mm Hg on at least two occasions measured 4 hours apart in previously normotensive women accompanied by ≥1 of the following new-onset conditions at or after 20 weeks gestation:

- Proteinuria (i.e., ≥30 mg/mol protein: creatinine ratio; ≥300 mg/24 hours; or ≥2 + dipstick).
- Evidence of other maternal organ dysfunction, including acute kidney injury (creatinine ≥90 µmol/L; 1.1 mg/dL), liver involvement (elevated transaminases, e.g., alanine aminotransferase or aspartate aminotransferase >40 IU/L) with or without right upper quadrant or epigastric abdominal pain, neurological complications (e.g., eclampsia, altered mental status, blindness, stroke, clonus, severe headaches, and persistent visual scotomata), or hematological complications (platelet count <150,000/µL, disseminated intravascular coagulation, hemolysis).

Exclusion Criteria

- If the patient experienced an adverse outcome before fulfilling the PIERS eligibility criteria or collecting study predictor variables.
- If they got admitted to the hospital in spontaneous labor.

Methodology

Enrolled in the study were patients who met the inclusion and exclusion criteria and gave their consent for the current investigation. We performed thorough clinical examinations, including obstetric,

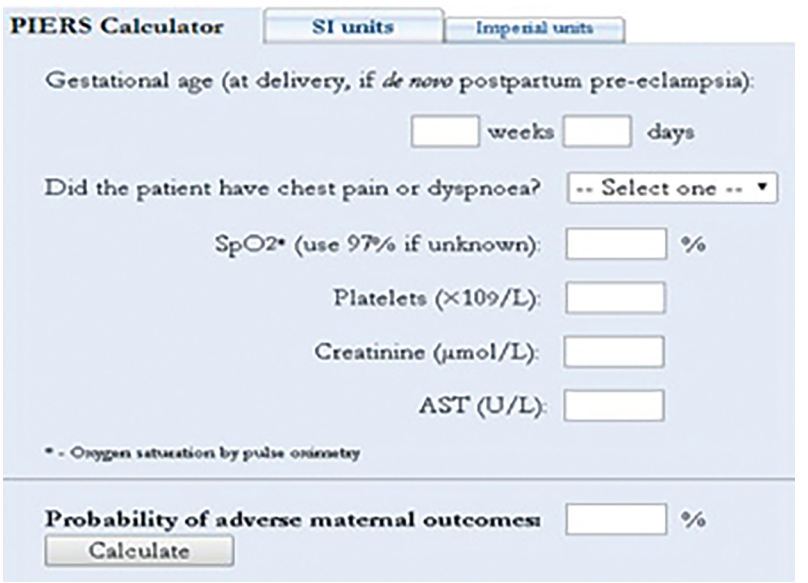

Fig. 1: Preeclampsia integrated estimate of risk (PIER) calculator

systemic, and general examinations, and we took thorough histories. We sent all of the investigations—complete blood counts, coagulation profiles, liver and renal function tests, and oxygen saturation measured by a pulse oximeter—in accordance with the institutional protocol for the workup of HDPs. We performed Doppler, ultrasonography, and cardiotocography (CTG) (daily) for fetal surveillance and amniotic fluid volume assessment. To get the risk of unfavorable outcomes for both the mother and the fetus, we employed the complete PIERS calculator. For patients requiring preterm birth, all patients were closely watched and treated with antihypertensive medications and steroids to promote fetal lung development. The period of gestation, cervix favorability, and necessity of termination all influenced the method of pregnancy termination.

The data was entered into a Microsoft Excel spreadsheet. The Statistical Package for the Social Sciences (SPSS) program version 21 was used, along with ×2 and other pertinent tests, to do statistical analysis. A statistically significant *p*-value was defined as one that was <0.05.

Results

Maternal characteristics and unfavorable maternal outcomes are displayed in Table 1. It demonstrates that in the present study, the mean gestational age was 33.5 weeks, the mean SpO_2 was 96.77%, and 593.3% of the 54 HDP patients who experienced a poor maternal outcome were primigravida, which is highly statistically significant.

