



Analysis of Risk Factors for The Severity of Hyaline Membrane Disease in Preterm Infants Based on Modality Chest X-Ray

Aulia Kusuma Dewi¹, Farah Hendara Ningrum²,
Adhie Nur Radityo Suswihardhyono³, Lydia Widyastuti Setjadinigrat Kuntjoro²

¹Faculty of Medicine Diponegoro University Semarang, Indonesia

²Department Radiology, Faculty of Medicine Diponegoro University / Kariadi Hospital Semarang, Indonesia

³Department Pediatric Faculty of Medicine Diponegoro University / Kariadi Hospital Semarang, Indonesia

Abstract

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Author Affiliation:

Department Radiology,
Faculty of Medicine Diponegoro University /
Kariadi Hospital Semarang, Indonesia

Author Correspondence:

Farah Hendara Ningrum
Dr. Sutomo 16 street, Semarang,
Central Java 50244, Indonesia

E-mail:

farahhendara@fk.undip.ac.id

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Background : Hyaline membrane disease is one of the leading causes of morbidity and mortality in premature infants. Chest X-ray examination can significantly improve the diagnosis of hyaline membrane disease. This study aims to examine the relationship between risk factors and the severity of hyaline membrane disease using chest X-ray modalities.

Methods : An analytic observational study with a cross sectional and retrospective approach was conducted. Consecutive sampling of 30 preterm infants's medical records and thoracic X-ray at Dr. Kariadi Hospital Semarang was used. Data collection was carried out from April to July 2023. Statistical tests included the *Contingency Coefficient Correlation Test* and *Intraclass Correlation Coefficient (ICC)*.

Results : Findings indicate that HMD severity is associated with lower birth weights ($p = 0.020$; $r = 0.392$); gestational ages ($p = 0.011$; $r = 0.420$) and maternal hypertension ($p = 0.013$; $r = 0.414$). Preeclampsia, delivery method, and gender not significantly related to the HMD severity ($p > 0.05$).

Conclusion : Infant birth weight, gestational age, and maternal hypertension are significantly associated with the severity of hyalin membrane disease.

Keywords : Risk Factors, Hyaline Membrane Disease, Chest X-ray, Premature Infant

INTRODUCTION

Hyaline membrane disease, also known as respiratory distress syndrome (RDS) is a major cause of morbidity and mortality in premature infants.¹ The incidence varies internationally with rates 4.24% in Arabia; 6.4% in India; and 88.4% in Egypt.²⁻⁴ Causes of respiratory distress include infection (68.6%), transient tachypnea of the newborn (30.7%), congenital heart defect (18%), surgery (9.6%), and hyaline membrane disease (9%). Studies show that hyaline membrane disease is particularly prevalent in India and Nigeria.⁵⁻⁷ Chest x-ray examination can significantly indicate the diagnosis of hyaline membrane disease (27.36%).⁸ Preterm infants less than 1500 grams are a risk factor for hyaline membrane disease.⁹ Severe preeclampsia, infant gender, and cesarean delivery method are also risk factors hyaline membrane disease. For this reason, early diagnosis, supporting examinations, and appropriate interventions are very important for newborns, especially premature babies.

Diagnosis relies on clinical signs (tachypnea, cyanosis, retractions), laboratory tests (PaO₂ levels below 50 mmHg), and radiological examinations.^{10,11} Chest X-rays are crucial, revealing lung opacities and correlating with disease severity. The disease can be classified into four grades based on X-ray findings, ranging from ground glass appearance to homogeneous opacity.^{1,12-14}

Based on the classification of grade hyaline membrane disease based on chest x-ray images and by looking at risk factors and the high mortality rate of newborns with hyaline membrane disease, researchers are interested to research on the analysis of risk factors with the severity of hyaline membrane disease in newborns based on chest x-ray modalities at Dr. Kariadi Hospital Semarang. The goal is to enhance early diagnosis and intervention, thereby reducing severity and mortality rates in affected newborns.

METHODS

The study was conducted at Dr. Kariadi Hospital Semarang from April to July 2023, using an analytic observational design with a cross-sectional, retrospective approach. Thirty subjects were selected through consecutive sampling from electronic medical records, adhering to inclusion and exclusion criteria. Inclusion criteria included premature infants diagnosed with hyaline membrane disease based on clinical and radiological exams (initial imaging) with a gestational age under 37 weeks and a birth weight below 2500 grams. Exclusion criteria involved incomplete medical records and infants who had received surfactant therapy. Data was collected from the initial thoracic X-ray imaging through HER (Electronic Health Record) and subsequently evaluated by two radiologists to determine

the disease grade. Descriptive analysis was employed to characterize the respondents, while bivariate analysis was conducted to assess the relationships between variables. The strength of the relationships between risk factors and disease severity was evaluated using the contingency coefficient correlation test. The reliability of the instrument in this study was assessed using inter-rater reliability (IRR). This study received ethical clearance from the Health Research Ethics Commission (KEPK) of Diponegoro University (Number 130/EC/KEPK/FK-UNDIP/IV/2023).

RESULTS

Table 1 shows that the study included 30 premature infants diagnosed with hyaline membrane disease, with 21 (70%) classified as grade I and II. Infants weighing ≤ 1500 grams comprised the largest group (56.7%), while those born at ≥ 30 weeks accounted for 66.7%. Most infants were born to mothers without hypertension (56.7%) or preeclampsia (93.3%), and cesarean section was the most common delivery method (80%). Males made up 56.7% of the sample.

