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Fetal and neonatal deaths among cases of maternal near miss

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A B S T R A C T

**Objective:** To determine the prevalence of fetal and neonatal deaths among patients with maternal near miss and the factors associated with this fatal outcome.

**Methods:** The authors conducted a descriptive, cross-sectional, analyzing medical records of patients admitted to the ICU of a tertiary obstetric Recife (Brazil), between January 2007 and December 2010, who had at least one criterion of near miss defined by WHO. Statistical analysis was performed with Epi-Info 3.3.2, using chi-square and Fisher's exact test, considering a significance level of 5%. For multivariate analysis was constructed as a hierarchical model with the response variable fetal and neonatal deaths.

**Results:** We included 246 cases of maternal near miss. Among women in the study, hypertensive disorders occurred in 62.7% to 41.2% in HELLP syndrome and the laboratory criteria for near miss in 59.6%. There were 48 (19.5%) stillbirths and 19 (7.7%) neonatal deaths. After analyzing the variables that remained statistically associated with fetal and neonatal deaths were: severe preeclampsia, placental abruption, endometritis, cesarean delivery, prematurity and the laboratory criteria for maternal near miss.

**Conclusion:** The high incidence of fetal and neonatal deaths among patients with maternal near miss. Among these women there is an overlap of factors contributing to this fatal outcome, in our study, those who had severe preeclampsia, placental abruption, endometritis, premature birth or laboratory criteria positively associated with deaths.

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Óbitos fetais e neonatais entre casos de *near miss* materno

R E S U M O

**Objetivo:** Determinar a prevalência dos óbitos fetais e neonatais entre as pacientes com *near miss* materno e os fatores associados a esse desfecho fatal.

**Métodos:** Realizou-se um estudo descritivo, tipo corte transversal, analisando-se prontuários das pacientes admitidas na UTI obstétrica de um hospital terciário do Recife (Brasil), entre janeiro de 2007 e dezembro de 2010, que apresentavam pelo menos um critério de *near miss* definido pela OMS. A análise estatística foi realizada com o programa Epi-Info 3.3.2,

Palavras-chave:

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Morbidade materna grave

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Óbito neonatal

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usando os testes Qui-quadrado de associação e exato de Fisher, considerando-se o nível de significância de 5%. Para análise multivariada foi construído um modelo hierarquizado tendo como variável resposta os óbitos fetais e neonatais.

**Resultados:** Foram incluídos 246 casos de *near miss*. Entre as mulheres do estudo, os distúrbios hipertensivos ocorreram em 62,7%, a síndrome HELLP em 41,2% e os critérios laboratoriais de *near miss* em 59,6%. Ocorreram 48 (19,5%) óbitos fetais e 19 (7,7%) óbitos neonatais. Após a análise estatística as variáveis que permaneceram associadas aos óbitos fetais e neonatais foram: pré-eclâmpsia grave, DPP, endometrite, cesariana, prematuridade e os critérios laboratoriais de *near miss* materno.

**Conclusão:** É elevada a ocorrência de óbitos fetais e neonatais entre as pacientes com *near miss* materno. Entre essas mulheres há uma sobreposição de fatores que contribuem para esse desfecho fatal, em nosso estudo aquelas que apresentaram pré-eclâmpsia grave, DPP, endometrite, parto prematuro ou critérios laboratoriais apresentam associação positiva com os óbitos.

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## Introduction

Cases of maternal near miss, i.e., women in the pregnancy-childbirth cycle that were very close to death and survived, can occur up to 100 times more often than maternal deaths, and are currently used to evaluate the care provided by hospitals.<sup>1-4</sup> The prevalence of near miss varies widely; in Latin America, it ranges from 0.34% to 4.92%, depending on the defining criteria.<sup>5</sup> In a study conducted in Brazil, the prevalence of complications was 21.1/1,000 live births.<sup>6</sup>