Biochemical markers such as hemoglobin, platelet count, liver function test, and renal function test that are performed on all of our pregnant patients with hypertension disease are listed in Table 2. The average serum urea was 37.85 mg/dL, the average serum uric acid was 7.13 mg/dL, the average serum aspartate aminotransferase (AST) was 105.67 IU/L, the average serum alanine aminotransferase (ALT) was 106.56 IU/L, and the average serum lactate dehydrogenase (LDH) was 787.75 IU/L. The mean hemoglobin was 10.04 gm%.

The table shows that all the parameters have a *p*-value of <0.05, indicating that they are statistically significant in predicting adverse maternal outcomes. We also found that platelet count was <1.5 lakh in 59.3% of cases with adverse maternal outcome, creatinine was <1 in 77.8% of cases, and AST was > 40 in 59.3% cases and uric acid was >6 in 81.5% of patients with the adverse maternal outcome. All the above-mentioned biochemical markers have a *p*-value of <0.001, showing that they are statistically significant in predicting adverse maternal outcomes.

Table 1: Baseline characteristics of women in the total cohort comparing women with and without adverse outcomes

	With adverse maternal outcome (n = 54)		*Without adverse maternal outcome (n = 108)*		
Characteristic	*Mean*	*Standard deviation (SD)*	*Mean*	*SD*	*p-value*
Age	27.74	5.83	28.25	4.66	0.571
Gestational age	33.57	3.22	35.50	5.28	**0.005***
Systolic blood pressure (SBP)	155.38	24.45	154.75	22.01	0.875
Diastolic blood pressure (DBP)	99.61	9.95	101.21	13.17	0.399
SpO_2	96.77	2.06	98.40	1.13	**<0.001****
	With maternal outcome (n = 54)		*Without maternal outcome (n = 108)*		
Characteristic	*N*	*%*	*N*	*%*	*p-value*
Primigravida	32	59.3%	30	27.8%	**<0.001****
Multigravida	22	40.7%	78	72.2%	
Fetal heart sound (FHS) present	52	96.3%	106	98.1%	0.474
FHS absent	2	3.7%	2	1.9%	

**$p < 0.001$ highly significant; *$p < 0.05$ significant; Chi-squared test; Independent *t*-test

Table 2: Biochemical markers and maternal outcome

		Adverse maternal outcome		
Biochemical markers		*Present (n = 54)*	*Absent (n = 108)*	*p-value*
Platelet count	<1.5 lakh	32 (59.3%)	22 (20.4%)	<0.001**
	>1.5 lakh	22 (40.7%)	86 (79.6%)	
Creatinine	<1	42 (77.8%)	102 (94.4%)	0.001**
	>1	12 (22.2%)	6 (5.6%)	
AST	<40	22 (40.7%)	98 (90.7%)	<0.001**
	>40	32 (59.3%)	10 (9.3%)	
Uric acid	<6	10 (18.5%)	68 (63%)	<0.001**
	>6	44 (81.5%)	40 (37%)	

**$p < 0.001$ highly significant; Chi-squared test

Table 3 shows that out of 162 patients recruited for the current study, 54 (33.33%) patients with HDP had any of these adverse maternal outcomes like eclampsia, stroke, or reversible ischemic neurological deficit, transient ischemic attack, cortical blindness or retinal detachment, posterior reversible encephalopathy, myocardial ischemia or infarction, the need for intubation (other than for cesarean section), pulmonary edema, and 108 (66.66%) patients had a favorable outcome without any complications of HDP.

We applied the PIERS model to our study population of 162 patients. We found that patients with a PIER score of <2.5 had adverse maternal outcomes in 16.07% of cases. Among the patients with a PIER score between 2.6 and 29.9, 68.18% had adverse maternal outcomes. In patients with a PIER score of >30, 100% had adverse maternal outcomes. The *p*-value is <0.001, which is highly significant, indicating that the PIER score is an efficient tool for predicting adverse maternal outcomes in patients with HDP.

