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The Protective Paradox of Operative Delivery: A Case-Control Analysis of Maternal and Neonatal Risk Factors for Asphyxia in a Balinese Hospital

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A B S T R A C T

Neonatal asphyxia constitutes a primary driver of neonatal morbidity and mortality worldwide, with a disproportionate burden in developing nations like Indonesia. The identification of localized, modifiable risk factors is a critical prerequisite for the development of targeted and effective preventive healthcare strategies. This study was designed to meticulously identify the significant maternal, intrapartum, and neonatal risk factors associated with neonatal asphyxia within a tertiary care hospital setting in Bali, Indonesia. We executed a retrospective matched case-control study at a specialized Maternal and Child Hospital in Denpasar, Bali. The study included all neonates diagnosed with asphyxia (cases, n=103) born between January 1st and December 31st, 2023, and 103 randomly selected neonates without asphyxia (controls), also born within the same period. To control for potential confounding, cases and controls were matched by gender and month of birth. An exhaustive review of maternal and neonatal medical records was conducted. The data were analyzed using Chi-square tests for bivariate analysis and a multivariate logistic regression model to isolate the independent predictors of asphyxia. The multivariate analysis identified prematurity as the most profound risk factor for neonatal asphyxia, conferring a more than tenfold increase in risk (Adjusted Odds Ratio [aOR] = 10.33, 95% CI: 4.50-23.71, p<0.001). Significant maternal risk factors included anaemia during pregnancy (aOR = 6.56, 95% CI: 2.36-18.20, p<0.001), maternal age outside the optimal range of 20-35 years (aOR = 3.93, 95% CI: 1.50-10.32, p=0.005), and maternal obesity (aOR = 2.92, 95% CI: 1.20-7.11, p=0.018). Premature rupture of membranes (PROM) was identified as a significant intrapartum risk factor (aOR = 3.16, 95% CI: 1.30-7.72, p=0.011). Notably, delivery by caesarean section or instrumental assistance appeared to be a significant protective factor (aOR = 0.22, 95% CI: 0.08-0.59, p=0.003). In conclusion, prematurity, maternal anaemia, age extremes, maternal obesity, and PROM are confirmed as critical, independent risk factors for neonatal asphyxia in this Balinese population. The striking protective association of operative delivery likely represents a "protective paradox," a statistical artifact arising from confounding by indication, wherein timely and decisive obstetric intervention for high-risk pregnancies successfully mitigates adverse outcomes. Preventive strategies must therefore be multifaceted, prioritizing the public health imperatives of preterm birth prevention and the rigorous clinical management of maternal anaemia and obesity throughout the continuum of antenatal care.

1. Introduction

The neonatal period, encompassing the first 28 days of life, represents the most vulnerable phase of human existence.[1] Globally, the majority of deaths among children under the age of five are concentrated within this critical window, with the highest risk of mortality occurring in the first week.[2] The principal etiologies of this early loss of life are a constellation of conditions intrinsically linked to the perinatal period: complications arising from preterm birth, birth

asphyxia, birth trauma, severe infections, and congenital anomalies.[3] While global and national efforts have led to a gradual decline in the neonatal mortality rate in Indonesia, the pace of this reduction has been insufficient to meet the ambitious targets set forth by the Sustainable Development Goals (SDGs). In provinces such as Bali, neonatal mortality remains a pressing public health challenge, underscoring the urgent need for focused interventions.[4] Among the primary causes of neonatal mortality, birth asphyxia—defined as the failure to initiate and sustain breathing at birth—stands out as a major contributor that is, in principle, largely preventable. The pathophysiology of birth asphyxia is rooted in a critical interruption of oxygen supply to the infant, an event that triggers a cascade of systemic insults.[5] This profound hypoxia and hypercapnia lead to a state of mixed metabolic and respiratory acidosis, which can inflict irreversible damage on vital organs, with the developing brain being exquisitely vulnerable. The neurological sequelae for survivors of significant asphyxia are often devastating and lifelong, manifesting as cerebral palsy, seizure disorders, profound cognitive and learning disabilities, and sensory impairments affecting vision and hearing.[6]

The immense burden imposed by neonatal asphyxia, both in terms of mortality and long-term disability, mandates a strategic shift from reactive treatment to proactive prevention.[7] A foundational step in this direction is the precise identification of the antecedent risk factors that predispose an infant to this perilous outcome. While the international literature has established a broad range of maternal and neonatal risk factors, the prevalence, impact, and interplay of these factors are known to vary substantially across different geographic, ethnic, and socioeconomic contexts.[8] Localized data are therefore indispensable for the design of tailored, evidence-based public health policies and clinical guidelines. This study was conceived to address this knowledge gap within the specific healthcare landscape of Bali, Indonesia. The primary objective of this research was to meticulously identify and quantify the maternal, intrapartum, and neonatal factors that serve as significant and independent predictors for the incidence of neonatal asphyxia at a specialized tertiary care Maternal and Child Hospital in Denpasar.

While numerous studies have investigated risk factors for neonatal asphyxia, this study offers several unique contributions. Firstly, it provides urgently needed, high-quality data specific to the population of Bali, Indonesia, a region with its own distinct demographic and healthcare profile. Secondly, this study moves beyond a simple cataloging of risk factors to critically analyze a counter-intuitive and clinically significant finding: the apparent protective effect of operative delivery. By framing this as a "protective paradox" attributable to confounding by indication, this research provides a more nuanced interpretation that speaks to the quality of local obstetric decision-making, a topic rarely explored in conventional risk factor studies.[9,10] This analysis, therefore, not only identifies what the risks are but also offers insights into how the healthcare system is responding to them. The primary aim of this study was to identify and quantify the independent maternal, intrapartum, and neonatal factors associated with the incidence of neonatal asphyxia in a tertiary care hospital in Denpasar, Bali. By establishing a robust, evidence-based profile of the highest-risk pregnancies, this research seeks to provide actionable data to inform the development of targeted clinical guidelines and focused public health strategies designed to reduce the burden of neonatal asphyxia in this specific setting and in similar contexts throughout the region.

