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Study of Mortality and Morbidity in Neonates with Congenital Diaphragmatic Hernia

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Congenital diaphragmatic hernia may either lead to death or cause several complications such as increased pulmonary artery pressure.
Objective: The present study aimed to compare mortality and morbidity, vasopressor intake, and visceral hernia of CDH neonates with pulmonary hypertension and without pulmonary hypertension in Mahdieh and Mofid hospitals in Tehran.
Methods: This cross-sectional analytical study included 56 neonates with congenital diaphragmatic hernia who were admitted to Mofid and Mahdieh Children's Hospitals from 2014 to 2018. The sample size included 56 people selected based on census method. We compared the pulmonary hypertension and non-pulmonary hypertension groups in variables, such as gender, gestational age, birth weight, place of birth, and type of delivery and we examined relationship between pulmonary hypertension and mortality and morbidity and relationship between mortality and vasopressor intake.
Results: The OR value was calculated to be 1.106, which is significant at the level of 0.004 ($p < 0.01$). This finding indicated that the chance of death in the group of infants with severe pulmonary

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hypertension was increased by 1.106. Also, the relationship of visceral hernia (stomach, intestine, liver, kidney, and spleen) to thorax was examined by logistic regression. Only the OR value of liver hernia (9.42) was significant ($p < 0.001$), indicating that the chance of death was higher in infants with liver hernias. It also the OR value of dopamine, dobutamine, and milrinone was significant ($p < 0.01$).

Conclusion: In general, the results obtained in our study indicated that the mortality rate in the group of infants with pulmonary hypertension was significantly higher than the group without pulmonary hypertension. Also, liver hernia to thorax was associated with the severity of pulmonary hypertension, and the patients needed medication had a higher chance of death.

Keywords: Congenital diaphragmatic hernia; pulmonary hypertension; Mortality, Neonates.

1. INTRODUCTION

Congenital diaphragmatic hernia (CDH) is a life-threatening congenital anomaly, with an approximate prevalence of 1: 2500 live births [1, 2]. It is caused by incomplete development of the diaphragm in early pregnancy, leading to abdominal viscera to be herniated into the chest. Despite advances in prenatal diagnosis and postpartum management, the mortality rate is about 40-50% [3, 4]. Left-sided defects occur in 85-90% of cases. Bilateral and right defects generally have worse outcomes than left defects [5, 6].

One of the complications of this disease is increased pulmonary blood pressure, which displaces the heart and mediastinum and causes compression of the lungs due to the pressure of viscera on the lungs and the contents of the thorax. In this condition, the normal growth of the lungs is disrupted and the lungs are damaged. Whereas hypoplasia reduces the development of bronchi, the number of alveoli and structural abnormalities of the pulmonary arteries, it increases the muscularity of the pulmonary arteries, the vascular resistance of the lungs, and pulmonary blood pressure [7].

Most patients with CDH develop acute respiratory distress shortly after birth. The severity of symptoms depends on the severity of pulmonary hypoplasia. Immediate intubation is often necessary [8]. The mild form of CDH can manifest itself months or even years later with respiratory or gastrointestinal symptoms [9].

Neonatal pulmonary disease is characterized by severe respiratory failure and hypoxemia due to persistent increased pulmonary vascular resistance. Changes within the pulmonary arteries include thick-walled vessels that cause the lumen of the arteries to shrink and the abnormal vaso-reactive response. In the early stages of the pulmonary vascular disease, the treatment would be achieved by pharmacological strategies in the postpartum period. However, in some cases, high blood pressure and pulmonary stasis associated with right ventricular hypertrophy, leads to increased rate the mortality and morbidity [10].

Although survival has improved in these patients, overall mortality is still high due to pulmonary hypoplasia and pulmonary hypertension [11,12] .The present study aimed to compare mortality and morbidity and vasopressor intake in with pulmonary hypertension and without pulmonary hypertension groups.

2. METHODS

In a cross-sectional analytical study from 2014 to 2018, we examined all CDH neonates hospitalized at Mofid and Mahdieh Children's Hospitals. Data were collected by reviewing the records of infants with congenital diaphragmatic hernias. The study sampling was a census in which all neonates with neonatal diaphragmatic hernia who were admitted to Mahdieh and Mofid children's hospitals from 2014 to 2018. According to the earlier studies, the minimum number of required sample size with 95% confidence and 80% power was determined to be 56 for the final analysis.

