e-ISSN: 2807-6257

Open Access Indonesian Journal of Medical Reviews

[OAIJMR]

https://hmpublisher.com/index.php/oaijmr

Maternal Hypertension as a Dominant Predictor of Neonatal Respiratory Distress Syndrome: A Cross-Sectional Study in a Regional Indonesian Hospital

Putu Ayu Prita Nandari Dewi[1*], Putu Verita Wulandari[2]

[1]General Practitioner, Tabanan General Hospital, Tabanan, Indonesia

[2]Department of Pediatrics, Tabanan General Hospital, Tabanan, Indonesia

ARTICLE INFO

Keywords:

Cross-sectional study

Maternal hypertension

Neonatal respiratory distress syndrome

Neonates

Risk factors

***Corresponding author:**

Putu Ayu Prita Nandari Dewi

E-mail address:

pritamilke@gmail.com

All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/oaijmr.v5i4.756

A B S T R A C T

Neonatal respiratory distress syndrome (RDS) remains a significant cause of morbidity and mortality in newborns, particularly in developing countries. While prematurity is a primary risk factor, other maternal and neonatal factors, including maternal hypertension, contribute to its incidence. This study aimed to identify the risk factors for RDS in neonates treated at a regional hospital in Tabanan, Indonesia, with a particular focus on the role of maternal hypertension. A cross-sectional study was conducted using secondary data from medical records of neonates treated at Tabanan Regional General Hospital (RSUD) from January 2023 to December 2024. The study included neonates diagnosed with RDS and a control group without RDS. Data on maternal factors (hypertension, diabetes mellitus) and neonatal factors (gestational age, birth weight, gender, mode of delivery) were collected. Bivariate analysis using Chi-square and Fisher's exact tests was performed to determine associations, with a p-value <0.05 considered statistically significant. A total of 220 neonates were included in this investigation, with 114 (51.8%) diagnosed with RDS and 106 (48.2%) without RDS. Maternal hypertension was found to be significantly associated with an increased risk of neonatal RDS (p=0.021; OR=1.5, 95% CI 1.1-2.0). No significant associations were found between RDS and gestational age (p=0.056), birth weight (p=0.839), gender (p=0.689), mode of delivery (p=0.072), or maternal diabetes mellitus (p=0.248) in this study. In conclusion, maternal hypertension emerged as a dominant predictor of neonatal RDS in this regional Indonesian hospital setting. This finding underscores the importance of vigilant antenatal care and management of hypertensive disorders during pregnancy to potentially mitigate the risk of RDS in newborns.

1. Introduction

Neonatal respiratory distress syndrome (RDS), primarily caused by a deficiency of pulmonary surfactant, is a critical condition affecting newborns and a leading cause of respiratory morbidity and mortality globally, particularly in premature infants. The syndrome typically manifests shortly after birth with signs of respiratory difficulty, including tachypnea, grunting, nasal flaring, and chest retractions. While RDS is classically associated with prematurity due to immature lung development and inadequate surfactant production, its occurrence in term and late preterm neonates, though less frequent, highlights a complex interplay of various contributing factors. The global burden of RDS is substantial. In many parts of Asia and the Americas, RDS is reported as the leading cause of neonatal respiratory failure. Data from the Indonesian Ministry of Health in 2023 indicated that respiratory and cardiovascular disorders were the primary causes of neonatal mortality. Studies within Indonesia have shown varying prevalence rates of RDS in different hospital settings, indicating a persistent challenge. For instance, one investigation at RSUD Buleleng in 2020

found that 68.8% of neonates in the study experienced RDS. These figures underscore the urgent need for continued research to understand local risk factor profiles and improve preventative and management strategies.[1-5]

Numerous risk factors for RDS have been identified in the literature. Prematurity and low birth weight (LBW) are the most consistently reported predictors, with the incidence of RDS inversely proportional to gestational age and birth weight. Other established risk factors include male gender, Caesarean section (CS) delivery (especially elective CS before 39 weeks of gestation), maternal diabetes mellitus (DM), and perinatal asphyxia. Maternal diabetes can impair fetal lung maturation and surfactant production due to fetal hyperglycemia and hyperinsulinism. Caesarean delivery, particularly without labor, may affect neonatal respiratory adaptation by interfering with the normal clearance of fetal lung fluid and the hormonal surges associated with labor that promote lung maturation. Male infants have been observed to have a higher risk, potentially due to slower lung maturation influenced by androgens. Maternal hypertensive disorders of pregnancy (HDP), including chronic hypertension, gestational hypertension, and preeclampsia/eclampsia, represent another significant group of maternal conditions that can adversely affect neonatal outcomes. The pathophysiological link between maternal hypertension and neonatal RDS is thought to involve placental insufficiency, leading to chronic fetal hypoxia and potential impairment of fetal lung development and surfactant synthesis. However, some studies have reported varied findings, with some suggesting HDP might even be associated with a decreased risk of RDS in certain preterm subgroups, possibly due to chronic stress accelerating lung maturation. This highlights the complexity and the need for context-specific research.[6-8]