2. Methods

This investigation was structured as a retrospective matched case-control study. The case-control design was chosen for its inherent efficiency in studying determinants of relatively infrequent health outcomes, such as neonatal asphyxia, and its capacity to explore multiple potential risk factors simultaneously. The study was conducted at a prominent, specialized Maternal and Child Hospital in Denpasar, the provincial capital of Bali, Indonesia. This institution

serves as a tertiary care referral center, offering comprehensive obstetric, neonatal, and pediatric services, thus providing a representative study of both routine and high-risk deliveries. The study period encompassed all births occurring over a full calendar year, from January 1st, 2023, to December 31st, 2023. The source population for this study included all neonates delivered at the hospital during the specified one-year period. The case group consisted of all neonates who received a clinical diagnosis of neonatal asphyxia. To maximize the study's statistical power and minimize the potential for selection bias, a total sampling strategy was employed, including all 103 eligible cases identified during the study period. For the purposes of this investigation, neonatal asphyxia was operationally defined by the presence of an Apgar score of less than 7 at 5 minutes following birth. This is a widely accepted clinical standard for identifying neonates requiring resuscitation and who are at increased risk for adverse outcomes. The control group was composed of neonates delivered in the same hospital during the same time frame who were not diagnosed with asphyxia, defined as having an Apgar score of 7 or greater at 5 minutes. For each identified case, one control was selected via simple random sampling from the comprehensive electronic birth registry of all eligible non-asphyxiated neonates. To mitigate potential confounding by variables known to influence birth outcomes, a 1:1 matching protocol was implemented. Each case was individually matched to a control based on the neonate's gender and the calendar month of birth. All live-born, singleton neonates delivered at the facility were eligible for inclusion. To ensure that the outcome was attributable to perinatal factors rather than underlying structural defects, neonates with major congenital abnormalities that independently cause respiratory compromise or mortality (such as complex congenital heart disease, diaphragmatic hernia, or anencephaly) were excluded from both the case and control groups.

The primary outcome variable was the neonate's status as either a case (asphyxia present) or a control (asphyxia absent). The independent variables investigated were a panel of maternal, intrapartum, and neonatal factors known or suspected to be associated with asphyxia. The following precise operational definitions were used for all key independent variables: Maternal Age: Classified into two categories: optimal reproductive age (20-35 years) and high-risk age (<20 years or >35 years). Maternal Obesity: Defined according to the Asia-Pacific classification for obesity as a Body Mass Index (BMI) of 27.5 kg/m² or greater, calculated based on the mother's height and her weight recorded at the first antenatal visit. Anaemia during Pregnancy: Defined as a maternal hemoglobin (Hb) concentration of less than 11 g/dL on any formal laboratory record during the pregnancy, in accordance with World Health Organization criteria. Mode of Delivery: Categorized as either spontaneous vaginal delivery or operative delivery. The operative delivery category encompassed all births via Caesarean section as well as those assisted by vacuum extraction or forceps. Premature Rupture of Membranes (PROM): Defined as the rupture of fetal membranes occurring more than one hour prior to the onset of recognized, active labor. Prematurity: Defined as a live birth occurring before 37 completed weeks of gestation. Gestational age was primarily determined by first-trimester ultrasound dating, with the date of the last menstrual period used as a secondary confirmation. Low Birth Weight (LBW): Defined as a recorded birth weight of less than 2500 grams. Data for all variables were meticulously abstracted from the hospital's electronic and paper-based maternal and neonatal medical records. This process was carried out by two trained research assistants who were blinded to the study's primary hypotheses to prevent observer bias. A standardized data abstraction form was utilized to ensure uniformity and completeness of the collected information.

All statistical analyses were conducted using IBM SPSS Statistics, Version 26.0. The analysis proceeded in two main stages. First, a descriptive and bivariate analysis was performed. Baseline characteristics of the

study population were summarized. The Chi-square test was used to examine the initial, unadjusted association between each independent variable and the case-control status. To ensure that potentially important variables were not prematurely discarded, any factor with a p-value less than 0.25 in this bivariate analysis was considered a candidate for the subsequent multivariate model. Second, a multivariate logistic regression analysis was conducted to identify the independent predictors of neonatal asphyxia while simultaneously controlling for the confounding effects of other variables in the model. Adjusted odds ratios (aOR) and their corresponding 95% confidence intervals (CI) were calculated to quantify the magnitude and precision of the association for each significant predictor. For all tests in the final model, a p-value of less than 0.05 was considered to indicate statistical significance.

3. Results and Discussion

Table 1 showed a comprehensive bivariate analysis of the baseline demographic, maternal, and neonatal characteristics of the study population, providing a foundational, unadjusted comparison between neonates who suffered from birth asphyxia (cases) and those who did not (controls). This table serves as the crucial first step in the analytical process, meticulously screening a wide array of potential risk factors to identify which variables demonstrate a statistically significant association with the outcome of interest within this specific Balinese hospital setting. It presents a stark and compelling preliminary narrative, painting a detailed portrait of the pregnancies and infants most vulnerable to this devastating condition before these factors are entered into a multivariate model to control for confounding effects. The data, derived from a study of 206 singleton neonates (103 cases and 103 controls) born in a single calendar year, are instrumental in building the evidence-based profile of high-risk pregnancies that the study aims to establish. The analysis begins with an examination of Maternal Age, a well-established factor in perinatal outcomes. The data reveals a highly significant association ($p<0.001$) between maternal age extremes and the incidence of neonatal asphyxia. In the control group, representing the general obstetric population of the hospital, a vast majority of mothers (89.3%) were within the optimal reproductive age range of 20-35 years. Conversely, in the case group, this figure dropped to 68.9%. The critical finding lies in the high-risk category (<20 or >35 years): nearly one-third of mothers of asphyxiated infants (31.1%) fell into this group, a proportion almost three times higher than that observed in the control group (10.7%). This strong unadjusted association underscores the "U-shaped" risk profile of maternal age. The study's discussion provides the pathophysiological context for this finding, explaining that adolescent mothers (<20 years) often face risks stemming from biological immaturity, such as potential cephalopelvic disproportion, and higher rates of nutritional deficiencies like anaemia. At the other end of the spectrum, advanced maternal age (>35 years) is associated with a decline in oocyte quality, uterine senescence, and a significantly higher prevalence of pre-existing medical conditions like chronic hypertension and diabetes, all of which can impair placental function and compromise fetal oxygenation. This initial finding from the bivariate analysis strongly suggests that pregnancies at the extremes of the reproductive age spectrum require heightened surveillance.