The collection tool in the present study was a checklist including gender, type of delivery, first and fifth minute APGAR score at birth, duration of ventilator dependence, length of hospital stay, presence of right or left diaphragmatic defect.

Exclusion criteria were congenital heart disease, severe asphyxia, major anomalies, and other syndromes, and infants with these conditions are excluded from the study.

Inclusion criteria were all infants with congenital diaphragmatic hernia admitted to the NICU of

Mofid and Mahdieh Children's Hospital. During the first week of hospitalization and then at weekly intervals they underwent echocardiography and measurement of pulmonary blood pressure by a pediatric cardiologist. The intensity of pulmonary hypertension was divided into three types: severe pulmonary hypertension (pressure gradient above 60 mm Hg), moderate pulmonary hypertension (pressure gradient between 60-40 mm Hg) and mild pulmonary hypertension (pressure gradient between 25-40 mm Hg), and the necessary treatments were performed. A relationship was examined between pulmonary hypertension and mortality and morbidity of the neonates. All echocardiographs were performed with one device.

For data analysis, at the first, the checklist information was entered into SPSS software version 19. We have applied the mean, SD, frequency and percentage as descriptive statistics. Frequency and percentage were used to describe qualitative variables. In this regard, logistic regression was used to measure the relationship and prediction.

3. RESULTS

Of the 56 cases studied, 37 were male (66.10%) and 19 (33.90%) were female infants. It was also observed that 29 patients (51.80%) had pulmonary hypertension and 27 patients (48.20%) hadn't it. Table 1 shows the frequency of two groups with pulmonary hypertension and non-pulmonary hypertension in variables, such as gender, gestational age, birth weight, place of birth, and type of delivery. It is mentioned all the tables are based on ECHO findings.

Table 2 shows the frequency of two groups with pulmonary hypertension and no pulmonary hypertension in the variable of visceral displacement to the thorax.

Table1. Comparison of two groups with pulmonary hypertension and no pulmonary hypertension in the variables of gender, gestational age, birth weight, place of birth, and type of delivery

Variable		With pulmonary hypertension	Without pulmonary hypertension	P
Gender	Female	10 (34.5)	9 (33.3)	0.57
	Male	19 (65.5)	18 (66.7)	
Gestational age	< 37 w	6 (20.7)	1 (3.7)	0.06
	> 37 w	23 (79.3)	26 (96.3)	
Birth weight	< 1500 gr	1 (3.5)	1 (3.7)	0.50
	1500-3000 gr	13 (44.8)	10 (37)	
	> 3000 gr	15 (51.7)	16 (59.3)	
Place of birth	Inborn	11 (37.9)	14 (51.9)	0.21
	Out born	18 (62.1)	13 (48.1)	
Type of delivery	Cesarean section	23 (73.9)	13 (51.9)	0.02
	Normal	6 (20.7)	14 (48.1)	

Table 2. Comparison of two groups with pulmonary hypertension and no pulmonary hypertension in the variable of visceral to thoracic displacement

Variable		With pulmonary hypertension	Without pulmonary hypertension
Stomach	Yes	9 (31)	6 (22.2)
	No	20 (69)	21 (77.8)
Spleen	Yes	11 (37.9)	14 (51.9)
	No	18 (62.1)	13 (48.1)
Kidney	Yes	1 (3.4)	1 (3.7)
	No	28 (96.6)	26 (96.3)
Liver	Yes	3(10.3)	2 (7.4)
	No	26 (89.7)	25 (92.6)
Intestine	Yes	27 (93)	27 (100)
	No	2 (3)	0

Tables 3 and 4 show the relationship between the severity of pulmonary hypertension and mortality. The relationship between pulmonary hypertension and mortality in infants was tested by logistic regression.

To find whether or not the severity of pulmonary hypertension is related to mortality in infants, we used the logistic regression and calculated OR value as 1.13, which was significant at the level of 0.002 ($p < 0.01$). This finding indicates that the chance of death in the neonatal group with severe pulmonary hypertension increases to 1.13. The analysis revealed that only the OR value of liver hernia (9.42) was significant ($p< 0.001$), indicating that the chance of death was higher in infants with a liver hernia.