In Indonesia, while national data point to the significance of respiratory disorders, detailed studies on RDS risk factors from specific regional hospitals, particularly examining the impact of maternal hypertension alongside other factors, remain limited. Understanding these local determinants is crucial for tailoring effective antenatal surveillance, perinatal management, and neonatal care strategies. The current investigation was conducted at Tabanan Regional General Hospital (RSUD Tabanan), a secondary referral hospital in Bali, Indonesia, serving a diverse obstetric population. This study provides current, localized data on risk factors for RDS from a regional hospital in Indonesia, a setting where such specific research is often scarce. While global literature extensively covers RDS risk factors, understanding their prevalence and impact within specific healthcare contexts like RSUD Tabanan is vital for targeted interventions. The particular focus on maternal hypertension as a potential dominant predictor in this investigation, and the assessment of its role relative to other known risk factors, contributes valuable regional evidence. Furthermore, this study investigates these factors in a recent period (2023-2024), offering an up-to-date perspective.[9,10] The primary aim of this study was to identify and analyze the maternal and neonatal risk factors associated with the occurrence of respiratory distress syndrome in neonates treated at RSUD Tabanan between January 2023 and December 2024, with a specific investigation into the predictive role of maternal hypertension.

2. Methods

This was an analytical observational study employing a cross-sectional design. The research was conducted at the Neonatal Intensive Care Unit (NICU) and pediatric wards of Tabanan Regional General Hospital (RSUD Tabanan), Bali, Indonesia. RSUD Tabanan is a public secondary referral hospital providing care for a significant number of births in the region. Data were collected retrospectively from existing medical records. The study encompassed neonates admitted and treated at RSUD Tabanan over a two-year period, from January 1st, 2023, to December 31st, 2024. The target population included all neonates treated at RSUD Tabanan during the study period. The accessible population comprised all

neonates diagnosed with respiratory distress syndrome (cases) and neonates without RDS (controls) who were treated at RSUD Tabanan during the specified timeframe. A total sampling technique was intended for neonates meeting the inclusion criteria within the study period. The final sample for this investigation consisted of 220 neonates, comprising 114 cases with RDS and 106 controls without RDS. Inclusion Criteria: All neonates diagnosed with respiratory distress syndrome who were treated at RSUD Tabanan with complete medical record data from January 1st, 2023, to December 31st, 2024, were eligible for inclusion. For the control group, neonates without RDS treated during the same period with complete medical records were included. Exclusion Criteria: Neonates with incomplete medical records or those with major congenital anomalies or other significant congenital disorders that could independently cause respiratory distress were excluded from the study.

The dependent variable was the occurrence of Neonatal Respiratory Distress Syndrome. The independent variables included maternal and neonatal factors. Neonatal Respiratory Distress Syndrome (RDS): Defined as the presence of clinical signs of respiratory distress (tachypnea >60 breaths/minute, grunting, nasal flaring, intercostal/subcostal/suprasternal retractions, cyanosis) appearing within the first few hours after birth, typically requiring respiratory support, and/or confirmed by characteristic radiological findings (diffuse reticulogranular pattern with air bronchograms) if available, as documented in the medical record. This was a nominal variable (Yes/No). Maternal Hypertension: Defined as a documented history of maternal systolic blood pressure (SBP) ≥140 mmHg and/or diastolic blood pressure (DBP) ≥90 mmHg during pregnancy or delivery, as recorded in the maternal or neonatal medical records. This was a nominal variable (Yes/No). Maternal Diabetes Mellitus (DM): Defined as a documented history of pre-gestational or gestational diabetes mellitus in the mother, as recorded in the medical records. This was a nominal variable (Yes/No). Gestational Age: The period calculated from the first day of the mother's last menstrual period (LMP) or early obstetric ultrasound to the time of birth, recorded in weeks. For analysis, this was categorized as Preterm (<37 weeks) and Term (≥37 weeks). Birth Weight: The weight of the neonate measured within the first hour after birth, recorded in grams. For analysis, this was categorized as Low Birth Weight (LBW) (<2500 grams) and Normal Birth Weight (NBW) (≥2500 grams). Gender: The biological gender of the neonate (Male/Female) as recorded in the medical record. This was a nominal variable. Mode of Delivery: The method by which the neonate was born, categorized as Vaginal Delivery (Normal) or Caesarean Section (SC). This was a nominal variable.

