

## Original Research Article

# Maternal risk factors for neonatal asphyxia in severe pre-eclampsia: study at the University Hospital of Obstetrics and Gynecology, Befelatanana

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## ABSTRACT

**Background:** Severe pre-eclampsia remains a major cause of perinatal morbidity and mortality. Neonatal asphyxia is one of its most serious complications. This study aimed to identify maternal factors associated with neonatal asphyxia in cases of severe pre-eclampsia.

**Methods:** A retrospective analytical case-control study was conducted at the University Hospital Center of Obstetrics and Gynecology Befelatanana over a 13-month period (January 2020-January 2021). Cases were newborns with an Apgar score  $\leq 7$  at 5 minutes or absence of immediate cry. Controls were vigorous newborns with an Apgar score of 10 at 5 minutes. A 1:2 sampling ratio was used. Data were analyzed with Epi-Info™ 7.2.5.0. Associations were expressed using odd ratios (OR) with 95% confidence intervals.

**Results:** Among 6,252 live births, 105 cases of severe pre-eclampsia were recorded, including 35 newborns with neonatal asphyxia (33.33%). The strongest risk factors were gestational age  $< 37$  weeks (OR 48.07;  $p=7.3 \times 10^{-9}$ ), low birth weight  $< 2500$  g (OR 21.80;  $p=5.6 \times 10^{-9}$ ), maternal convulsive crisis (OR 10.69;  $p=1.8 \times 10^{-6}$ ), elevated serum creatinine  $\geq 120$   $\mu\text{mol/L}$  (OR 25.5;  $p=4.96 \times 10^{-7}$ ), vaginal bleeding (OR 20.44;  $p=0.00057$ ), and severe hypertensive symptoms (OR 4.14;  $p=0.0025$ ). Referral admission also increased the risk (OR 3.22;  $p=0.016$ ).

**Conclusions:** Neonatal asphyxia in severe pre-eclampsia is strongly associated with prematurity, low birth weight, maternal complications, organ dysfunction, and delayed referral. Early recognition, improved antenatal surveillance, timely maternal stabilisation, and effective referral systems are essential to reduce neonatal morbidity and mortality.

**Keywords:** Severe pre-eclampsia, Neonatal asphyxia, Risk factors, Prematurity, Low birth weight, Maternal complications

## INTRODUCTION

Pre-eclampsia is a pregnancy-specific hypertensive disorder defined by elevated blood pressure and proteinuria after 20 weeks of gestation.<sup>1</sup> It remains a major global health problem, responsible for 15-20% of maternal

deaths and significant neonatal mortality.<sup>2</sup> Its prevalence ranges from 3-14% worldwide and 4-18% in Africa, where it is a leading cause of perinatal morbidity.<sup>3,4</sup> In Madagascar, it is among the main causes of maternal complications and accounts for 5.10% of severe cases at CHUGOB.<sup>5,6</sup> Birth asphyxia is a major contributor to

neonatal mortality. Globally, 4-9 million newborns are affected each year, representing 29% of neonatal deaths.<sup>7</sup> It is clinically defined by a 5-minute Apgar score <7 or absence of immediate cry.<sup>8</sup> In Madagascar, perinatal asphyxia accounts for 18% of neonatal admissions, similar to rates in Africa and much higher than those reported in high-income countries.<sup>9-11</sup> Previous studies have identified multiple risk factors for neonatal asphyxia, including prolonged pregnancy, premature rupture of membranes, eclampsia, thrombocytopenia, renal failure, and maternal infections.<sup>8,9</sup> However, few studies have focused specifically on neonatal asphyxia in the context of *severe pre-eclampsia*, despite the high maternal–fetal risk associated with this condition. This gap highlights the need to investigate maternal factors associated with neonatal asphyxia in severe pre-eclampsia.

## METHODS

### Study design

This was a retrospective analytical case–control study.