Until recently, there was no consensus regarding the criteria used to define a case as maternal near miss. Some authors used criteria based on a specific disease, while others used interventions or organ dysfunction.<sup>7-11</sup> In 2009, the World Health Organization (WHO) established its own criteria to define maternal near miss, and recommended its worldwide use. They are: clinical (acute cyanosis, gasping, respiratory rate > 40 or < 6/rpm, shock, oliguria unresponsive to fluids or diuretics, coagulation disorders, loss of consciousness for 12 hours or more, loss of consciousness and absence of pulse or heartbeat, stroke, uncontrolled seizures, jaundice in the presence of PE), laboratory criteria (SO<sub>2</sub> < 90% for 60 minutes or more, PaO<sub>2</sub>/FiO<sub>2</sub> < 200 mmHg, creatinine ≥ 3.5 mg/dL, bilirubin ≥ 6.0 mg/dL, pH < 7.1, lactate > 5, acute thrombocytopenia [ $< 50,000$ ], loss of consciousness, and presence of glucose and ketone in the urine), and management criteria<sup>3</sup> (use of vasoactive drugs, hysterectomy by infection or bleeding, transfusion ≥ five units of PRBC, intubation and ventilation for ≥ 60 minutes unrelated to anesthesia, dialysis for acute renal failure, and cardiorespiratory arrest).

Maternal status during pregnancy and childbirth affect fetal and neonatal conditions.<sup>12,13</sup> Thus, the maternal near miss, a condition in which the woman is critically ill, and which increases maternal morbidity, may also contribute to the increase in perinatal morbimortality.<sup>3,14</sup> Its association with adverse perinatal events is expected, and is very strong.<sup>15,16</sup>

In addition to the increased risk of stillbirth, newborns of women with near miss present a higher risk of dying in the first week of life, of requiring intensive care unit (ICU

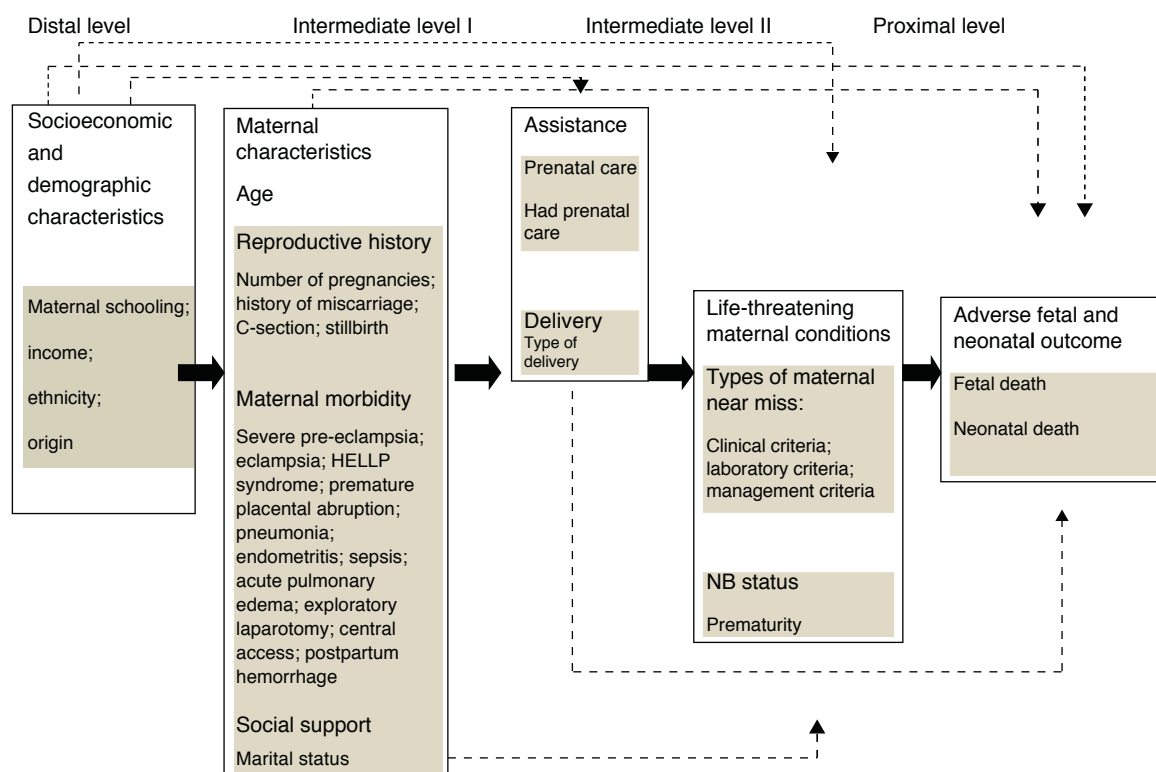
hospitalization, and of being small for gestational age.<sup>16</sup> A WHO survey compared 2,952 cases of maternal near miss with 94,083 women who did not have this morbidity and found an approximately four-fold higher risk of stillbirth and neonatal death among the near miss cases.<sup>16</sup> However, the near miss criteria used (ICU admission, blood transfusion, hysterectomy, eclampsia, and renal or cardiac complications) were different from that recommended by the WHO.<sup>3,16</sup>