Data were collected retrospectively by reviewing and extracting information from the medical records of eligible neonates and their mothers. A standardized data collection form was used to ensure consistency in data extraction for all variables of interest, including demographic characteristics, maternal history, and neonatal outcomes. Data were entered and analyzed using SPSS (Statistical Package for the Social Sciences) software version 27. Descriptive statistics, including frequencies and percentages, were calculated for all categorical variables (RDS, maternal hypertension, maternal DM, categorized gestational age, categorized birth weight, gender, mode of delivery) to describe the characteristics of the study sample. The association between each independent variable and the occurrence of RDS was assessed using the Chi-square test or Fisher's exact test, where appropriate (when expected cell counts were less than. The strength of association was estimated by calculating the odds ratio (OR) with a 95% Confidence Interval (CI). A p-value of <0.05 was considered statistically significant. This study utilized secondary data from medical records. Permission to conduct the research and access medical records was obtained from the relevant authorities at RSUD Tabanan. Patient confidentiality was maintained by anonymizing all data collected.

3. Results and Discussion

Table 1 provides a comprehensive overview of the baseline maternal and neonatal characteristics of the 220 neonates included in this study, meticulously stratified by the presence or absence of respiratory distress syndrome (RDS). This stratification allows for a comparative understanding of the profiles of neonates who developed RDS (N=114) versus those who did not (N=106). Observing gestational age, a critical determinant of neonatal outcomes, the RDS group comprised a higher proportion of preterm infants (<37 weeks) at 45.6% (52 neonates), compared to 33.0% (35 neonates) in the No RDS group. Consequently, term neonates (≥37 weeks) were more represented in the No RDS group (67.0%) than in the RDS group (54.4%). The total sample had 39.5% preterm infants. Regarding birth weight, the distribution of low birth weight (<2500g) infants was quite similar between the two groups, with 43.0% in the RDS group and 44.3% in the No RDS group. The mean birth weight was slightly lower in the RDS group (2450 ± 550 grams) compared to the No RDS group (2510 ± 520 grams), with an overall sample mean of 2478 ± 535 grams. The gender distribution was nearly balanced in both groups and overall; male neonates constituted 51.8% of the RDS group and 49.1% of the No RDS group. Data on Apgar scores suggest that neonates in the RDS group tended to have lower scores indicative of greater initial physiological stress; for instance, 30.7% of the RDS group had an Apgar score <7 at 1 minute, compared to 17.0% in the No RDS group. This trend continued at 5 minutes, where 15.8% of the RDS group had an Apgar <7, versus 7.5% in the No RDS group. The majority of births were singleton, with data showing a slightly higher, though comparable, percentage of multiple gestations (twins) in the RDS group (7.9%) compared to the No RDS group (5.7%). The maternal age distribution, based on data, was broadly similar across both groups, with the largest proportion of mothers in the 20-34 year age bracket (70.2% for RDS mothers, 73.6% for No RDS mothers). The mean maternal age was also comparable (29.5 ± 6.2 years for the RDS group vs. 28.9 ± 5.8 years for the No RDS group). Similarly, parity, whether primiparous or multiparous, showed a comparable distribution between the groups in the data. A striking feature of this study population was the high rate of Caesarean section (CS) deliveries, accounting for 80.5% of all births. When stratified, CS was the mode of delivery for 85.1% of infants in the RDS group and 75.5% in the No RDS group, suggesting a higher prevalence of CS births among neonates who subsequently developed RDS. Vaginal deliveries were correspondingly less frequent, particularly in the RDS group (14.9%). Maternal diabetes mellitus was a rare condition in this study sample, noted in only 1.4% of all mothers. All three cases of maternal DM were in the RDS group, meaning no infants born to mothers with DM were in the No RDS group based on the study's data. In contrast, maternal hypertension was notably more prevalent among mothers whose infants developed RDS (16.7%, or 19 mothers) compared to those whose infants did not (6.6%, or 7 mothers). Overall, 11.8% of mothers in the total sample had hypertension. Finally, for the subset of preterm infants (N=87), data on antenatal corticosteroid (ACS) use suggests that exposure to ACS was less common among preterm infants who developed RDS (15 out of 52, or 28.8%) compared to preterm infants who did not develop RDS (18 out of 35, or 51.4%). This highlights a potential area of intervention, as ACS is crucial for fetal lung maturation. Table 1 delineates the baseline profiles, revealing a higher proportion of preterm births and maternal hypertension in the RDS group. The high Caesarean section rate across the entire study population is also a significant characteristic. While other factors showed some numerical differences, the most apparent distinctions at baseline related to maternal hypertension and, to a lesser extent, gestational age and mode of delivery when observing the raw distributions.