### Study setting

The study was conducted at the University Hospital Center of Obstetrics and Gynecology Befelatanana (CHUGOB), a national referral facility in Madagascar.

### Study period and duration

Data collection covered 13 months, from 1 January 2020 to 31 January 2021. The study process started in January 2024 and will conclude at the time of publication.

### Study population

The study involved women diagnosed with severe pre-eclampsia who delivered at  $\geq 28$  weeks of gestation, and their newborns. Cases were newborns with neonatal asphyxia; controls were vigorous newborns.

### Inclusion criteria

Women with severe pre-eclampsia delivering at  $\geq 28$  weeks; newborns with Apgar  $\leq 7$  at 5 minutes and/or absence of immediate cry; newborns with Apgar score of 10 at 5 minutes.

### Non-inclusion criteria

Women who delivered before 28 weeks of gestation.

### Exclusion criteria

Maternal use of neuroleptics or benzodiazepines during the third trimester; general anesthesia during labor; multiple pregnancies.

### Sampling method

A 1:2 case–control ratio was used. Sampling was exhaustive for all eligible mother–newborn pairs.

### Sample size

All subjects meeting the inclusion criteria were included. Of the 6252 patients registered during the study period, 105 patients presented with severe preeclampsia, of which 35 patients met the inclusion criteria for cases and 70 patients for controls.

### Variables

#### Maternal sociodemographic variables

Age, gravidity, parity, educational level, mode of admission (direct or referred), number of antenatal care (ANC) visits, ANC provider (midwife, physician, obstetrician–gynecologist).

#### Maternal clinical variables

Gestational age, previous caesarean section, symptoms of severe hypertension (headache, tinnitus, visual disturbances, epigastric pain), vaginal bleeding, amniotic fluid characteristics, convulsive crisis, mode of delivery, fetal presentation, birth weight.

#### Maternal biological variables

Hemoglobin <10.5 g/dl, serum creatinine >120  $\mu\text{mol/l}$ , transaminases.

### Data collection

Data were extracted using a standardized form and completed from the medical records of eligible patients.

### Statistical analysis

Data were analyzed using Epi-Info™ version 7.2.5.0. Categorical variables were presented as numbers and percentages and compared using Chi-square or Fisher's exact test. Quantitative variables were expressed as mean  $\pm$  standard deviation. Statistical significance was set at  $p < 0.05$  with 95% confidence intervals. Associations with neonatal asphyxia were measured using odds ratios (OR). An OR > 1 indicated a risk factor.

### Ethical approval

Administrative authorization was obtained from the hospital director. Data were anonymized and securely stored to ensure confidentiality.

## RESULTS

Neonatal asphyxia was observed in 33.33% of newborns from severe pre-eclampsia cases (35/105) (Figure 1). Sociodemographic characteristics were not significantly associated with the neonatal asphyxia. Maternal age, gravidity, and parity showed no significant differences between the groups. Primary education was more frequent among cases (Table 1). Preterm birth was the strongest predictor of neonatal asphyxia (OR 48.07;  $p=7.3\times 10^{-9}$ ). Low birth weight also showed a strong association (OR 21.80;  $p=5.6\times 10^{-9}$ ) (Table 2). Maternal convulsive crisis

significantly increased the risk of neonatal asphyxia (OR 10.69;  $p=1.8\times 10^{-6}$ ). Elevated serum creatinine ( $\geq 120$   $\mu\text{mol/L}$ ) was also a major risk factor (OR 25.5;  $p=4.96\times 10^{-7}$ ) (Table 2). Vaginal bleeding was strongly associated with the neonatal asphyxia (OR 20.44;  $p=0.00057$ ). Severe hypertensive symptoms also increased the risk (OR 4.14;  $p=0.0025$ ) (Table 2).

Referred patients had a higher likelihood of neonatal asphyxia compared with those admitted directly (OR 3.22;  $p=0.016$ ) (Table 2).

