

## Original Article



# Congenital diaphragmatic hernia: Prognostic value of hernia sac and size of defect

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### Abstract

**Introduction:** Congenital diaphragmatic hernia (CDH) is a congenital malformation with challenging management. The aim of this study was to evaluate the effect of the presence of hernia sac and defect size on the prognosis of CDH in Tabriz children's hospital.

**Methods:** In this prospective study, all the infants with the diagnosis of CDH that were admitted to the Tabriz children's hospital since 2016-2019 were enrolled. The presence or absence of a hernia sac was evaluated, and the largest diameter on diaphragmatic defect was measured before the repair. Postoperative outcomes, including instability, duration of mechanical ventilation, mortality rate, or hospital discharge were obtained and analyzed.

**Results:** Over the study period, 30 patients with CDH met the inclusion criteria, consisting of 15 males and 15 females. Fifteen cases were diagnosed during the first 24 hours of life and 16 cases experienced hypoxia in the first hour after birth. Defect size was significantly smaller in survived patients ( $P=0.041$ ). Postoperative death occurred in 9 (42.85%) patients without a hernia sac. Results showed that none of the cases with hernia sac expired ( $P=0.035$ ).

**Conclusion:** In our study, the presence of the hernia sac was related to a lower postoperative mortality rate. Defect size in survived group was also smaller. It can be suggested that the presence of hernia sac and lower diameter of defect size act as good prognostic factors in the outcome of patients with CDH.

### Introduction

Congenital diaphragmatic hernia (CDH) is characterized by a developmental defect in the diaphragm leading to protrusion of abdominal organs into the thoracic cavity and abnormal lung development.<sup>1</sup> CDH complicates about 1 per 3300 live births and could range from a small defect in the posterior portion of the diaphragmatic rim to a complete absence of diaphragm.<sup>2</sup> The diaphragmatic defect is usually placed on the left side (85%-90%), whereas the right and bilateral side defects are less common. The common form of involvement is the posterolateral defect of the diaphragm, also called Bochdalek hernia. Hernia involving the anterior (Morgagni; 25%-30%) or central regions (2%-5%) are less common.<sup>3</sup> CDH is accompanied by pulmonary hypoplasia and lack of normal bronchial and vascular branching patterns. This developmental anomaly leads to increased pulmonary vascular resistance and resultant significant pulmonary hypertension.<sup>4</sup> The exact etiology of CDH remains unclear but is currently suggested to be multifactorial. Even though the majority of cases might have an isolated diaphragmatic defect with pulmonary hypoplasia, CDH can be associated with cardiac and gastrointestinal anomalies or with chromosomal anomalies such as trisomies.<sup>1</sup> Major

determinants of outcome in CDH are thought to be the presence of associated anomalies, especially heart disease, and the severity of lung hypoplasia. Late presentation is also associated with a good prognosis.<sup>5</sup> Surgical repair of CDH is not an urgent treatment, and could be delayed according to the stability of the cardiac and pulmonary status of the patient. In the circumstance that the pulmonary system is stabilized evidenced by adequate urine output, adequate preductal oxygenation, and reduced pulmonary artery pressure, surgery is undertaken. Repair of the CDH could be accomplished through a thoracic or abdominal approach, and both open and minimally invasive approaches were accepted and performed.<sup>5,6</sup> Management of CDH requires integrated multidisciplinary care across the perinatal phases up to childhood. Medical and surgical advances in the management of CDH resulted in the improvement of overall survival. The recent survival rate was reported to be 63%-90% in various studies.<sup>1,7</sup> Despite the pulmonary condition and associated anomalies, characteristics of the hernia such as liver herniation, presence of hernia sac, and size and diameter of the defect seem to be related to the post-operative outcome.<sup>8,9</sup> The aim of this study was to evaluate the effect of surgical and morphologic factors such as the presence of hernia sac and defect size on the

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prognosis of CDH in Tabriz children's hospital.