Table 2 presents the results of the reliability test using the Intraclass Correlation Coefficient (ICC), yielding a κ value of 0.889, indicating very good agreement in the grading of hyaline membrane disease. The correlation between birth weight and the severity of HMD was significant ($p = 0.020$; $r = 0.392$), reflecting a weak positive correlation, while gestational age also showed a significant moderate positive correlation with disease severity ($p = 0.011$; $r = 0.420$). In this study also indicate a correlation between maternal hypertension and the severity of hyaline membrane disease ($p = 0.013$; $r = 0.414$). However, maternal preeclampsia, delivery method, and gender did not show significant relationships with disease severity ($p > 0.05$).

DISCUSSION

This study identified a significant association between birth weight and the severity of hyaline membrane disease (HMD), demonstrating a weak positive correlation ($p = 0.020$; $r = 0.392$). Heavier infants exhibited milder disease, while those with lower birth weights experienced more severe cases. These findings are consistent with the research conducted by Warman *et al.*, which reported a 42% incidence of HMD in infants with birth weights below 1500 grams, as well as with Melamed *et al.*, who found that the majority of NICU patients with HMD weighed less than 1800 grams. Low birth weight emerged as a primary risk factor for HMD.^{15,16} Additionally, Pherson *et al.* demonstrated that the severity of HMD is inversely related to gestational age, while Mansoor *et al.* confirmed a positive correlation between gestational age and birth weight. Infants with

TABLE 1
Research Subject Characteristics

Variable	n	%
Total Sample	30	100.0
Grading HMD		
I – II	21	70.0
III – IV	9	30.0
Birth Weight		
≤ 1500 grams	17	56.7
> 1500 grams	13	43.3
Gestational Age		
< 30 weeks	10	33.3
≥ 30 weeks	20	66.7
Maternal Hypertension		
Yes	13	43.3
No	17	56.7
Maternal Preeclampsia		
Yes	2	6.7
No	28	93.3
Mode of Delivery		
SC	24	80.0
Spontaneous	6	20.0
Sex		
Male	17	56.7
Female	13	43.3

TABLE 2
Conformity of Hyaline Membrane Disease Degree of Observer I and Observer II

HMD (I)	HMD (II)								Total		κ
	I		II		III		IV		n	%	
	n	%	n	%	n	%	n	%			
I	7	23.3	1	3.3	0	0	0	0	8	26.7	0.889
II	1	3.3	11	36.7	1	3.3	0	0	13	43.3	
III	0	0	2	6.7	5	16.7	0	0	7	23.3	
IV	0	0	0	0	0	0	2	6.7	2	6.7	
Total	8	26.7	14	46.7	6	20.0	5	6.7	30	100	

TABLE 3
Test of Relationship to HMD Severity

Variable	Grading HMD				p	r
	I – II		III – IV			
	n	%	n	%		
Birth Weight						
≤ 1500 grams	9	42.9	8	88.9	0.020 [£]	0.392
> 1500 grams	12	57.1	1	11.1		
Gestational						
< 30 weeks	4	19	6	66.7	0.011 [£]	0.420
≥ 30 weeks	17	81	3	33.3		
Maternal Hypertension						
Yes	6	28.6	7	77.8	0.013 [£]	0.414
No	15	71.4	2	22.2		
Maternal Preeclampsia						
Yes	1	4.8	1	11.1	0.523 [£]	0.116
No	20	95.2	8	88.9		
Mode of Delivery						
SC	17	81	7	77.8	0.842 [£]	0.036
Spontaneous	4	19	2	22.2		
Sex						
Male	11	52,4	6	66.7	0.469 [£]	0.131
Female	10	47,6	3	33.3		

[£] Contingency Coefficient

low birth weights are often born prematurely, resulting in immature lung development and inadequate surfactant production, which contribute to respiratory distress and HMD.^{11,17}

The study also identified a significant correlation between gestational age and the severity of hyaline membrane disease (HMD), demonstrating a moderate positive correlation ($p = 0.011$; $r = 0.420$). Specifically, as gestational age approaches 37 weeks, the severity of HMD diminishes. This finding is consistent with the observations of Pherson *et al.*, who reported an inverse relationship between HMD severity and gestational age, and Wicaksono *et al.*, who documented a 60–80% incidence of HMD in infants born at gestational ages less than 28 weeks and 15–30% incidence of HMD in infant born at 32–36 gestational age.^{15,18} Additionally, Pickerd *et al.* identified both prematurity and deficiencies in surfactant production as significant risk factors for the development of HMD.^{16,19}

This study identified a significant correlation

between maternal hypertension and HMD severity, with a moderate positive correlation ($p = 0.013$; $r = 0.414$). Elevated maternal blood pressure was associated with increased severity of HMD, corroborating the findings of Condo *et al.* and Wang *et al.*, who emphasized the influence of maternal hypertension on neonatal outcomes. Pathological pregnancy (maternal hypertension and maternal diabetes) is associated with the incidence of hyaline membrane disease.^{20,21} Efriza *et al.* also reported a significant relationship between maternal hypertension and HMD.²² Hypertension in pregnant women can lead to vasospasm in the blood vessels, resulting in compromised blood flow that may disrupt overall circulation, including uteroplacental perfusion. This reduction in perfusion can adversely affect fetal oxygenation, increasing the risk of respiratory distress in neonates. In contrast, this study found no significant association between maternal preeclampsia, delivery method, or infant gender and the severity of hyaline membrane disease.

CONCLUSION

There is a significant correlation between birth weight, gestational age, and maternal hypertension with the severity of hyaline membrane disease.

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