A descriptive Brazilian study that used the new WHO criteria identified, among cases of maternal near miss, a high frequency of prematurity and low birth weight, as well as a perinatal mortality rate two times higher than that observed in that hospital during the same period.<sup>17</sup> A study conducted in Africa that followed near miss women and their children for 12 months, which compared them with women without near miss, demonstrated that the risk of death among the children was five times higher among cases of near miss.<sup>18</sup> However, when adjusting for other factors, the odds ratio increased and the significance decreased ( $p = 0.08$ ), making this association uncertain.<sup>18</sup>

Although maternal near miss has been the subject of many studies, there have been few studies dealing with perinatal complications among these patients.<sup>14,19</sup> With this purpose, the present article described the impact of maternal near miss on fetal and neonatal mortality and sought to identify the factors associated with fetal and neonatal deaths among patients with near miss.

## Methods

The study was conducted after approval by the Research Ethics Committee of the Instituto de Medicina Integral Prof. Fernando Figueira (IMIP), according to the principles that regulate research in humans, and in accordance with resolution 196/96 of the Brazilian Health Council, Case No. 2028-10, on November 19, 2010. The study was performed at IMIP, a charity organization located in Recife (Pernambuco, Brazil), which is divided into obstetric emergency and maternity wards (obstetrics, fetal medicine, human reproduction, and



**Fig. 1 – Hierarchical model for fetal and neonatal adverse outcome among patients with maternal near miss, adapted from the model of Lima<sup>20</sup>.**

postpartum care). IMIP also has a 12-bed obstetric ICU; annual admission is approximately 800 patients.

This was a cross-sectional and retrospective study that identified, among patients admitted to the obstetric ICU of IMIP from January of 2007 to December of 2010, those who had maternal near miss according to the WHO criteria. During the study period, 2,997 women in the pregnancy-childbirth cycle were admitted to the obstetric ICU of IMIP. After analyzing the medical records, 255 women who met some of the WHO maternal near miss criteria were identified. Live children born to these participants also had their records analyzed to determine neonatal outcome. Data were collected from November of 2010 to January of 2012 by the main investigator and research assistants, trained in the School of Medicine of the Faculdade Pernambucana de Saúde, linked to the Institutional Program for Scientific Initiation Scholarships.

The variables studied were age, ethnicity, marital status, educational level, origin, income, reproductive history, pre-existing diseases, prenatal care, diagnosis of hypertensive disorders, postpartum hemorrhage, premature placental abruption, sepsis, endometritis, pneumonia, pulmonary edema, thrombocytopenia, laparotomy, central access, length of hospital stay, gestational age at delivery, type of delivery, types of WHO maternal near miss criteria and their moment of onset, fetal and neonatal death, Apgar score, and birth weight.

All data were entered into specific files created in Microsoft Excel spreadsheets, 2003 version, and statistical analysis was performed using the Epi-info software, release 3.5.3. For categorical variables, descriptive analysis was performed with

a study of frequency and percentage, while for quantitative variables, measures of central tendency and their dispersions were calculated. Cases of fetal and neonatal death were considered adverse fetal and neonatal outcome (AFNO). AFNO analysis excluded cases of maternal near miss associated with miscarriage (seven), gestational trophoblastic disease (one), and ectopic pregnancy (one), as these situations do not include viable fetuses. Cases of twin pregnancies were recorded as a single outcome, classified by the twin with worse outcome.