Table 4 demonstrates that of these 162 individuals, 100 experienced unfavorable fetal outcomes, including intrauterine mortality, fetal growth restriction, oligohydramnios, aberrant Doppler changes, stillbirth, admission to the neonatal intensive care unit, and neonatal death. About 50% of the 162 patients had unfavorable fetal outcomes if their PIER score was <2.5, 86% if their PIERS value was between 2.6 and 29.9, and 100% if their PIER score was greater than 30. Given that the *p*-value is <0.001, it is highly significant and suggests that the PIER score is a useful tool for predicting unfavorable fetal outcomes in patients with HDP.

The receiver operating characteristic (ROC) curve obtained by PIER score at different cutoffs is shown in Figure 2. It was found that the area under the curve (AUC) is $C = 0.903$ with SE = 0.024 and 95% confidence interval (CI) from 0.855 to 0.951. It seems from the ROC that PIER score is a very good indicator ($p < 0.001$) to predict maternal outcome. The best cutoff that maximizes (sensitivity + specificity) is 2.85.

The ROC curve obtained by PIER score at different cutoffs is shown in Figure 3. It was found that the AUC is $C = 0.753$ with SE = 0.039 and 95% CI from 0.676 to 0.829. It seems from the ROC that PIER score is a very good indicator ($p < 0.001$) to predict fetal outcome. The best cutoff that maximizes (sensitivity + specificity) is 0.95.

Discussion and Conclusion

Preeclampsia (PE) and eclampsia in particular are two of the HDP that continue to rank among the top three causes of maternal death and morbidity worldwide.[14] Preterm birth, intrauterine growth restriction, stillbirth, and neonatal mortality are among the additional fetal hazards that are elevated by PE.[15] The full-PIERS study was performed to validate a prediction model for assessing risk in women with confirmed diagnoses of PE in high- and mid-resourced settings.[11,13] After applying the full-PIERS prediction model to the study population, we found that 33.33% of patients with hypertensive diseases of pregnancy experienced adverse maternal outcomes. This was statistically significant as the prediction of adverse maternal and fetal outcomes had a *p*-value

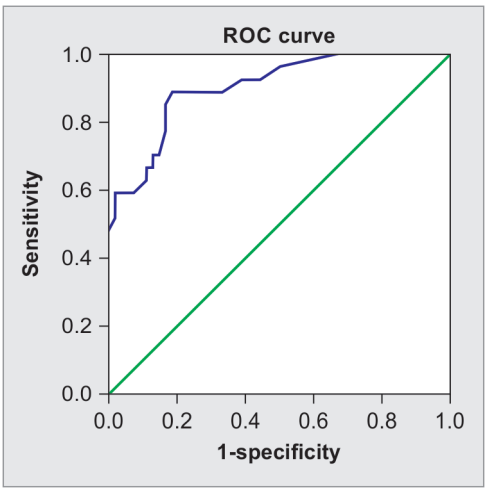

Fig. 2: Receiver operating characteristic (ROC) curve for performance of the full-PIERS model in predicting adverse maternal outcome patients with PE combined cohort within 48 hours of admission

Table 3: Preeclampsia integrated estimate of risk score (PIER) and maternal outcome

	Adverse maternal outcome		
PIER score	*Present (n = 54)*	*Absent (n = 108)*	*p-value*
<30	48 (88.9%)	108 (100%)	<0.001**
>30	6 (11.1%)	0	
<2.5	18 (33.3%)	94 (87%)	
2.6–29.9	30 (55.6%)	14 (13%)	