Table 1. Baseline maternal and neonatal characteristics of the study population, stratified by respiratory distress syndrome (RDS) status (N=220).

Characteristic	RDS Group (N=114)	No RDS Group (N=106)	Total sample (N=220)
Neonatal factors			
Gestational age			
Preterm (<37 weeks)	52 (45.6%)	35 (33.0%)	87 (39.5%)
Term (≥37 weeks)	62 (54.4%)	71 (67.0%)	133 (60.5%)
Birth weight (grams)			
Low birth weight (<2500g)	49 (43.0%)	47 (44.3%)	96 (43.6%)
Normal birth weight (≥2500g)	65 (57.0%)	59 (55.7%)	124 (56.4%)
Mean birth weight (grams) ± SD	2450 ± 550	2510 ± 520	2478 ± 535
Gender			
Male	59 (51.8%)	52 (49.1%)	111 (50.5%)
Female	55 (48.2%)	54 (50.9%)	109 (49.5%)
Apgar score at 1 minute			
<7	35 (30.7%)	18 (17.0%)	53 (24.1%)
≥7	79 (69.3%)	88 (83.0%)	167 (75.9%)
Mean ± SD	6.8 ± 1.5	7.5 ± 1.2	7.1 ± 1.4
Apgar score at 5 minutes			
<7	18 (15.8%)	8 (7.5%)	26 (11.8%)
≥7	96 (84.2%)	98 (92.5%)	194 (88.2%)
Mean ± SD	7.8 ± 1.3	8.5 ± 1.0	8.1 ± 1.2
Multiple gestation			
Singleton	105 (92.1%)	100 (94.3%)	205 (93.2%)
Multiple (Twins)	9 (7.9%)	6 (5.7%)	15 (6.8%)
Maternal factors			
Maternal age (years)			
<20	10 (8.8%)	8 (7.5%)	18 (8.2%)
20-34	80 (70.2%)	78 (73.6%)	158 (71.8%)
≥35	24 (21.1%)	20 (18.9%)	44 (20.0%)
Mean ± SD	29.5 ± 6.2	28.9 ± 5.8	29.2 ± 6.0
Parity			
Primiparous	40 (35.1%)	35 (33.0%)	75 (34.1%)
Multiparous (≥1 previous birth)	74 (64.9%)	71 (67.0%)	145 (65.9%)
Mode of Delivery			
Caesarean section	97 (85.1%)	80 (75.5%)	177 (80.5%)
Vaginal delivery	17 (14.9%)	26 (24.5%)	43 (19.5%)
Maternal diabetes mellitus			
Yes	3 (2.6%)	0 (0.0%)	3 (1.4%)
No	111 (97.4%)	106 (100.0%)	217 (98.6%)
Maternal hypertension			
Yes	19 (16.7%)	7 (6.6%)	26 (11.8%)
No	95 (83.3%)	99 (93.4%)	194 (88.2%)
Antenatal corticosteroid use			
(Among preterm births, N=87)	(N=52 RDS)	(N=35 No RDS)	
Yes	15 (28.8%)	18 (51.4%)	33 (37.9%)
No	37 (71.2%)	17 (48.6%)	54 (62.1%)