In the bivariate analysis, AFNO was the outcome variable, and all others were considered exposure variables, categorized as yes/no dichotomous variables. The prevalence ratio (PR) was calculated as a measure of risk, with a 95% confidence interval (95% CI). Chi-squared or Fisher's association tests were used when pertinent.

Since this was an epidemiological study with a large number of mediating or intervening variables conceptually related to AFNO, a hierarchical model was constructed for multiple logistic regression analysis, as in these situations the use of only one hierarchical level is not adequate.<sup>20</sup> The model was based on another proposed by Lima<sup>20</sup> (Fig. 1). The variables were positioned hierarchically in four levels (distal, intermediate I, intermediate II, and proximal), following a temporal and logical order among the events that led to AFNO.

The distal level of the model consisted of maternal socioeconomic and demographic characteristics (education, income, ethnicity, origin), which precede or partly determine the occurrence of maternal morbidity and reproductive history.<sup>20,21</sup> These characteristics, in turn, were included in the intermediate

I level (age, marital status, number of births, miscarriages, previous C-section, previous stillbirth, PE, eclampsia, HELLP syndrome, premature placental abruption, pneumonia, endometritis, sepsis, acute pulmonary edema, exploratory laparotomy, central access, and postpartum hemorrhage).

The intermediate level II included aspects related to prenatal care and childbirth (presence or absence of prenatal care and type of delivery), as a good quality prenatal care should be able to ensure access to an appropriate obstetrics unit and to identify the necessities and morbidities of the mother.<sup>20</sup> The proximal factors included the birth status of the newborn (prematurity) and maternal life-threatening situations (clinical, laboratory, and management criteria of maternal near miss) due to the close association with neonatal morbidity and mortality.<sup>13,20</sup>

It is also noteworthy that among the selection criteria of the study participants was the presence of at least one criterion of maternal near miss. Thus, there were women who had only clinical, laboratory, or management criteria, or an association of them. The criteria for near miss could then be divided and grouped as proximal factors directly associated with AFNO, and it was thus possible to discover among the three (clinical, laboratory or management), which would have a greater association with AFNO.

The introduction of the variables into a multiple regression model was performed in steps. First, a multivariate analysis with variables from the distal level showed a significance level of up to 20%. In this analysis, the variables with the highest p-value were removed from the model, one at a time, until only those that had a statistically significant difference remained ( $p < 0.05$ ), which were then selected for the next phase, and thereafter were not excluded from the model. The PR obtained in this step did not change with the addition of the variables from the following levels, reflecting the different weight assigned to each level of the model. Then, all variables from intermediate level I whose p-value was less than 0.20 were included in the model, as well as the variables from the previous level (distal) with statistical significance. The process was repeated with the following levels, obtaining in the final model the variables that remained significantly associated with AFNO ( $p < 0.05$ ).

To demonstrate the representativeness of the present sample, after collection, sample size was calculated with the help of the StatCalc Epi Info program, release 3.5.1, using data from the study "Severe maternal morbidity and near miss events in a regional referral hospital", in which the prevalence of fetal and neonatal death was 12.5% among patients with maternal near miss.<sup>17</sup> Thus a sample of 168 patients was obtained, for an alpha error of 0.05 and a beta error of 0.20. Considering a predicted loss rate of 20%, the total number of participants was 202. Because this was a descriptive study, as many patients as possible were obtained during the time of the study, so the number found by calculation was rounded to the total number collected in the four years of the study period (246).

## Results

Between January of 2007 and December of 2010, 255 cases of maternal near miss were identified among the obstetric patients

admitted to the ICU of IMIP. During the same period, there were 19,940 live births in the institution, with a maternal near miss ratio of 12.8/1,000 live births. The length of stay ranged from five to 86 days, with a mean of 14.8 days (SD = 10.27).