**Table 1 : Sociodemographic characteristics and educational level of the participants.**

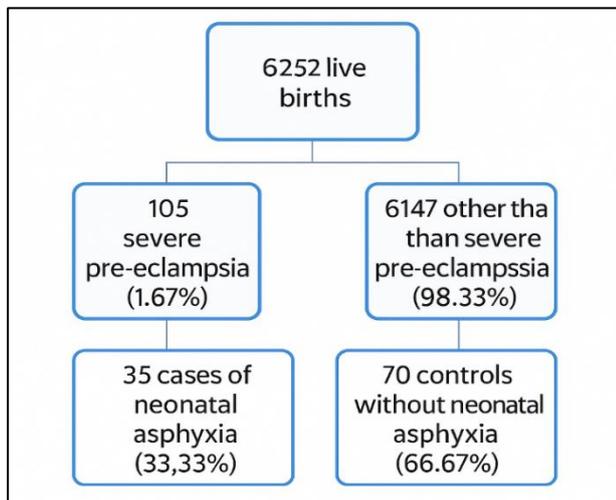
Variables	Cases (n=35)	Controls (n=70)	P value
<b>Age (years), mean<math>\pm</math>SD</b>	25.77 $\pm$ 4.86	29.83 $\pm$ 7.03	0.20
<b>Gravidity, mean<math>\pm</math>SD</b>	2.54 $\pm$ 1.85	2.55 $\pm$ 1.87	0.49
<b>Parity, mean<math>\pm</math>SD</b>	1.30 $\pm$ 1.57	1.31 $\pm$ 1.60	0.14
<b>Educational level, N (%)</b>			
Non-schooled	2 (5.7)	1 (1.4)	0.257
Primary	21 (60.0)	16 (22.9)	0.00041
Secondary	9 (25.7)	42 (60.0)	0.00101
University	3 (8.6)	11 (15.7)	0.377

**Table 2 : Maternal clinical, obstetric and biochemical factors associated with neonatal asphyxia.**

Variables	Cases (n=35)	Controls (n=70)	Or (95% CI)	P value
<b>Mode of admission</b>				
Referred	14 (40.0%)	12 (17.1%)	3.22 (1.28-8.07)	0.016
Direct admission	21 (60.0%)	58 (82.9%)	Reference	
<b>Antenatal care provider</b>				
Physician + obstetrician/gynecologist	17 (48.6%)	50 (71.4%)	0.38 (0.16-0.88)	0.026
Midwife	18 (51.4%)	20 (28.6%)	Reference	
<b>Number of ANC visits</b>				
<4 visits	12 (34.3%)	19 (27.1%)	1.40 (0.58-3.35)	0.500
$\geq 4$ visits	23 (65.7%)	51 (72.9%)	Reference	
<b>Gestational age</b>				
<37 weeks	34 (97.1%)	29 (41.4%)	48.07 (6.22-371)	$7.3\times 10^{-9}$
$\geq 37$ weeks	1 (2.9%)	41 (58.6%)	Reference	
<b>Previous caesarean section</b>				
Yes	3 (8.6%)	8 (11.4%)	0.73 (0.18-2.92)	0.748
No	32 (91.4%)	62 (88.6%)	Reference	
<b>Hypertensive symptoms</b>				
Present	17 (48.6%)	13 (18.6%)	4.14 (1.69-10.14)	0.0025
Absent	18 (51.4%)	57 (81.4%)	Reference	
<b>Convulsive crisis</b>				
Present	19 (54.3%)	7 (10.0%)	10.69 (3.83-29.8)	$1.8\times 10^{-6}$
Absent	16 (45.7%)	63 (90.0%)	Reference	
<b>Vaginal bleeding</b>				
Present	8 (22.9%)	1 (1.4%)	20.44 (2.43-171.3)	0.00057
Absent	27 (77.1%)	69 (98.6%)	Reference	
<b>Amniotic fluid appearance</b>				
Abnormal	13 (37.1%)	34 (48.6%)	0.63 (0.27-1.43)	0.303
Normal	22 (62.9%)	36 (51.4%)	Reference	
<b>Mode of delivery</b>				
Caesarean section	34 (97.1%)	10 (14.3%)	204.0 (26.7-1558)	$1.7\times 10^{-17}$

Continued.