Table 2 meticulously outlines the associations between various maternal and neonatal factors and the occurrence of neonatal respiratory distress syndrome (RDS) among the 220 neonates in this study. The analysis employed odds ratios (OR) with 95% confidence intervals (CI) to quantify these associations, alongside corresponding p-values to assess statistical significance. The most striking finding from this analysis was the statistically significant association between maternal hypertension and neonatal RDS. Neonates born to mothers with hypertension exhibited 2.83 times the odds of developing RDS compared to those born to normotensive mothers (OR 2.83; 95% CI 1.14 - 7.04; p=0.021). This robust association highlights maternal hypertensive status as a substantial predictor of RDS

in this study population, with 73.1% of infants from hypertensive mothers developing RDS compared to 49.0% from normotensive mothers. Regarding gestational age, preterm infants (<37 weeks) had 1.70 times the odds of developing RDS compared to term infants (OR 1.70; 95% CI 0.98 - 2.94). While 59.8% of preterm infants developed RDS versus 46.6% of term infants, the p-value of 0.056 suggests this finding was at the cusp of statistical significance, with the confidence interval narrowly including 1.0, indicating a strong trend towards increased odds for preterm infants. The analysis of birth weight did not reveal a significant association with RDS. Infants with low birth weight (<2500g) had odds of developing RDS similar to those with normal birth weight (OR 0.95; 95% CI 0.56 - 1.61; p=0.839). The proportion of RDS was 51.0% in the low birth weight group and 52.4% in the normal birth weight group. Similarly, neonatal gender was not found to be significantly associated with RDS. Male neonates had slightly higher odds (OR 1.11; 95% CI 0.66 - 1.89; p=0.689) of developing the syndrome compared to females, but this difference was not statistically significant. Approximately 53.2% of male infants and 50.5% of female infants developed RDS. For Apgar score at 5 minutes**,** infants with a score of less than 7 exhibited 2.30 times the odds of developing RDS compared to those with an Apgar score of 7 or higher (OR 2.30; 95% CI 0.95 - 5.53). With a p-value of 0.06, this association approached statistical significance, suggesting that lower Apgar scores at 5 minutes may indicate increased odds for RDS. Within this group, 69.2% of infants with a 5-minute Apgar score <7 developed RDS. The study also examined multiple gestations. Infants from multiple gestation pregnancies had 1.42 times the odds of developing RDS compared to singletons (OR 1.42; 95% CI 0.48 - 4.18). However, this finding was not statistically significant (p=0.21, indicating a p-value >0.05), with 60.0% of neonates from multiple gestations developing RDS. The mode of delivery showed a trend towards increased odds of RDS for infants born via Caesarean section. These infants had 1.85 times the odds of RDS compared to those delivered vaginally (OR 1.85; 95% CI 0.94 - 3.66). The p-value of 0.072 indicates this did not reach statistical significance, although a higher percentage of RDS cases (54.8%) was observed in the Caesarean section group versus the vaginal delivery group (39.5%). Maternal diabetes mellitus was a rare condition in this study sample. While infants born to mothers with diabetes showed markedly increased odds of RDS (OR 6.69), the 95% confidence interval was extremely wide (0.34 - 130.99), reflecting the instability due to the small number of cases (n=3, all of whom developed RDS, with no cases of RDS among infants of non-diabetic mothers in this specific comparison for the OR calculation with correction). The p-value of 0.248, derived from Fisher's exact test in the original analysis, confirms this lack of statistical significance in the context of sparse data. Finally, among the subset of preterm infants (N=87), the absence of antenatal corticosteroid (ACS) use was significantly associated with increased odds of developing RDS. Preterm infants whose mothers did not receive ACS had 2.61 times the odds of developing RDS compared to preterm infants whose mothers did receive ACS (OR 2.61; 95% CI 1.07 - 6.39; p<0.05). This finding underscores the protective effect of antenatal corticosteroids in the preterm population, as 68.5% of preterm infants without ACS exposure developed RDS, compared to 45.5% of those with ACS exposure. Table 2 highlights maternal hypertension as a statistically significant factor increasing the odds of RDS. Antenatal corticosteroid non-use in preterm infants also showed a significant association with higher odds of RDS. Gestational age, mode of delivery, and Apgar score at 5 minutes showed trends towards increased odds, though not reaching conventional statistical significance in this particular analysis.

Table 2. Association between potential risk factors and neonatal respiratory distress syndrome (RDS) (N=220).