The age of the participants ranged from 14-45 years with a mean of 25.6 (SD = 6.99), and among them 57.3% were mixed-race, 41.2% had a stable relationship with a partner, 43.2% had less than eight years of schooling, and 18.8% were from Recife. Regarding the obstetric history, 50% of patients were nulliparous, 18.8% had a history of miscarriage, 6.3% of stillbirth, and 20.5% had had a previous C-section delivery. Regarding the analysis of prenatal care, only 12 (4.9%) did not receive it.

Among the 160 cases of hypertensive disorders, there were 125 cases (49%) of severe PE, and 35 cases of eclampsia (13.7%). HELLP syndrome occurred in 105 (41.2%) participants. The most frequent infection was endometritis (25.1%), followed by pneumonia (19.6%), and 16.9% of patients developed sepsis. There were 90 cases (35.3%) of postpartum hemorrhage, 29 (11.4%) cases of premature placental abruption (PPA), four cases of placenta accreta, three uterine ruptures, and one placenta praevia.

The laboratory criteria for near miss were present in 59.6% of the participants, while the clinical and management criteria were observed in 50.2% and 49%, respectively. C-section was the most common type of delivery, with 188 cases (76.4%). The mean gestational age at delivery was 34 weeks and two days, with 54.5% premature births (gestational age at birth less than 37 weeks).

For the analysis of AFNO, seven cases of miscarriage, one ectopic pregnancy, and one choriocarcinoma were excluded. Thus, among 246 cases of maternal near miss, there were 67 (27.2%) cases of AFNO, of which 48 (19.5%) occurred due to fetal death and 19 (7.7%) due to neonatal death; 44.4% of live births were discharged, 9.8% were hospitalized for more than 28 days, and there was loss of data on neonatal outcome in 18% of cases. Among the 198 live births, 42 (17.1%) had birth weight  $< 1.5$  kg, 30 (12.2%) were less than 30 gestational weeks at birth, and 22 (9%) had five-minute Apgar score  $< 7$ . There were 12 twin pregnancies.

The highest frequency of fetal and neonatal deaths occurred in women who had PPA (73.1%). Among the criteria for maternal near miss, the laboratory criteria showed the highest number of cases of AFNO (45.1%) (Table 1). In the bivariate analysis, AFNO was significantly associated ( $p < 0.05$ ) with the following variables: history of miscarriage, severe PE, HELLP syndrome, PPA, endometritis, postpartum hemorrhage, C-section delivery, prematurity, and laboratory criteria for maternal near miss (Table 1).

Considering the possible inter-associations between the study variables, a logistic regression model with hierarchical levels was applied. Among the distal level variables, only one had  $p < 0.20$  (Black ethnicity), but it was greater than 0.05, so it was not included in the regression analysis. Among the intermediate I level variables, a p-value  $< 0.20$  was found for age, marital status, nulliparity, history of stillbirth and miscarriage, severe PE, HELLP syndrome, PPA, endometritis, central access, laparotomy, and postpartum hemorrhage. When performing the multiple regression analysis, those with p-values  $< 0.05$  were severe PE, PPA, and endometritis (Table 2).