Logistic regression was used to find whether there is a relationship between mortality and vasopressor intake in neonates. We used these drugs upon the treatment protocol. The results indicated that the OR ratios of dopamine, dobutamine, and milrinone were 12.73, 8.36, and 10.50 respectively ($p < 0.01$). This finding indicates that patients in need of medication had a higher chance of mortality (Table 5).

4. DISCUSSION

We examined the findings on the relationship between the severity of pulmonary hypertension and mortality in neonates with logistic regression and calculated the OR value to be 1.106, which is significant at the level of 0.004 ($p < 0.01$). It revealed that the chance of death in the group of infants with severe pulmonary hypertension increases by 1.106. The findings were consistent with the research of Lusk et al. (2015). The researchers observed a cohort of 140 infants with a congenital diaphragmatic hernia (CDH) who were cared for at the University of California, San Francisco between 2002 and 2012. They found persistence of pulmonary hypertension by echocardiography predicts short-term outcomes in congenital diaphragmatic hernia [13].

We also investigated the relationship between visceral hernia (stomach, intestine, liver, kidney, and spleen) to thorax and mortality in neonates. The results indicated a higher chance of death in infants with liver hernias. The findings were consistent with those of Ruža Grizelj et al. The researchers also showed that out of 228 infants with a congenital diaphragmatic hernia, 140 (61%) had isolated congenital diaphragmatic hernia, and 88 (39%) had a complex congenital diaphragmatic hernia [14].

Regarding the relationship between mortality and vasopressor intake (dopamine, dobutamine, milrinone) in neonates, the OR value of dopamine, dobutamine, and milrinone was 12.73, 8.36, and 10.50, respectively. It suggests that patients who require medication had a higher chance of death. Inconsistent with the findings of

Table 3. Frequency table of the severity of pulmonary hypertension by mild, moderate, and severe levels

Variable	Level	Frequency	%
Severity of pulmonary hypertension	Mild	40	71.4
	Moderate	15	26.8
	Severe	1	1.8
	Total	56	100.0

Table 4. Logistic regression of the relationship between pulmonary hypertension and mortality

Variable	OR	CI(confidence interval)	P value
pulmonary hypertension	1.13	1.04-1.22	0.002

Table 5. Logistic regression of the relationship of mortality and vasopressor intake in neonates

Variable	OR	CI(confidence interval)	P value
Dopamine intake	12.73	2.35-69.05	0.003
Dobutamine intake	8.36	1.87-37.43	0.006
Milrinone intake	10.50	2.10-52.47	0.004

Malowitz et al., in a study titled Controlling Infant Mortality with Congenital Diaphragmatic Hernias, the researchers found that out of 760 identified neonates, between 1999-2001 and 2008-2012, the use of inhaled nitric oxide has been increased from 20% to 50%, sildenafil, has been increased from zero percent to 14 percent and milrinone has been increased from zero to 22 percent. In general, the mortality rate (28%) in this period has not changed significantly compared to the same period in the past [15].

5. CONCLUSION

In general, the results obtained in our study indicated:

1. In general, the results obtained in our study showed that the mortality rate in the group of infants with pulmonary hypertension was significantly higher than the group without pulmonary hypertension. Neonatal specialists can use the findings of the present study in the diagnosis and treatment of affected CDH neonates.
2. The mortality rate is higher in the group of infants with a liver hernia in the thorax.
3. Intake of Dopamine, dobutamine, and Milrinone are independently associated with neonatal death.

6. RESEARCH LIMITATIONS

- Limited research sample to infants hospitalized in Mahdieh and Mofid hospitals in Tehran
- The study was a cross-sectional study and causal conclusion should be taken cautiously.

7. RESEARCH SUGGESTIONS

Based on the results obtained in the present study, it is suggested:

- The present study should be conducted on other samples in other cities.
- Due to association between pulmonary hypertension and mortality in infants with congenital diaphragmatic hernias, it is suggested that future studies examine the effectiveness of strategies to control pulmonary hypertension.

CONSENT

As per international standard, parental written consent has been collected and preserved by the author(s).

ETHICAL CONSIDERATION

This article is taken from the thesis of the children's subspecialty course with the code of ethics 1398.680.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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