In contrast, Parity (the number of previous births) did not show a statistically significant association with neonatal asphyxia in this initial analysis, with a p-value of 0.094. While there was a slight trend showing that mothers in the case group were more likely to be in their first or fourth (or more) pregnancy (59.2%) compared to the control group (47.6%), this difference did not meet the threshold for statistical significance. This suggests that, in this study, when considered in isolation, parity may be less influential than other biological and health-related factors. The analysis then moves to critical maternal health indicators, beginning with Maternal Obesity. Here, the data reveals a statistically significant relationship

(p=0.003). While obesity was present in 15.5% of mothers in the control group, the prevalence of obesity was more than double in the case group, at 32.0%. This finding points to obesity as a powerful, independent stressor on the pregnancy. The study's discussion elaborates on the dual metabolic and mechanical pathways driving this risk. Metabolically, obesity is a chronic inflammatory state that negatively affects placental development and blood flow. Mechanically, it increases the likelihood of delivering a large baby (macrosomia), which can lead to difficult, prolonged, or obstructed labor, directly increasing the risk of fetal distress and asphyxia.

Even more striking is the association with Anaemia during Pregnancy, which demonstrated a very strong statistical significance (p<0.001). The disparity between the groups is dramatic: only 7.8% of mothers in the control group were anaemic, whereas this figure surged to 30.1% among mothers of infants with asphyxia. This more than threefold difference highlights maternal haematological status as a critical determinant of fetal well-being. The study provides a profound physiological explanation for this link, framing maternal anaemia as a "silent hypoxic insult". Anaemia directly reduces the oxygen-carrying capacity of the mother's blood. While the maternal cardiovascular system can compensate at rest, it may fail under the intense stress of labor, where uterine contractions transiently reduce placental blood flow. A fetus already existing in a state of chronic, low-grade hypoxia due to maternal anaemia has severely diminished physiological reserves and cannot tolerate the additional stress of labor, leading to rapid decompensation into acidosis and asphyxia. Hypertension in Pregnancy showed a trend towards significance (p=0.060). The prevalence of hypertension was more than double in the case group (13.6%) compared to the control group (5.8%). While this did not cross the p<0.05 threshold in this unadjusted analysis, it suggests a clinically relevant association that may be influenced by other factors. Hypertensive disorders in pregnancy are known to cause placental vasculopathy and insufficiency, directly impairing the transfer of oxygen and nutrients to the fetus. Regarding the intrapartum factors, Mode of Delivery presents a nuanced preliminary finding. With a p-value of 0.052, the association narrowly misses the threshold for statistical significance. However, the data shows an interesting distribution: spontaneous vaginal deliveries were more common in the case group (20.4%) than the control group (9.7%), while operative deliveries were slightly more common in the control group (90.3%) than the case group (79.6%). This counter-intuitive finding, even in its non-significant bivariate form, hints at the "protective paradox" that becomes a central theme of the study. It suggests that operative delivery is not a random event but a deliberate clinical response to high-risk situations. This initial look provides the first clue that timely intervention may be successfully rescuing at-risk fetuses, a hypothesis that is later confirmed in the multivariate analysis.

Premature Rupture of Membranes (PROM) was found to be a significant predictor of asphyxia (p=0.002). The incidence of PROM in the case group (32.0%) was substantially higher than in the control group (18.4%). The primary mechanism for this risk, as explained in the study, is the pathway of intrauterine infection. A breach in the amniotic sac allows vaginal bacteria to ascend, potentially causing chorioamnionitis, a potent maternal and fetal inflammatory response that is directly neurotoxic and impairs placental gas exchange, making the fetus highly vulnerable to hypoxic injury during labor. The final section of the table reveals the most overwhelmingly dominant risk factors, which are intrinsically linked: Prematurity (<37 weeks) and Low Birth Weight (<2500g). Both factors show an extremely high statistical significance (p<0.001). The difference between the groups is profound. For prematurity, an astounding 57.3% of asphyxiated infants were born preterm, compared to a mere 3.9% in the control group. Similarly, for low birth weight, 58.3% of cases were LBW, while only 3.9% of controls were. This massive disparity underscores that the premature and low birth weight infant is fundamentally and

physiologically ill-equipped for extrauterine life. The study's discussion provides a detailed explanation for this vulnerability, citing a constellation of factors: immature lungs lacking surfactant, leading to respiratory collapse; a fragile cerebral vasculature prone to bleeding (intraventricular hemorrhage); an immature brainstem with poor respiratory drive; and severely limited metabolic reserves (glycogen and fat) coupled with an inability to maintain body temperature. This combination of vulnerabilities means the preterm neonate has a drastically reduced physiological reserve, making them unable to tolerate even minor perinatal stresses that a term infant would easily overcome. Finally, Meconium Aspiration also showed a significant association (p=0.002). Critically, while 8.7% of the cases had meconium aspiration, not a single infant in the control group did. The passage of meconium in utero is itself a sign of fetal distress and hypoxia, and its aspiration can cause severe respiratory distress through airway obstruction and chemical pneumonitis, thus directly contributing to or exacerbating the asphyxial state. Figure 1 provides a powerful narrative through its unadjusted data. It clearly identifies a profile of vulnerability long before the final multivariate analysis. The mothers of asphyxiated infants in this Balinese study were significantly more likely to be at the extremes of reproductive age, obese, and, most critically, anaemic. The infants themselves were overwhelmingly more likely to be born prematurely and with low birth weight. Intrapartum complications like PROM and the presence of meconium were also strong indicators of risk.