Risk factor (Variable)	Category / Level	Neonates with RDS (N=114)	Neonates without RDS (N=106)	Total in category	Odds Ratio (OR) (95% CI)	P-value
Neonatal factors						
Gestational age		N (%)	N (%)	N (%)		
	Preterm (<37 weeks)	52 (59.8%)	35 (40.2%)	87 (100%)	1.70 (0.98 - 2.94)	0.056
	Term (≥37 weeks)	62 (46.6%)	71 (53.4%)	133 (100%)	Reference	
Birth weight		N (%)	N (%)	N (%)		
	Low Birth Weight (<2500g)	49 (51.0%)	47 (49.0%)	96 (100%)	0.95 (0.56 - 1.61)	0.839
	Normal (≥2500g)	65 (52.4%)	59 (47.6%)	124 (100%)	Reference	
Gender		N (%)	N (%)	N (%)		
	Male	59 (53.2%)	52 (46.8%)	111 (100%)	1.11 (0.66 - 1.89)	0.689
	Female	55 (50.5%)	54 (49.5%)	109 (100%)	Reference	
Apgar score at 5 min		N (%)	N (%)	N (%)		
	<7	18 (69.2%)	8 (30.8%)	26 (100%)	2.30 (0.95 - 5.53)	0.06
	≥7	96 (49.5%)	98 (50.5%)	194 (100%)	Reference	
Multiple gestation		N (%)	N (%)	N (%)		
	Multiple	9 (60.0%)	6 (40.0%)	15 (100%)	1.42 (0.48 - 4.18)	0.21
	Singleton	105 (51.2%)	100 (48.8%)	205 (100%)	Reference	
Maternal factors						
Mode of delivery		N (%)	N (%)	N (%)		
	Caesarean Section	97 (54.8%)	80 (45.2%)	177 (100%)	1.85 (0.94 - 3.66)	0.072
	Vaginal Delivery	17 (39.5%)	26 (60.5%)	43 (100%)	Reference	
Maternal diabetes mellitus		N (%)	N (%)	N (%)		
	Yes	3 (100.0%)	0 (0.0%)	3 (100%)	6.69 (0.34 - 130.99)	0.248
	No	111 (51.2%)	106 (48.8%)	217 (100%)	Reference	
Maternal hypertension		N (%)	N (%)	N (%)		
	Yes	19 (73.1%)	7 (26.9%)	26 (100%)	2.83 (1.14 - 7.04)	0.021
	No	95 (49.0%)	99 (51.0%)	194 (100%)	Reference	
Antenatal corticosteroid use		N (%)	N (%)	N (%)		
(Among preterm births, N=87)	No	37 (68.5%)	17 (31.5%)	54 (100%)	2.61 (1.07 - 6.39)	0.031
	Yes	15 (45.5%)	18 (54.5%)	33 (100%)	Reference	

This study, conducted at RSUD Tabanan in Indonesia, aimed to elucidate risk factors for Neonatal Respiratory Distress Syndrome (RDS), revealing maternal hypertension as a particularly prominent predictor in this regional setting. While a statistically significant association with maternal hypertension was observed, other established risk factors such as gestational age, birth weight, neonatal gender, mode of delivery, and maternal diabetes mellitus did not demonstrate a significant independent association within this specific investigation, although certain trends warrant further exploration of underlying complex biological interactions. The key finding of this investigation was the significant association between maternal hypertension and an increased risk of neonatal RDS (RR=1.5, p=0.021). This aligns with numerous studies globally and within Indonesia that have identified hypertensive disorders of pregnancy

(HDP) as a critical contributor to adverse neonatal respiratory outcomes. The pathophysiological impact of maternal hypertension on fetal lung development and neonatal adaptation is profound and multifaceted. The placenta plays a central role in this interaction. Maternal hypertensive states, particularly preeclampsia, often lead to placental vasculopathy, characterized by incomplete spiral artery remodeling, endothelial dysfunction, vasospasm, and an increased likelihood of placental infarcts or abruption. These pathological changes compromise uteroplacental blood flow, resulting in a state of chronic fetal hypoxia and undernutrition. This chronic intrauterine stress has significant implications for fetal lung organogenesis.[11,12]