**Table 1 – Bivariate analysis between the study variables and AFNO among women with near miss.**

	AFNO		OR (95% CI)	p
	Yes n (%)	No n (%)		
<i>Distal factors</i>				
Ethnicity (black)	7 (53.8)	6 (46.2)	1.74 (1.00-3.03)	0.08 <sup>a</sup>
Schooling (< 8 years)	31 (34.1)	60 (65.9)	1.14 (0.74-1.75)	0.55
Origin (countryside or RMR)	55 (34)	107 (66)	1.08 (0.64-1.80)	0.78
Income (no income)	44 (30.6)	100 (69.4)	0.82 (0.50-1.35)	0.45
<i>Intermediate factors I</i>				
Age (35 or older)	11 (50)	11 (50)	1.59 (0.99-2.54)	0.08
Marital status (no partner)	8 (21.1)	30 (78.9)	0.60 (0.31-1.14)	0.09
Nulliparous	27 (26.7)	74 (73.3)	0.70 (0.46-1.06)	0.09
History of C-section	48 (31.8)	103 (68.2)	0.95 (0.59-1.55)	0.85
History of stillbirth	8 (53.3)	7 (46.7)	1.76 (1.04-2.97)	0.06 <sup>a</sup>
History of miscarriage	19 (46.3)	22 (53.7)	1.64 (1.08-2.48)	0.03
Severe pre-eclampsia	44 (43.6)	57 (56.4)	1.88 (1.23-2.86)	< 0.05
Eclampsia	8 (25.8)	23 (74.2)	0.74 (0.40-1.39)	0.32
HELLP syndrome	39 (44.8)	48 (55.2)	1.81 (1.22-2.69)	< 0.05
PPA	19 (73.1)	7 (26.9)	2.65 (1.89-3.70)	< 0.05
Pneumonia	11 (26.2)	31 (73.8)	0.74 (0.43-1.28)	0.26
Endometritis	22 (45.8)	26 (54.2)	1.55 (1.04-2.29)	0.03
Sepsis	10 (31.3)	22 (68.8)	0.92 (0.53-1.60)	0.77
Acute pulmonary edema	8 (28.6)	20 (71.4)	0.83 (0.45-1.55)	0.55
Exploratory laparotomy	6 (20.7)	23 (79.3)	0.58 (0.28-1.22)	0.11
Central access	16 (47.1)	18 (52.9)	1.53 (1.00-2.34)	0.07
Postpartum hemorrhage	36 (50)	36 (50)	2.06 (1.41-3.03)	< 0.05
<i>Intermediate factors II</i>				
C-section delivery	37 (24.8)	112 (75.2)	0.42 (0.29-0.61)	<0.05
Lack of prenatal	4 (44.4)	5 (55.6)	1.44 (0.67-3.08)	0.31 <sup>a</sup>
<i>Proximal factors</i>				
Prematurity	52 (44.1)	66 (55.9)	4.22 (2.03-8.75)	< 0.05
Clinical near miss	33 (33.3)	66 (66.7)	0.99 (0.67-1.46)	0.96
Laboratory near miss	51 (45.1)	72 (58.5)	2.00 (1.23-3.24)	< 0.05
Management near miss	28 (31.1)	62 (68.9)	0.88 (0.59-1.31)	0.52

95% CI, 95% confidence interval; AFNO, adverse fetal and neonatal outcome; OR, odds ratio; PPA, premature placental abruption; RMR, Recife metropolitan region.

<sup>a</sup>Analysis performed with Fisher's test.

**Table 2 – Multivariate analysis of factors associated with adverse fetal and neonatal outcome among women with near miss.**

	Adjusted risk odds ratio	95% CI	p
<i>Proximal factors</i> <sup>a</sup>	—	—	—
<i>Intermediate factors I</i>			
Endometritis	3.82	1.71-8.58	< 0.05
PPA	8.86	3.03-25.91	< 0.05
Severe pre-eclampsia	3.21	1.55-6.63	< 0.05
<i>Intermediate factors II</i>			
C-section delivery	0.20	0.08-0.44	< 0.05
<i>Proximal factors</i>			
Prematurity	7.20	2.52-20.53	< 0.05
Laboratory near miss	2.83	1.08-7.39	0.03

95% CI, 95% confidence interval; PPA, premature placental abruption.

<sup>a</sup>Among the proximal factors, none showed statistical significance.



The intermediate level II variable, C-section, whose adjusted risk was 0.20 ( $p < 0.05$ ), was added to the model with the intermediate level I variables. After this step, the proximal level variables; prematurity and laboratory criteria for near miss with  $p$ -values  $< 0.20$  were then added. Through a multivariate logistic regression analysis, using a hierarchical model, only the variables severe PE, PPA, endometritis, C-section delivery, prematurity, and laboratory criteria for maternal near miss remained significantly associated with AFNO (Table 2). The variables history of miscarriage, HELLP syndrome, and postpartum hemorrhage lost significance after adjusted analysis.