Table 2 showed the culmination of the study's statistical analysis, presenting the results of a multivariate logistic regression model designed to isolate the most powerful, independent predictors of neonatal asphyxia. Whereas the bivariate analysis in Figure 1 provided a preliminary look at potential associations, this multivariate model represents a far more sophisticated and definitive step. By simultaneously considering all significant variables from the initial analysis, this model mathematically adjusts for the confounding effects that these factors have on one another, thereby revealing the true, independent contribution of each variable to the risk of asphyxia. The table elegantly distills a complex web of interrelated factors into a clear hierarchy of risk, providing clinicians and public health officials in Bali and similar settings with a precise, evidence-based roadmap of the conditions that most potently endanger a newborn's successful transition to extrauterine life. It moves beyond simple correlation to establish a statistically robust profile of the high-risk pregnancy, a critical achievement for the development of targeted preventive strategies. The most profound and clinically significant finding presented in the table is the overwhelming impact of Prematurity. The adjusted odds ratio (aOR) for this variable is a staggering 10.325, with a 95% confidence interval (CI) ranging from 4.496 to 23.714. The statistical significance is unequivocal ($p<0.001$). The aOR of 10.325 can be interpreted to mean that, even after accounting for all other factors in the model—such as maternal age, obesity, anaemia, and mode of delivery—a neonate born before 37 completed weeks of gestation is more than ten times as likely to suffer from birth asphyxia compared to a neonate born at term. The sheer magnitude of this odds ratio establishes prematurity not merely as a risk factor, but as the single most dominant determinant of neonatal asphyxia in this study population. The confidence interval, while wide, does not cross 1.0, reinforcing the certainty of this strong association. This finding is deeply rooted in the fundamental principles of fetal and neonatal physiology. The study's discussion provides the biological narrative behind these statistics, explaining that the preterm infant is a study in systemic immaturity. Their lungs are structurally and functionally underdeveloped, often profoundly deficient in surfactant, the substance essential for preventing alveolar collapse and enabling efficient gas exchange. This leads to respiratory distress syndrome, a state of progressive atelectasis, hypoxia, and hypercapnia—the very definition of asphyxia.

Table 1. Baseline characteristics of the study population.

Bivariate Analysis of Factors between Asphyxia Cases and Controls (N=206)

CHARACTERISTIC	TOTAL COHORT (N=206) N (%)	CASES (N=103) N (%)	CONTROLS (N=103) N (%)	BIVARIATE P-VALUE
Maternal Age (years)				**<0.001**
20-35	163 (79.1)	71 (68.9)	92 (89.3)	
<20 or >35	43 (20.9)	32 (31.1)	11 (10.7)	
Parity				**0.094**
2-3	96 (46.6)	42 (40.8)	54 (52.4)	
1 or ≥4	110 (53.4)	61 (59.2)	49 (47.6)	
Maternal Obesity				**0.003**
No	157 (76.2)	70 (68.0)	87 (84.5)	
Yes	49 (23.8)	33 (32.0)	16 (15.5)	
Anaemia during Pregnancy				**<0.001**
No	167 (81.1)	72 (69.9)	95 (92.2)	
Yes	39 (18.9)	31 (30.1)	8 (7.8)	
Hypertension in Pregnancy				**0.060**
No	186 (90.3)	89 (86.4)	97 (94.2)	
Yes	20 (9.7)	14 (13.6)	6 (5.8)	
Mode of Delivery				**0.052**
Spontaneous Vaginal	31 (15.0)	21 (20.4)	10 (9.7)	
Operative (CS/Assisted)	175 (85.0)	82 (79.6)	93 (90.3)	
PROM				**0.002**
No	154 (74.8)	70 (68.0)	84 (81.6)	
Yes	52 (25.2)	33 (32.0)	19 (18.4)	
Prematurity (<37 weeks)				**<0.001**
No (Term)	143 (69.4)	44 (42.7)	99 (96.1)	
Yes (Preterm)	63 (30.6)	59 (57.3)	4 (3.9)	
Low Birth Weight (<2500g)				**<0.001**
No	142 (68.9)	43 (41.7)	99 (96.1)	
Yes	64 (31.1)	60 (58.3)	4 (3.9)	
Meconium Aspiration				**0.002**
No	197 (95.6)	94 (91.3)	103 (100)	
Yes	9 (4.4)	9 (8.7)	0 (0)	

Notes:

- Values are presented as n (%), representing the count and percentage within that column's group.
- **Bivariate p-value:** Calculated using the Chi-square test to assess the association between each characteristic and the case/control status. A p-value < 0.05 (highlighted in red) indicates a statistically significant difference between the groups.

Furthermore, the preterm brain possesses an exquisitely fragile germinal matrix and poor cerebrovascular autoregulation, making it highly susceptible to both hypoxic-ischemic injury and intraventricular hemorrhage. Compounding this is the infant's limited metabolic reserve and inability to