**$p < 0.001$ highly significant; Chi-squared test

Table 4: Preeclampsia integrated estimate of risk score (PIER) and fetal outcome

	Adverse fetal outcome		
PIER score	*Present (n = 100)*	*Absent (n = 62)*	*p-value*
<30	94 (94%)	62 (100%)	0.049*
>30	6 (6%)	0	
<2.5	56 (56%)	56 (90.3%)	<0.001**
2.6–29.9	38 (38%)	6 (9.7%)	

*$p < 0.05$ significant; **$p < 0.001$ highly significant; Chi-squared test

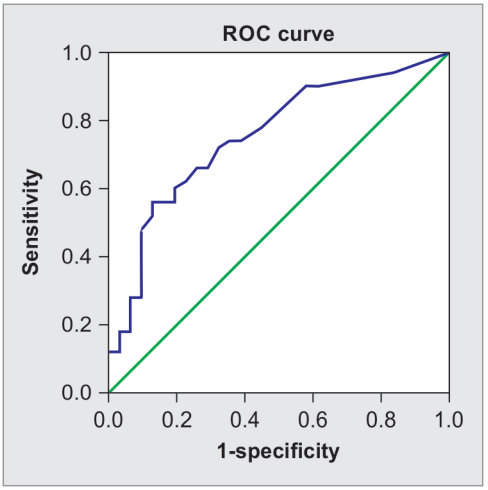

Fig. 3: Receiver operating characteristic (ROC) curve for performance of the full-PIERS model in predicting adverse fetal outcome in patients with PE combined cohort within 48 hours of admission

of <0.05. The mini-PIERS model worked well in terms of accuracy and discrimination ability to predict adverse outcome in women with hypertensive disorder of pregnancy in low-resource settings.[16] The mini-PIERS prediction model was validated by van der Meij et al. They discovered a low sensitivity, positive predictive value, and positive likelihood ratio for the model, as well as an adverse outcome rate of 13.6%, which is not particularly significant.[17]

In addition to the full-PIERS and mini-PIERS risk prediction models, prediction of complications in early-onset preeclampsia (PREP) evaluates predictors that are currently used in routine practice in high-resource settings and can be used to predict unfavorable maternal outcomes. The risks of complications were predicted using the PREP-S (survival model) model at different intervals, up to 48 hours. On the other hand, the total risk during postnatal discharge was provided by the PREP-L (logistic regression). Maternal age, gestation, medical history, systolic blood pressure, deep tendon reflexes, platelets, serum alanine amino transaminases, urea, creatinine, oxygen saturation, and antihypertensive or magnesium sulfate medication were all included in the PREP-S model. With the exception of creatinine, serum alanine amino transaminases, and deep tendon reflexes, all of the above were present in the PREP-L model. When it came to predicting unfavorable outcomes within 48 hours, the PREP-S model demonstrated good discrimination (C-statistic 0.75 and slope 0.80). The two external datasets demonstrated that the simplified PREP-L model performed exceptionally well in terms of calibration [slope: 0.93 PIERS, 0.90 pregnancy-related emergency triage and acuity score (PETRA)] and discrimination (0.81 PIERS, 0.75 PETRA) when predictive risk by discharge was included.[18] Predictive value of this PREP model is comparable to that of the complete PIER model. In our study, we discovered that the entire PIERS model is quite simple to apply and that in patients with HDP, a total PIER score of >30 has a 100% predictive value for unfavorable maternal outcomes. According to a research by Agrawal et al. that took individual maternal outcomes into account, the estimated probability of the whole PIERS model is greater than 30%.[19]

According to our research, poor mother outcomes were linked to early gestational age, low SpO_2, elevated ALT, AST, LDH, and serum uric acid levels. In our study, the patients with unfavorable maternal effects (33.3%) had a mean gestational age of 33.5 weeks. Our findings are in line with those of Srivastava et al.'s study using the full-PIERS calculator, which discovered that out of 27 women in their research with gestational ages under 34 weeks, nine (33.3%) had unfavorable outcomes, and 12 of 98 (12.24%) women with gestational ages over 34 weeks experienced an unfavorable maternal outcome.[20]