## Discussion

The ratio of maternal near miss in this study was 12.8/1,000 live births, similar to that found in a Brazilian study (9.35/1,000) that also used the new WHO criteria, and within the wide range reported in the literature.<sup>5,11,17,22</sup>

The number of fetal deaths (19.5%) was higher than that observed by other authors<sup>16,17</sup> (3.6% and 12.5%). Conversely, Souza showed an almost four times higher risk of fetal death among patients with maternal near miss when compared to women without near miss.<sup>16</sup> He also concluded that the babies of these patients were small for gestational age, more often required neonatal ICU admission, and had a higher risk of perinatal death.<sup>16</sup> The number of neonatal deaths (7.7%) was also higher than that found by Souza (3.2%); this difference can be explained by the maternal near miss criteria adopted by Souza, which were different from those currently recommended by the WHO.<sup>14,16</sup>

In spite of these differences, it is undeniable that the severe obstetric conditions experienced by these women with maternal near miss determined a high number of fetal and neonatal deaths, as observed in the present study.

Among the children of women with maternal near miss, there was a significant proportion of infants with very low birth weight ( $< 1.5$  kg), severe hypoxia (5-minute Apgar score  $< 7$ ) and extreme prematurity (gestational age  $< 30$  weeks), which were even higher than that reported by other authors.<sup>16,17</sup> This corroborates the hypothesis that near miss increases not only fetal but also neonatal morbidity, as such conditions have high sensitivity and specificity to identify neonatal complications.<sup>12</sup>

When performing the multivariate analysis with a hierarchical model, PPA, severe PE, endometritis, C-section delivery, prematurity, and laboratory criteria for maternal near miss remained significantly associated with AFNO. PPA is an obstetric complication with high potential for maternal and fetal morbimortality. Adverse perinatal outcomes such as low birth weight, prematurity, and perinatal death often accompany this diagnosis.<sup>23,24</sup> In the present study, PPA remained strongly associated with AFNO (PR = 8.86; 95% CI = 3.03 to 25.91;  $p < 0.05$ ), corroborating the findings of other studies.<sup>23,24</sup>

Hypertensive disorders are among those most often associated with maternal near miss and perinatal morbidity and mortality.<sup>15,19</sup> In the present study, among women with severe PE, almost half had AFNO. The fetuses of mothers

with severe PE have worse perinatal prognosis, with increased risk of prematurity, low birth weight, and death when compared with fetuses of normotensive mothers or those with gestational hypertension.<sup>25</sup> In this study, in addition to severe PE, women had another factor associated with a worse fetal and neonatal outcome, which was the near miss. This overlap of maternal near miss and severe PE resulted in a strong association with AFNO; women with maternal near miss who had severe PE had a three times greater association with AFNO when compared with patients with near miss who did not have severe PE.

An analysis with a specific group of patients with severe PE (those with HELLP syndrome) was also performed. In the bivariate analysis, this group showed statistical significance, but in the multivariate analysis, only severe PE was strongly associated with AFNO, and HELLP syndrome lost significance (PR = 1.29; 95% CI = 0.52 to 3.21;  $p = 0.58$ ). The literature shows conflicting results of studies that compared the perinatal outcome of patients with HELLP syndrome and cases of severe PE.<sup>26,27</sup> Among women with near miss, fetal and neonatal deaths were more often related with severe PE than with its complications (eclampsia or HELLP syndrome).

This prevalence of hypertensive disorders among cases of maternal near miss and its association with AFNO indicates the need for prenatal care improvement aimed at the early identification and implementation of measures to prevent progression to complications and minimize the effects on the fetus. This is feasible, as in developed countries there has been a reduction in cases of hypertensive disorders; they do not appear as the main maternal condition associated with near miss, having been replaced by bleeding disorders.<sup>28</sup>

In a study conducted in Italy with over 1,200 cases of maternal near miss, and in another conducted by the WHO with almost 3,000 cases, C-section was the main route of pregnancy termination, with frequencies of 70% and 59.5%, respectively, similar to that found in this study<sup>16,28</sup> (76.4%). Some authors consider C-section delivery as a factor that increases the chance of a woman to become a near miss case by five times; however, this association may be influenced by confounding factors.<sup>29</sup> Thus, it is still debatable whether C-section is a risk factor for near miss, or if it is actually a consequence of this condition.<sup>17,29</sup>