maintain thermal stability, creating a vicious cycle where hypothermia and hypoglycemia exacerbate the underlying asphyxial insult. This statistical finding, therefore, is the numerical expression of a state of profound biological vulnerability. The second most powerful independent predictor identified was Maternal Anaemia, with an aOR of 6.556 (95% CI: 2.362–18.195; p<0.001). This indicates that a fetus gestating in an anaemic mother has over six and a half times the odds of being born with asphyxia compared to a fetus of a non-anaemic mother, independent of all other measured variables. This is a critical public health finding, as maternal anaemia is a common and, crucially, modifiable condition. The study explains this powerful link through the lens of oxygen transport physiology, framing it as a "silent hypoxic insult." Maternal anaemia fundamentally reduces the oxygen-carrying capacity of the blood delivered to the placenta. While maternal compensatory mechanisms, such as increased cardiac output, may suffice during the relative calm of gestation, they are often overwhelmed by the immense physiological stress of labor. During contractions, uterine blood flow is temporarily impeded, causing transient dips in fetal oxygenation. For a fetus whose baseline oxygen supply is already chronically compromised by maternal anaemia, this intermittent stress can be catastrophic. Their physiological reserves are eroded, and they are unable to mount an adequate response, leading to a rapid decompensation into profound metabolic acidosis and asphyxia. The strength of this association highlights that the antenatal period is a critical window of opportunity for intervention; by identifying and treating maternal anaemia, clinicians can directly and significantly mitigate a major risk factor for one of the most severe neonatal outcomes. The analysis further confirms the well-documented U-shaped risk curve associated with Maternal Age. With an aOR of 3.934 (95% CI: 1.500–10.315; p=0.005), the model shows that mothers at the extremes of the reproductive age spectrum (<20 or >35 years) have nearly four times the odds of having an asphyxiated infant compared to mothers in the optimal age range of 20-35 years. The study elucidates the distinct pathophysiological pathways at play. In adolescent mothers, the risk is often linked to biological immaturity, leading to higher rates of cephalopelvic disproportion and obstructed labor, as well as a greater likelihood of nutritional deficiencies, including the aforementioned anaemia. For mothers of advanced age, the risk stems from the cumulative effects of aging on the reproductive system, including declining oocyte quality and uterine senescence, and, most importantly, a much higher prevalence of co-morbid medical conditions such as chronic hypertension and diabetes, which can impair placental function.

Intrapartum and pregnancy-related complications also emerged as significant independent predictors. Premature Rupture of Membranes (PROM) carried an aOR of 3.164 (95% CI: 1.297–7.720; p=0.011), indicating that the odds of asphyxia are more than tripled when the amniotic sac ruptures well before the onset of labor. The primary mediating pathway is intrauterine infection. The breach of this sterile barrier allows for ascending infection (chorioamnionitis), which triggers a potent fetal inflammatory response syndrome. This systemic inflammation is not only directly neurotoxic but also impairs placental gas exchange, rendering the fetus highly susceptible to hypoxic injury during labor contractions. Similarly, Maternal Obesity was identified as a significant risk factor, with an aOR of 2.919 (95% CI: 1.198–7.112; p=0.018). This finding reveals that, independent of other factors, maternal obesity nearly triples the odds of neonatal asphyxia. The risk is driven by both metabolic and mechanical forces. Metabolically, obesity creates a chronic inflammatory and insulin-resistant state that adversely affects placental development and function. Mechanically, it increases the risk of macrosomia, shoulder dystocia, and prolonged, obstructed labor, all of which are direct causes of fetal distress. Perhaps the most intellectually intriguing and epidemiologically complex finding presented in Figure 2 is the strong apparent protective effect of the Mode of Delivery. With an aOR of 0.218 (95% CI: 0.080–0.596; p=0.003), the data suggests

that infants delivered via operative means (Caesarean section or instrumental assistance) were approximately 78% less likely to be diagnosed with asphyxia compared to those delivered via spontaneous vaginal birth. Interpreted literally and without clinical context, this would lead to the dangerously flawed conclusion that surgery is inherently safer than spontaneous birth. However, the study correctly identifies this as a classic example of "confounding by indication," which it terms the "Protective Paradox." In clinical reality, the decision to perform an operative delivery is not random; it is a deliberate medical intervention made precisely because a threat to fetal well-being has been identified. Obstetricians intervene with a Caesarean section in response to non-reassuring fetal heart rate patterns, arrest of labor, or other signs indicating that the fetus is already in distress or is failing to tolerate the stress of labor. Therefore, the group of infants delivered operatively is, by its very nature, enriched with high-risk pregnancies where an adverse outcome was likely imminent. The fact that this high-risk group ultimately had a *lower* incidence of diagnosed asphyxia is a testament to the *success* of the intervention. The operative delivery acted as a rescue mission, effectively truncating the injurious process before it could evolve into the full-blown clinical syndrome of severe asphyxia. This "protective" odds ratio is not a measure of the inherent safety of surgery, but rather a powerful statistical marker of a well-functioning obstetric service that is capable of vigilant intrapartum monitoring and performing timely, decisive, and life-saving interventions. It highlights that the availability of emergency obstetric care is critical to preventing the most severe outcomes in high-risk deliveries.

Table 2. Multivariate logistic regression analysis.

Identifying the Independent Predictors of Neonatal Asphyxia

VARIABLE	COMPARISON GROUP	ADJUSTED ODDS RATIO (AOR)	95% CONFIDENCE INTERVAL (CI)	P-VALUE
Prematurity Major Risk Factor	Preterm (<37 weeks) vs. Term	10.325	4.496 – 23.714	<0.001
Maternal Anaemia Major Risk Factor	Yes vs. No	6.556	2.362 – 18.195	<0.001
Maternal Age Significant Risk Factor	<20 or >35 years vs. 20-35 years	3.934	1.500 – 10.315	0.005
PROM Significant Risk Factor	Yes vs. No	3.164	1.297 – 7.720	0.011
Maternal Obesity Significant Risk Factor	Yes vs. No	2.919	1.198 – 7.112	0.018
Mode of Delivery Protective Paradox*	Operative vs. Spontaneous Vaginal	0.218	0.080 – 0.596	0.003

Notes:

- **aOR (Adjusted Odds Ratio):** An aOR > 1 indicates an increased risk, while an aOR < 1 indicates a protective effect.
- **p-value:** A p-value < 0.05 is considered statistically significant.
- ***The Protective Paradox:** The strong protective association of operative delivery (aOR = 0.218) is an example of 'confounding by indication'. This means that operative delivery was likely performed in response to fetal distress, and the timely intervention successfully prevented a diagnosis of asphyxia, rather than being inherently protective in all cases. It highlights effective obstetric care.