Normal lung development involves intricate processes of branching morphogenesis, alveolar septation, and capillary network formation. Chronic hypoxia can disrupt these processes, leading to lungs with fewer, larger alveoli (reducing surface area for gas exchange) and abnormal pulmonary vascular development. This structural immaturity can directly predispose to respiratory insufficiency at birth. The production of pulmonary surfactant by type II alveolar cells is a complex biochemical process that is exquisitely sensitive to the fetal hormonal milieu and oxygen tension. While acute stress can sometimes accelerate surfactant production (a fetal stress response), chronic hypoxia and the associated metabolic disturbances seen in HDP can impair type II pneumocyte function, reduce the synthesis of crucial surfactant phospholipids (like dipalmitoylphosphatidylcholine) and surfactant-associated proteins (SP-A, SP-B, SP-C, SP-D), or alter their composition, rendering the surfactant less effective. For example, SP-B is critical for spreading and stabilizing surfactant films, and its deficiency is incompatible with effective air breathing. Preeclampsia and other hypertensive disorders are associated with a systemic maternal inflammatory response and increased oxidative stress. Pro-inflammatory cytokines and reactive oxygen species can cross the placenta or be generated within the feto-placental unit. These mediators can directly injure the developing fetal lung tissue, inducing an inflammatory response (fetal inflammatory response syndrome - FIRS) that can further impair lung maturation and surfactant function, making the neonate more susceptible to RDS. Maternal endothelial dysfunction, a hallmark of preeclampsia, may also have parallels in the fetal pulmonary vasculature, potentially contributing to altered vascular reactivity and an increased risk of persistent pulmonary hypertension of the newborn (PPHN), which can complicate or mimic RDS. The 1.5-fold increased risk observed in this study underscores the direct or indirect detrimental impact of maternal hypertension on neonatal respiratory adaptation in this specific regional population. It suggests that the mechanisms linking maternal hypertension to fetal lung compromise are actively at play and are clinically significant in this setting.[13,14]

In this particular investigation, the association between preterm birth (<37 weeks) and RDS (p=0.056) approached, but did not achieve, statistical significance with the broad categorization used. This finding, while seemingly divergent from the overwhelming global evidence establishing prematurity as the paramount risk factor for RDS, invites a deeper consideration of biological nuances. The risk of RDS is not uniform across all gestational ages; it follows a steep inverse gradient, being extremely high in very preterm infants and diminishing as term approaches. The "term" category (≥37 weeks) includes "early term" infants (37 0/7 to 38 6/7 weeks), who are known to have higher respiratory morbidity, including RDS, compared to full-term infants (39 0/7 to 40 6/7 weeks). Similarly, "late preterm" infants (34 0/7 to 36 6/7 weeks) represent a significant proportion of the "preterm" category and, while at higher risk than term infants, may have variable degrees of lung maturity. If the current study's "term" group included a substantial number of early term infants, and the "preterm" group was predominantly late preterm, the physiological differences in lung maturity between these specific subgroups might be less stark than if comparing very

preterm to full-term infants. This could dilute the statistical strength of the association when using a simple preterm/term dichotomy. Certain intrauterine stressors, if not overwhelmingly severe, can paradoxically accelerate fetal lung maturation as a stress response, involving earlier release of fetal cortisol. While chronic severe hypoxia (as seen in some HDP cases) is detrimental, other stressors might have this effect. If specific local factors (e.g., certain maternal conditions or subclinical infections prevalent in the region, not measured in this study) contributed to such accelerated maturation in some preterm infants, it could modify the expected incidence of RDS. In a setting where maternal hypertension is a strong predictor, its influence might overshadow or interact with the effect of gestational age, particularly if hypertensive pregnancies disproportionately lead to deliveries across a spectrum of gestational ages. The borderline p-value suggests a complex relationship that may be influenced by such interactions or other unmeasured population-specific characteristics. This study did not find a statistically significant independent association between low birth weight (<2500g) and RDS (p=0.839). Low birth weight is a heterogeneous category, encompassing infants who are small due to prematurity (appropriate for gestational age but born early) and those who are small due to intrauterine growth restriction (IUGR) (smaller than expected for their gestational age, whether preterm or term).[15,16]

In these infants, RDS risk is primarily driven by the immature surfactant system and structural lung immaturity characteristic of their early gestational age. Infants with IUGR, often resulting from placental insufficiency (which can also be linked to maternal hypertension), experience chronic intrauterine nutrient and oxygen deprivation. Some evidence suggests that chronic stress in IUGR may *accelerate* certain aspects of lung maturation, including surfactant production, as a fetal adaptive response. If this were a prominent effect in the LBW infants in this study who were growth-restricted, it might counteract the increased RDS risk typically associated with being small. Conversely, severe or prolonged IUGR can lead to impaired lung growth (hypoplasia), reduced alveolar numbers, and abnormal pulmonary vascular development, thereby *increasing* RDS risk or susceptibility to other respiratory complications. The overall non-significant finding in this study might reflect a balance of these opposing effects within the LBW group, or a scenario where other factors, like maternal hypertension itself (a cause of both RDS and potentially IUGR), are stronger drivers of outcome, obscuring the independent effect of birth weight in a bivariate analysis. No significant association was found between neonatal gender and RDS risk in this investigation (p=0.689). The "male disadvantage" in neonatal respiratory outcomes is a widely discussed phenomenon in literature, with many studies reporting higher RDS incidence and severity in male infants, particularly preterm males. Androgens, present in higher concentrations in male fetuses, are thought to delay lung maturation. They may inhibit the differentiation of type II pneumocytes or delay the synthesis and secretion of surfactant components. Conversely, estrogens, relatively more influential in female fetuses, may promote lung maturation and surfactant production. Despite this biological rationale, the clinical expression of this sex difference can vary. The magnitude of the sex-based difference might be more pronounced at very early gestational ages. If the proportion of extremely preterm infants in this study was low, the effect might be less apparent. Other genetic or epigenetic factors, potentially varying across populations, might interact with sex hormones to modulate lung development and RDS susceptibility. Environmental factors or co-existing maternal conditions could also modify the baseline sex-related risk.[17,18]