As also shown in other studies, the C-section was the predominant type of delivery among cases of maternal near miss.<sup>16,28</sup> These high rates may be acceptable among these patients due to the urgent gestational resolution and unfavorable cervical or fetal status.<sup>30</sup> C-section also appeared as a protective factor for AFNO (PR = 0.20; 95% CI = 0.08 to 0.44;  $p < 0.05$ ). This finding may be due to the fact that early pregnancy termination can prevent maternal near miss effects from appearing in the fetus, and thus there is a decrease in AFNO.

Premature birth occurred in 54.5% of cases. This high rate of prematurity, also observed in a study performed in Campinas, Brazil (65%) and one in Rio de Janeiro, Brazil (50%), can be explained by the severe situations experienced by these patients that can affect the fetus and lead to the need for premature pregnancy termination.<sup>15,17</sup> Prematurity is referred to as the main factor associated with neonatal mortality.<sup>31</sup> In the present study, the rate of AFNO among premature births

was high (44.1%), and preterm birth remained strongly associated with AFNO after the multivariate analysis (PR = 7.20; 95% CI = 2.52 to 20.53;  $p < 0.05$ ).

Neonatal infection is among the three leading causes of fetal and neonatal death, and it is closely related with maternal infection.<sup>31</sup> In the present study, women who developed endometritis had an almost four-fold higher association with AFNO. A review of antibiotic therapy protocols for the specific group of patients with maternal near miss can be evaluated in the future for treatment optimization and consequent improvement of fetal and neonatal morbidity and mortality.

Another interesting finding was the positive association between the laboratory criteria for near miss and AFNO (PR = 2.83; 95% CI = 1.08 to 7.39;  $p < 0.05$ ), which was not observed with the clinical and management criteria. This could be explained by a higher frequency of laboratory criteria in patients still pregnant (56.2%), whereas the management criteria emerged more often postpartum (46.7%), and the clinical criteria had a lower percentage of pregnant women (40.2%). Thus, laboratory near miss can be investigated in other studies as a marker of not only severe maternal morbidity, but also of neonatal morbidity and mortality.

The association found in the present study between history of miscarriage and AFNO was not maintained after multivariate analysis (PR = 2.42; 95% CI = 1.16 to 5.03;  $p < 0.05$ ). A case-control population-based study demonstrated that among women with a history of miscarriage, the risk of fetal death was three times higher among nulliparous women, whereas among multiparous, there was no association between miscarriage and stillbirth, although this study did not analyze cases of maternal near miss.<sup>30</sup>

This supports the present model of multiple regression analysis that considers the inter-relationships of the variables, reducing the occurrence of erroneous findings that may eventually appear in the bivariate analysis. It can thus be inferred that, among patients with near miss, factors directly related to the pathology of the patient (severe PE, endometritis, PPA, and laboratory criteria for near miss) have greater influence on fetal and neonatal deaths than maternal characteristics, such as the obstetric background.

The study limitations include the fact that the data were collected from medical records, which did not allow for the characterization of some near miss criteria, such as gasping, while some other information may not have been recorded, such as cyanosis and lactate levels.

## Conclusion

The present study demonstrated the high frequency of fetal and neonatal deaths among women with near miss. It also disclosed the main factors associated with this fatal outcome, among which are severe PE, PPA, prematurity, and endometritis were already known to be associated with fetal and neonatal deaths. Others, such as C-section delivery, have shown conflicting results in the literature, but in patients with near miss this variable can be truly a protective factor against AFNO. The present study also suggested the association

between laboratory criteria for near miss with AFNO, which was not observed with clinical or management criteria.

In this specific group of patients with maternal near miss, there is an overlap of factors that can lead to stillbirths and neonatal deaths. Identifying them is the first step to achieve decrease in neonatal and fetal mortality, as they can be used as basis for changes in antenatal and neonatal treatment protocols of maternal near miss cases.

## Conflicts of interest

All authors declare to have no conflicts of interest.

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