The most potent and unequivocal finding from our analysis is the profound impact of prematurity. An odds ratio exceeding 10 demonstrates that being born preterm is not merely a risk factor; it is the single most dominant determinant of neonatal asphyxia in our study. This finding is deeply rooted in the fundamental biology of fetal development. The preterm neonate is a physiologically fragile being, ill-equipped for the rigors

of extrauterine life.[9] This vulnerability is multifaceted. The lungs are among the last organs to fully mature. The preterm lung is often deficient in surfactant, a complex lipoprotein that reduces alveolar surface tension and prevents end-expiratory collapse.[10] Without adequate surfactant, the infant must exert tremendous effort with each breath, leading to rapid respiratory fatigue, progressive atelectasis, ventilation-perfusion mismatch, and ensuing hypoxia and hypercapnia—the very definition of asphyxia. Furthermore, the central respiratory drive, controlled by the brainstem, is itself immature, predisposing the infant to apnea and periodic breathing, further compromising gas exchange. The cerebral vasculature of the preterm infant is exceptionally fragile.[11] The germinal matrix, a highly cellular and vascularized region of the developing brain, is prone to rupture under the hemodynamic stress of hypoxic-ischemic events. This leads to intraventricular hemorrhage (IVH), a devastating complication that can exacerbate the primary brain injury from asphyxia. The immature brain also lacks the robust autoregulatory capacity of the term brain, meaning it is less able to maintain stable cerebral blood flow during fluctuations in systemic blood pressure, making it more susceptible to both ischemic and reperfusion injury. The preterm infant has markedly limited glycogen and fat stores, depriving them of the necessary energy reserves to mount a sustained response to stress.[11] The hypoxic stress of asphyxia rapidly depletes these meager stores, leading to hypoglycemia, which can cause independent brain injury. Concurrently, their large surface area to body mass ratio and thin skin lead to rapid heat loss and hypothermia. Hypothermia increases metabolic demand and oxygen consumption, creating a vicious cycle that worsens the underlying asphyxial state.[12] This constellation of vulnerabilities explains why prematurity so dramatically increases the risk of asphyxia. The preterm neonate enters the world with a severely diminished physiological reserve, unable to tolerate even minor perinatal insults that a term infant would readily overcome.

Our study identified maternal anaemia as the second most powerful predictor of neonatal asphyxia. An odds ratio of 6.56 signifies a profound link between maternal hemoglobin concentration and fetal oxygenation. This relationship can be understood through the principles of oxygen transport physiology.[13] The total amount of oxygen delivered to the uterus and, by extension, the placenta, is a direct product of uterine blood flow and the oxygen content of the arterial blood (CaO_2). The CaO_2 is, in turn, critically dependent on the mother's hemoglobin concentration. When a mother is anemic, her blood has a reduced oxygen-carrying capacity. To compensate and maintain adequate oxygen delivery to her own tissues and the fetus, her cardiovascular system must increase cardiac output. While this may be sufficient at rest, the intense physiological stress and intermittent uterine contractions of labor can overwhelm this compensatory mechanism. Each contraction temporarily reduces blood flow to the placenta, causing a transient drop in fetal oxygen levels. A healthy fetus with a well-oxygenated baseline tolerates these dips easily.[14] However, a fetus whose baseline oxygenation is already compromised due to maternal anaemia has a much smaller margin of safety. This state of chronic, low-grade intrauterine hypoxia erodes the fetus's physiological reserves. When the acute stress of labor is superimposed on this chronic hypoxic state, the fetus is unable to mount an adequate response, leading to a rapid decompensation into profound acidemia and asphyxia.[15] The finding highlights that the uterine environment is not isolated; maternal health, specifically her hematological status, directly dictates the fetal capacity to survive the perinatal transition.

The U-shaped relationship between maternal age and adverse perinatal outcomes is a well-established phenomenon, and our findings confirm its relevance to asphyxia risk. The nearly fourfold increase in odds for mothers younger than 20 or older than 35 reflects distinct pathophysiological pathways. Adolescent Pregnancy (<20 years), The increased risk in very young mothers is often multifactorial. From a

biological standpoint, these mothers may not have achieved full physical and pelvic maturity, leading to a higher incidence of cephalopelvic disproportion and obstructed labor—a direct cause of fetal distress.[16] Nutritionally, adolescents are at higher risk for deficiencies, including iron-deficiency anaemia, which, as established above, is a major independent risk factor for asphyxia. Furthermore, adolescent pregnancies are associated with a higher rate of pre-eclampsia, a condition characterized by placental vasculopathy and insufficiency. Advanced Maternal Age (>35 years), In older mothers, the increased risk stems from the cumulative effects of aging on the reproductive system and overall health. Oocyte quality declines with age, leading to a higher risk of chromosomal abnormalities and early placental dysfunction. The aging uterus (uterine senescence) may have less efficient blood flow and contractility, predisposing to labor dystocia. Most importantly, advanced maternal age is strongly associated with a higher prevalence of pre-existing medical conditions such as chronic hypertension, pre-gestational diabetes, and obesity. These conditions create a hostile intrauterine environment, often characterized by endothelial dysfunction and vascular damage, which directly impairs placental function and fetal oxygenation.[17]

Our study identified two other key factors that increase the risk of asphyxia during the intrapartum period: PROM and maternal obesity. The threefold increase in risk associated with PROM is primarily mediated through the pathway of intrauterine infection. When the protective barrier of the amniotic sac is breached, vaginal flora can ascend into the uterine cavity, leading to chorioamnionitis.[17] This infection triggers a potent maternal and fetal inflammatory response, characterized by the release of pro-inflammatory cytokines such as Tumor Necrosis Factor-alpha (TNF-α) and Interleukin-6 (IL-6). These cytokines are not only directly neurotoxic to the fetal brain but also can induce uterine contractions and preterm labor. The systemic fetal inflammatory response increases metabolic demand and can cause placental vasculitis, further impairing gas exchange and rendering the fetus highly susceptible to hypoxic injury during labor. The nearly threefold risk associated with maternal obesity is driven by both metabolic and mechanical factors. Metabolically, obesity is a state of chronic, low-grade inflammation and insulin resistance. These conditions are known to adversely affect placental development and function, leading to a state of relative placental insufficiency.[18] Altered levels of adipokines, such as increased leptin and decreased adiponectin, contribute to endothelial dysfunction and reduced placental blood flow. Mechanically, obesity is associated with an increased risk of macrosomia, which can lead to shoulder dystocia and prolonged, obstructed labor. The increased adipose tissue can also make external fetal monitoring less reliable, potentially delaying the detection of fetal distress. The combination of a metabolically inefficient placenta and a mechanically challenging labor creates a perfect storm for the development of neonatal asphyxia.