Variables	Cases (n=35)	Controls (n=70)	Or (95% CI)	P value
Vaginal delivery	1 (2.9%)	60 (85.7%)	Reference	
<b>Type of fetal extraction</b>				
Breech presentation	15 (42.9%)	16 (22.9%)	2.53 (1.05-6.05)	0.043
Cephalic presentation	20 (57.1%)	54 (77.1%)	Reference	
<b>Birth weight</b>				
< 2500 g	32 (91.4%)	23 (32.9%)	21.80 (6.03-78.7)	5.6×10 <sup>-9</sup>
≥ 2500 g	3 (8.6%)	47 (67.1%)	Reference	
<b>Maternal anemia</b>				
HB <10.5 g/dl	17 (48.6%)	52 (74.3%)	3.06 (1.27-7.34)	0.016
HB ≥10.5 g/dl	18 (51.4%)	18 (25.7%)	Reference	
<b>Serum creatinine</b>				
≥120 μmol/l	15 (42.9%)	2 (2.9%)	25.5 (5.37-121)	4.96×10 <sup>-7</sup>
<120 μmol/l	20 (57.1%)	68 (97.1%)	Reference	
<b>Transaminases</b>				
Elevated (2–3× normal)	2 (5.7%)	2 (2.9%)	2.06 (0.27-15.28)	0.599
Normal	33 (94.3%)	68 (97.1%)	Reference	



**Figure 1: Frequency of neonatal asphyxia among severe pre-eclampsia cases.**

## DISCUSSION

During the study period, the University Hospital Center of Obstetrics and Gynecology Befelatanana recorded 6,252 live births, among which 105 cases of severe pre-eclampsia were identified, representing an incidence of 1.67%. Among these complicated pregnancies, 35 newborns presented neonatal asphyxia (33.33%). This high proportion is comparable to findings from African series where hypertensive disorders during pregnancy constitute a leading cause of neonatal asphyxia, as reported by Ndiaye et al, Senegal, 2017 and Ouedraogo et al, Burkina Faso, 2015.<sup>12,13</sup>

Preterm birth was the strongest predictor of neonatal asphyxia, with an Odds Ratio of 48 (95% CI:6.22-371; p =7.3×10<sup>-9</sup>). This agrees with data from Ndiaye et al, Senegal, 2017 and Ouedraogo et al, Burkina Faso,

2015.<sup>8,10</sup> In severe pre-eclampsia, preterm delivery is often iatrogenic to prevent maternal complications. Chronic placental underperfusion may impede fetal maturation, increasing vulnerability to neonatal depression. Timely corticosteroid administration and optimal timing of delivery are essential interventions.

Severe hypertensive manifestations significantly increased the risk of neonatal asphyxia (OR=4.14; 95% CI:1.69-10.14; p=0.001). This is consistent with findings from Koné et al, Mali, 2018 and Diallo et al, Guinea, 2018.<sup>1-16</sup> Endothelial dysfunction and systemic vasoconstriction contribute to chronic placental hypoperfusion, predisposing to fetal hypoxia. Strict control of severe hypertension is therefore essential.

Convulsive episodes were another major determinant of neonatal asphyxia (OR=10.68; 95% CI:3.83-29.8; p=7.19×10<sup>-7</sup>). This finding is consistent with observations from African studies, where eclampsia has been repeatedly identified as a significant contributor to fetal compromise. Ndiaye et al, Senegal, 2017, and Ouedraogo et al, Burkina Faso, 2015, similarly reported increased neonatal morbidity in the presence of maternal seizures.<sup>12,13</sup> Such crises cause an abrupt reduction in uteroplacental perfusion, aggravating fetal distress. Systematic administration of magnesium sulfate and early maternal stabilization remain essential components of the management of severe pre-eclampsia.

