Study of Mortality and Morbidity in Neonates with Congenital Diaphragmatic Hernia

Zainab Elahi1,2*, Seyyed Abolfazl Afje1, Mohammad Kazemian1, Maryam Shariati1, Naeeme Taslimi Taleghani1 and Minoo Fallahi1

1Neonatal Health Research Center, Research Institute for Children’s Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
2Department of pediatrics, Faculty of Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.

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

Article Information
DOI: 10.9734/JPRI/2021/v33i37B32050
Editor(s):
(1) Dr. Dharmesh Chandra Sharma, G. R. Medical College & J. A. Hospital, India.
Reviewers:
(1) Megha Kumra, Medanta – The Medicity, India.
(2) Manas Nayak, Dr. D. Y. Patil Hospital, India.
Complete Peer review History: https://www.sdiarticle4.com/review-history/71380

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 hypertension was significantly greater.
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 musculature 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
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.

Table 1. 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         | Mild  | 40        | 71.4 |
| hypertension                  | 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.

REFERENCES

1. Stege G, Fenton A, Jaffray B. Nihilism in the 1990s: the true mortality of congenital diaphragmatic hernia. Pediatrics. 2003; 112(3):532-5. Available: https://doi.org/10.1542/peds.112.3.532
2. Colvin J, Bower C, Dickinson JE, Sokol J. Outcomes of congenital diaphragmatic hernia: a population-based study in Western Australia. Pediatrics. 2005;116(3):e356-e63. Available: https://doi.org/10.1542/peds.2004-2845
3. Vanamo K. A 45-year perspective of congenital diaphragmatic hernia. British journal of surgery. 1996;83(12):1758-62. Available: https://doi.org/10.1002/bjs.1800831231
4. Azarow K, Messineo A, Pearl R, Filler R, Barker G, Bohn D. Congenital diaphragmatic hernia—a tale of two cities: the Toronto experience. Journal of pediatric surgery. 1997;32(3):395-400. Available: https://doi.org/10.1016/S0022-3468(97)90589-3
5. Beaumier CK, Beres AL, Puligandla PS, Skarsgard ED, Network TCPS. Clinical characteristics and outcomes of patients with right congenital diaphragmatic hernia: a population-based study. Journal of pediatric surgery. 2015;50(5):731-3. Available: https://doi.org/10.1016/j.jpedsurg.2015.02.027
6. Partridge EA, Peranteau WH, Herkert L, Rendon N, Smith H, Rintoul NE, et al. Right-versus left-sided congenital diaphragmatic hernia: a comparative outcomes analysis. Journal of pediatric surgery. 2016;51(6):900-2. Available: https://doi.org/10.1016/j.jpedsurg.2016.02.049
7. Peetsold M, Heij H, Kneepkens C, Nagelkerke A, Huisman J, Gemke R. The long-term follow-up of patients with a
congenital diaphragmatic hernia: a broad spectrum of morbidity. Pediatric surgery international. 2009;25(1):1-17. Available: https://doi.org/10.1007/s00383-008-2257-y

8. Öst E. Long-term follow-up in children born with congenital diaphragmatic hernia: Inst för kvinnor och barns hälsa/Dept of Women's and Children's Health; 2018. Available:https://doi.org/10.1007/s00383-018-4237-1

9. Chang SW, Lee HC, Yeung CY, Chan WT, Hsu CH, Kao HA, et al. A twenty-year review of early and late-presenting congenital Bochdalek diaphragmatic hernia: are they different clinical spectra? Pediatrics & Neonatology. 2010;51(1):26-30. Available:https://doi.org/10.1016/S1875-9572(10)60006-X

10. Jurcak-Zaleski S, Comstock C, Kirk JS. Eventration of the diaphragm. Prenatal diagnosis. Journal of ultrasound in medicine. 1990;9(6):351-4. Available:https://doi.org/10.7863/jum.1990.9.6.351

11. Muratore CS, Kharasch V, Lund DP, Sheils C, Friedman S, Brown C, et al. Pulmonary morbidity in 100 survivors of congenital diaphragmatic hernia monitored in a multidisciplinary clinic. Journal of pediatric surgery. 2001;36(1):133-40. Available:https://doi.org/10.1053/jpsu.2001.20031

12. Garriboli M, Duess JW, Ruttenstock E, Bishay M, Eaton S, De Coppi P, et al. Trends in the treatment and outcome of congenital diaphragmatic hernia over the last decade. Pediatric surgery international. 2012;28(12):1177-81. Available:https://doi.org/10.1007/s00383-012-3184-5

13. Lusk LA, Wai KC, Moon-Grady AJ, Steurer MA, Keller RL. Persistence of pulmonary hypertension by echocardiography predicts short-term outcomes in congenital diaphragmatic hernia. The Journal of pediatrics. 2015;166(2):251-6, e1. Available:https://doi.org/10.1016/j.jpeds.2014.10.024

14. Grizelj R, Bojanić K, Vuković J, Weingarten TN, Schroeder DR, Sprung J. Congenital diaphragmatic hernia: the side of diaphragmatic defect and associated nondiaphragmatic malformations. American Journal of Perinatology. 2017;34(09):895-904. Available:https://doi.org/10.1055/s-0037-1599821

15. Malowitz JR, Hornik CP, Laughon MM, Testoni D, Cotten CM, Clark RH, et al. Management practice and mortality for infants with congenital diaphragmatic hernia. American journal of perinatology. 2015;32(9):887. Available:https://doi.org/10.1055/s-0035-1544949

© 2021 Elahi et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle4.com/review-history/71380