Perhaps the most statistically striking, yet epidemiologically complex, finding is the strong apparent protective effect of operative delivery. An odds ratio of 0.22 suggests that infants delivered by Caesarean section or instrumental assistance were 78% less likely to be diagnosed with asphyxia. To interpret this finding literally—that surgery is inherently safer than spontaneous birth—would be a grave clinical and scientific error. This result is a classic example of confounding by indication, a common pitfall in observational research. In clinical practice, the decision to perform an operative delivery is not made at random. It is a deliberate response to a perceived or existing threat to maternal or fetal well-being. Obstetricians intervene with a Caesarean section precisely when they detect non-reassuring fetal heart rate patterns, arrest of labor, or other signs that indicate the fetus is already in distress or is failing to tolerate labor.[18] In this context, the operative delivery is not a preventative measure against a hypothetical risk; it is the treatment for an impending or evolving asphyxial event. Therefore, the group of

infants delivered operatively in our study is enriched with high-risk pregnancies where an adverse outcome was likely imminent. The control group, delivered spontaneously, consists largely of low-risk pregnancies that proceeded without complication. The fact that the operatively delivered babies had a lower incidence of asphyxia in our final diagnosis suggests that the intervention was not only necessary but also successful.[18] It successfully truncated the injurious process, rescuing the fetus from what might have been a much worse outcome had labor been allowed to continue. This "protective paradox" does not suggest that we should perform more Caesarean sections. Rather, it highlights the critical importance of vigilant intrapartum monitoring and the availability of timely, decisive emergency obstetric care. It is a marker of a well-functioning obstetric service that can recognize distress and act effectively to prevent the full-blown syndrome of severe neonatal asphyxia.

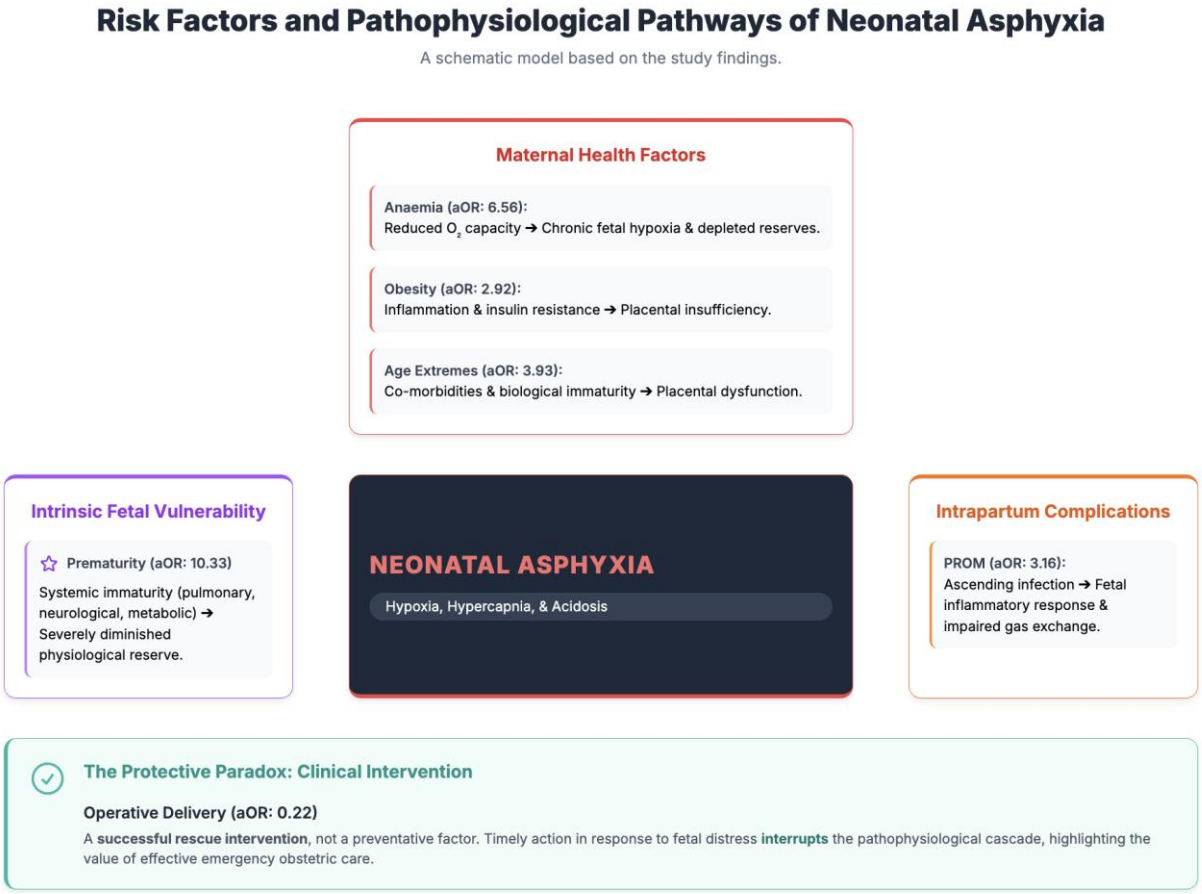

Figure 1. Risk factors and pathophysiological pathways of neonatal asphyxia.