The mode of delivery (Caesarean section vs. vaginal delivery) did not show a statistically significant association with RDS in this study (p=0.072), although a higher percentage of CS-born infants experienced RDS. This trend is consistent with the well-documented increased risk of neonatal respiratory problems, including RDS and transient tachypnea of

the newborn (TTN), following CS, particularly elective CS without labor. During labor and vaginal delivery, mechanical compression of the fetal thorax helps expel fluid from the lungs. Furthermore, the onset of breathing initiates a switch from active chloride (and fluid) secretion into the alveoli to active sodium (and fluid) absorption out of the alveoli. Labor itself, via hormonal changes (catecholamine surge), upregulates these sodium channels (ENaC). Infants born by CS, especially without labor, may miss some of these adaptive mechanisms, leading to delayed lung fluid clearance and potentially increasing the work of breathing. Labor triggers the release of fetal catecholamines and glucocorticoids, which play a role in final lung maturation, surfactant release, and the preparation of the lungs for air breathing.[1,14] Absence of exposure to the full labor process in elective CS might result in relatively less mature lungs at birth, even at similar gestational ages. The lack of statistical significance in this study, despite the observed trend and the high CS rate (80.5%), might be due to several factors influencing the local context. If elective CS procedures at RSUD Tabanan are generally performed closer to 39 weeks of gestation, and if post-CS neonatal care includes proactive measures for respiratory support (early nasal CPAP for at-risk infants), the differential risk might be attenuated. The reasons for CS (emergency vs. elective, maternal or fetal indications) can confound the association. If many CS procedures were performed due to conditions that themselves are risk factors for neonatal compromise (e.g., fetal distress, severe maternal illness like preeclampsia), it becomes challenging to isolate the independent effect of the mode of delivery itself without detailed stratification by indication. The high CS rate itself suggests that the comparison group (vaginal deliveries) might be smaller and potentially represent a lower-risk obstetric population.[19,20]

4. Conclusion

The association between maternal DM and RDS was not statistically significant (p=0.248) in this study, a finding primarily constrained by the very low prevalence of maternal DM (1.4%, n=3) within the study sample. While this limits definitive conclusions from the current data, the established biological link is important to consider. Maternal diabetes (both pre-gestational and gestational) is generally recognized as a risk factor for RDS. Maternal hyperglycemia leads to fetal hyperglycemia, stimulating excessive insulin production by the fetal pancreas. High levels of fetal insulin can interfere with lung maturation by antagonizing the effects of cortisol. Cortisol is a crucial hormone for stimulating the differentiation of type II pneumocytes and the synthesis of surfactant. Hyperinsulinemia can inhibit the expression of genes involved in surfactant protein production and phospholipid synthesis, leading to a quantitative or qualitative surfactant deficiency. This metabolic interference can delay lung maturation, even in term infants of diabetic mothers, making them more susceptible to RDS. The robust evidence from larger studies and meta-analyses supports this association, suggesting that in populations with a higher prevalence of maternal DM, this factor would likely play a more discernible role in RDS incidence. The findings from this investigation at RSUD Tabanan, particularly the prominent role of maternal hypertension, have direct implications for local clinical practice. Enhanced antenatal screening for, and optimal management of, hypertensive disorders of pregnancy are paramount. This includes early identification, appropriate pharmacological and non-pharmacological interventions, and timely decision-making regarding delivery to balance maternal and fetal well-being, potentially mitigating the risk of RDS. For neonates born to hypertensive mothers, heightened vigilance for early signs of RDS and proactive respiratory support strategies, in line with current international guidelines, are warranted.

5. References

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