The biochemical markers that we employed in our investigation were serum urea, uric acid, liver enzymes, and platelet count. These markers were useful in predicting the probability of unfavorable maternal outcomes in patients with HDP. In 59.3% of instances in our study, the platelet count was <1.5 lakh, the AST was greater than 40 in 59.3%, and the uric acid level was greater than six in 81.5% of patients who had poor maternal outcomes. Hawkins et al.'s study found that patients with elevated uric acid levels had a higher risk of both adverse maternal outcome [odds ratio (OR) 2.0; 95% CI 1.6–2.4] and adverse fetal outcome (OR 1.8; 95% CI 1.5–2.1).[21] Serum creatinine levels were not significantly associated with adverse outcomes, nor were serum AST levels of >40U/L. On the other hand, platelet counts of less than 1.5 lakh/cumm were significantly associated with increased incidence of adverse maternal outcome, according to a study by Srivastava et al. using a full-PIER calculator.[18] Kozic et al. found that 53% of the 2008 study participants had at least one abnormal liver function test result in a sub-analysis of the PIERS dataset, highlighting the significance of liver enzymes in predicting unfavorable outcomes for mothers.[22] Similar to our study, Agrawal et al.'s survey found that platelet count of <1.5 lakh/cumm was substantially related to unfavorable maternal outcomes, and that serum creatinine was an independent predictor of such outcomes.[17] Within 48 hours after admission, Ukah et al. found an unfavorable maternal outcome rate of 7.3% in a related study. They came to the conclusion that the model, with a calibration slope of 0.68 and an area under the ROC curve of 0.80 (95% CI, 0.75–0.86), exhibited good discrimination. With a probability of ≥30%, the calculated likelihood ratio was 23.4 (95% CI: 14.83–36.79), indicating substantial evidence to rule out unfavorable outcomes for mothers. According to the results of the current investigation, the AUC is $C = 0.903$, with a 95% CI of 0.855–0.951 and SE = 0.024. Based on the ROC, it appears that the PIER score is a highly reliable indication ($p < 0.001$) of maternal outcome. The optimal cutoff value to optimize (specificity + sensitivity) is 2.85. In a different investigation, no AUC ROC curve reached an AUC of 0.7, and all 95% CIs of the AUC ROC curves crossed the chance discriminating value of 0.5. Preeclamptic symptoms in mothers did not show sufficient discriminatory qualities to forecast our combined outcomes for mothers and perinatal.[23] It was discovered that the AUC in the current study is $C = 0.753$ with SE = 0.039 and a 95% CI ranging from 0.676 to 0.829. Based on the ROC curve, it appears that PIER score is a very reliable predictor ($p < 0.001$) of the fetal outcome. For maximizing (sensitivity + specificity), 0.95 is the ideal cutoff value. The full-PIERS model in our study was able to predict poor maternal outcomes in the women admitted with HDP within 24 hours of admission. Our results may guide decisions on the timing of the delivery, the continuation of conservative treatment, the patient's administration of blood products, and the patient's transfer to the critical care unit. The variables that demonstrated relevance were the potential predictors of unfavorable outcomes for both mothers and fetuses. After determining the likelihood of a negative outcome linked to the important variables using the OR, we determine the risk score for each case. The optimal cutoff score for the unfavorable maternal and fetal outcomes was

found by doing another ROC curve analysis. A *p*-value of <0.05 was deemed significant.

Recognitions

The study's volunteers are greatly appreciated by the authors.

Study Limitations

It was a single-center study with a modest sample size.

Research and clinical implications: It is simple to incorporate into healthcare environments in low- and middle-income nations and it may be utilized to determine which women would benefit most from treatments like magnesium sulfate, hypertension medications, or transportation to an advanced care facility.

Ethical Approval

Approval granted by the Institutional Ethics Committee (IEC) of AIIMS, Raipur with IEC approval number: AIIMS /RPR/IEC/220/437.

Patient Consent

Written informed consent was obtained.

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