Figure 1 showed a masterful schematic model that synthesizes the complex, multifactorial etiology of neonatal asphyxia, visually articulating the key findings of the study in a clear and compelling narrative. It moves beyond a simple list of risk factors to illustrate a dynamic and interconnected web of causality, where maternal health, intrapartum events, and intrinsic fetal characteristics converge upon a final, devastating common pathway. The diagram serves as a powerful conceptual framework, translating the statistical outputs of the multivariate analysis—specifically the adjusted odds ratios (aORs)—into a coherent story of physiological compromise. At its core, the figure posits that neonatal

asphyxia is not a singular event, but rather the culmination of a cascade of insults that begin long before the first moments of labor, ultimately defining the neonate's capacity to navigate the perilous transition from intrauterine to extrauterine life. The model is logically structured around three primary domains of risk that feed into the central outcome of neonatal asphyxia, which is defined by its core pathophysiological state: hypoxia, hypercapnia, and acidosis. The first domain, elegantly highlighted in red, is Maternal Health Factors, emphasizing that the mother's well-being is the foundational environment for the developing fetus. The schematic identifies three critical maternal conditions. The most powerful of these is Maternal Anaemia (aOR: 6.56), indicating a more than six-fold increase in the risk of asphyxia. The diagram succinctly illustrates its mechanism: a reduced oxygen-carrying capacity in the mother's blood leads to a state of chronic fetal hypoxia, which systematically depletes the fetus's physiological reserves. This creates a highly vulnerable state where the fetus, already living on a diminished oxygen budget, cannot withstand the additional, intermittent hypoxic stress of normal labor contractions, leading to rapid decompensation. Following this is Maternal Obesity (aOR: 2.92), nearly tripling the risk. Its pathway is described as a combination of inflammation and insulin resistance, which are known to cause placental insufficiency. This means the placenta itself, the vital interface for all nutrient and gas exchange, functions sub-optimally, effectively throttling the supply line to the fetus. The third factor is Age Extremes (<20 or >35 years), which carries an almost four-fold increase in risk (aOR: 3.93). The model attributes this to the dual challenges of co-morbidities (more common in older mothers) and biological immaturity (in adolescent mothers), both of which converge on the common problem of placental dysfunction. Together, these maternal factors paint a clear picture: a compromised maternal state directly translates to a compromised intrauterine environment, setting the stage for perinatal complications. Branching from the right, the orange-coded box represents Intrapartum Complications, focusing on events that unfold during the labor and delivery process itself. The key factor identified here is Premature Rupture of Membranes (PROM), which more than triples the risk of asphyxia (aOR: 3.16). The schematic clearly traces its pathological sequence: the breach of the protective amniotic sac allows for ascending infection from the maternal genital tract, leading to chorioamnionitis. This triggers a potent fetal inflammatory response syndrome (FIRS). This systemic inflammation is not a benign reaction; it is directly neurotoxic and can cause placental vasculitis, severely impairing gas exchange at the most critical time, rendering the fetus acutely susceptible to hypoxic injury. On the left, the purple-coded domain of Intrinsic Fetal Vulnerability highlights the characteristics of the fetus itself. This section is rightfully dominated by the single most powerful predictor identified in the entire study: Prematurity (aOR: 10.33). The star icon next to this factor appropriately denotes its overwhelming significance. A more than ten-fold increase in risk signifies that being born preterm is the most critical determinant of neonatal asphyxia. The diagram brilliantly summarizes the reason for this immense vulnerability as a state of global "systemic immaturity," affecting the pulmonary, neurological, and metabolic systems. This leads to what the model aptly calls a "severely diminished physiological reserve." The preterm infant's lungs lack surfactant, leading to respiratory collapse. Their brain's blood vessels are fragile and prone to hemorrhage, and their control of breathing is unstable. They lack the glycogen and fat stores needed to fuel a response to stress and cannot maintain their own body temperature.[19] This constellation of deficits means the preterm neonate is fundamentally unequipped for life outside the womb and cannot tolerate even minor perinatal insults. All three of these domains—maternal, intrapartum, and fetal—are shown to converge on the central, dark-colored box representing the ultimate outcome: Neonatal Asphyxia. This is the endpoint where the various upstream failures manifest as a critical failure of

physiology, defined by its core triad of hypoxia (insufficient oxygen), hypercapnia (excess carbon dioxide), and acidosis (a dangerous drop in blood pH). This central placement in the diagram visually reinforces that asphyxia is the final common pathway for a multitude of preceding risk factors. Finally, the diagram presents its most nuanced and intellectually sophisticated concept in the green-coded box at the bottom: The Protective Paradox: Clinical Intervention. This section addresses the counter-intuitive finding that Operative Delivery was associated with a dramatically reduced risk of asphyxia (aOR: 0.22). The schematic is careful to explain that this does not imply that surgery is inherently safer. Instead, it frames it as a "successful rescue intervention." This is a crucial distinction. The decision to perform a caesarean section or use instrumental assistance is not made randomly; it is made precisely because a problem, such as fetal distress, has been identified.[20] Therefore, the low odds ratio is a statistical testament to the effectiveness of the local obstetric care. It shows that when faced with an impending asphyxial event, the clinical team's timely action successfully interrupts the pathophysiological cascade, rescuing the fetus from a worse outcome.

4. Conclusion

This detailed analysis of neonatal asphyxia in a Balinese hospital setting confirms a cascade of risk that begins long before birth and culminates in the critical moments of labor and delivery. Our findings establish a clear hierarchy of risk, with prematurity standing as the single most powerful predictor, magnifying the odds of asphyxia by a factor of ten. This is closely followed by critical, and modifiable, aspects of maternal health, particularly anaemia during pregnancy and maternal obesity, which fundamentally compromise the fetal environment and its ability to withstand stress. Maternal age extremes and the intrapartum complication of PROM further compound this risk. The compelling "protective paradox" of operative delivery serves as a crucial reminder of the importance of clinical context in interpreting statistical data. It speaks not to the inherent safety of surgery, but to the life-saving value of skilled obstetric surveillance and timely intervention. Ultimately, our findings converge on a singular, powerful message: the prevention of neonatal asphyxia is inextricably linked to the promotion of maternal health. The battle against this devastating neonatal outcome is won not primarily in the delivery room with a resuscitation bag, but in the antenatal clinic and through public health initiatives. Strategies must be directed upstream, focusing on the prevention of preterm birth and the meticulous, aggressive management of maternal anaemia and obesity. By investing in the health of the mother, we make the most profound and lasting investment in the survival and well-being of the child.

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