Elevated maternal creatinine showed a strong association with neonatal asphyxia (OR=25.5; 95% CI:5.37-121; p=1.56×10<sup>-7</sup>), consistent with Coulibaly et al, Burkina Faso, 2016.<sup>17</sup> Renal dysfunction reflects multiorgan involvement, a hallmark of severe pre-eclampsia, and signals an increased risk of fetal hypoxia. Close biochemical follow-up may help identify candidates for urgent delivery.

Maternal anemia was also significantly associated with neonatal asphyxia (OR=3.05; 95% CI:1.30-7.17;  $p=0.008$ ). This finding aligns with Amsalu et al, Ethiopia, 2022.<sup>18</sup> Reduced oxygen-carrying capacity aggravates the impaired maternal–fetal oxygen transfer already present in severe pre-eclampsia. Strengthening antenatal anemia prevention and management could improve neonatal outcomes. Genital bleeding showed a strong association with neonatal asphyxia in our study (OR=20.44; 95% CI: 2.43-171.34;  $p=2.1 \times 10^{-4}$ ). This finding is consistent with reports from African studies showing that antepartum hemorrhage, especially in hypertensive pregnancies, markedly increases the risk of perinatal asphyxia due to impaired placental exchange. Ndiaye et al, Senegal, 2017, and Ouedraogo et al, Burkina Faso, 2015, similarly reported higher rates of neonatal compromise in the presence of suspected placental abruption.<sup>12,13</sup> This complication is frequently linked to the vascular fragility characteristic of severe pre-eclampsia. Immediate obstetric assessment and rapid access to operative facilities remain essential to reduce fetal mortality.

Referred patients were at a significantly higher risk of neonatal asphyxia (OR=3.22; 95% CI:1.28-8.07;  $p=0.01$ ). This finding is consistent with observations from Kaye et al, Uganda, 2003.<sup>19</sup> Delays in referral and late presentation at tertiary centers likely worsen maternal and fetal conditions. Improving the referral network, strengthening communication between healthcare levels, and ensuring timely transport are necessary measures. Other variables such as antenatal care provider, number of antenatal visits, mode of delivery, amniotic fluid abnormalities, history of caesarean section, and elevated transaminases were not significantly associated with neonatal asphyxia, consistent with findings from Alander et al, France, 2020 and Badawi et al, Australia, 1998.<sup>2-20</sup> In summary, neonatal asphyxia in severe pre-eclampsia is influenced by prematurity, low birth weight, maternal complications, organ dysfunction, placental pathology, and delays in care. Strengthening antenatal surveillance, improving stabilization of hypertensive disorders, and optimizing referral pathways remain essential strategies to reduce neonatal morbidity and mortality, as previously highlighted by Wayenberg et al, France, 1998.<sup>21</sup>

### Study limitations

This single-center design limits generalizability. The study period was relatively short, reducing statistical power for some variables. Neonatal asphyxia was assessed clinically, as cord pH and scalp lactate were unavailable at the institution.

### CONCLUSION

Neonatal asphyxia remains a major complication of severe pre-eclampsia, with a frequency of 33.33% in our study. Our findings show a strong correlation between neonatal asphyxia and key indicators of disease severity, including prematurity, low birth weight, maternal convulsive crises,

vaginal bleeding, biochemical abnormalities such as elevated serum creatinine, and referral delays. These factors reflect the profound placental insufficiency and multiorgan involvement characteristic of severe pre-eclampsia.

Improving early detection and management of severe pre-eclampsia, strengthening antenatal surveillance, and ensuring timely referral and delivery are essential strategies to reduce neonatal morbidity and mortality. Future multicentre studies with larger populations are needed to confirm these associations and guide evidence-based interventions.

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*Conflict of interest: None declared*

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

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