## Methods

This prospective study was approved by the Ethics Committee of Tabriz University of Medical Sciences in 2016 (IR.TBZMED.REC.1398.254). All the infants with the primary diagnosis of CDH that were admitted in the Tabriz children's hospital since 2016-2019 were enrolled in this study and informed consent was obtained from the patient's parents. Patients with unstable pulmonary and heart conditions which were undesirable to perform surgery or expired before surgery treatment were excluded from the study. Data was obtained from the parents and obstetrics and pediatric reports about the prenatal diagnosis and ultrasound findings, gestational age and birth weight, general condition and vital signs at birth time, intubation requirement, and diagnosis time before referral to the neonatal ward or neonatal intensive care unit of Tabriz children's hospital. Initial management was performed by the cooperation of pediatricians and pediatric surgeons in order to diagnose the disease and its associated anomalies as well as stabilizing pulmonary artery hypertension. Extracorporeal membrane oxygenation (ECMO) was not available in our center for advanced oxygenation support. When the patients were stabilized according to adequate urine output, adequate preductal oxygenation, and improved pulmonary condition were planned for surgery under the recommendation of pediatricians. Abdominal open surgery was the preferred surgery in our center and was performed after appropriate preoperative evaluations. During the surgery, herniated organs were reduced in to the abdominal cavity, the presence or absence of hernia sac was evaluated, and the largest diameter on diaphragmatic defect was measured using a sterile ruler. The defect was repaired by primary closure or a synthetic patch if the primary closure was not feasible. Concurrent malrotation (non-fixation of the bowel) or other abdominal abnormalities were investigated. Postoperative outcomes, including instability, duration of mechanical ventilation, mortality rate, or hospital discharge, were followed. Recurrence or need to additional abdominal surgery was also noted. All the data from the preoperative condition, surgical characteristics, and postoperative outcome were collected in checklists. Statistical analysis was performed using IBM SPSS statistics version 24.0. The power of this study was 80%. Descriptive statistics were expressed as mean and standard deviation for quantitative variables and frequency (percentage) for qualitative analysis. Chi-square/Fisher exact tests were used to compare categorical variables and a Student's *t* test for continuous variables.  $P \leq 0.05$  was considered significant in all statistical analysis.

## Results

Over the study period, 30 patients with CDH met the inclusion criteria, consisting of 15 males and 15 females. The mean age at diagnosis time was  $4.45 \pm 2.61$  days,

ranging from 3 hours to 28 days. Mean birth weight of patients was  $3.10 \pm 0.45$  kg.

Seven (23.33%) cases of CDH were diagnosed by prenatal ultrasound studies. Fifteen cases (50%) were diagnosed during the first 24 hours of life, the other 9 cases became symptomatic and admitted during the first week of life. Six patients had delayed manifestations. Sixteen cases experienced duo to hypoxia in the first hour after birth.

Echocardiographic study revealed severe pulmonary artery hypertension in 3 patients and mild to moderate pulmonary artery hypertension in 5 patients. There were no major cardiac anomalies in preoperative studies; patent ductus arteriosus in 13 cases was the most common echocardiographic findings, and atrial septal defect in 12 cases was the next common finding in which the majority were small in size or closing. During additional diagnostic studies, one case of congenital unilateral agenesis of the kidney was observed. Patients' characteristics and preoperative blood pH,  $\text{HCO}_3$  concentration and  $\text{PCO}_2$  and  $\text{O}_2$  saturation are listed in Table 1.

As expected, 26 (86.66%) patients had a defect in the left side, 3 (10%) patients had right-sided defects, and diaphragmatic defect was bilateral in one case. All patients were operated by abdominal open approach. The most common herniated organ was Spleen. Colon and small bowel was the next common herniated organ. Herniated organs into the thoracic cavity divided to the affected side are shown in Table 2. Mean diameter of the defect size was  $4.42 \pm 1.47$  cm and hernia sac were present in the 9 cases (30%). Bowel malrotation (non-fixation of the bowel) was noticed in 20 cases (66.66%).

The mortality rate was 9 cases (30%) in the postoperative period, and 21 (70%) patients were survived.

Mean diameter of defect size was measured  $4.12 \pm 0.61$  cm in survived group and  $4.61 \pm 0.48$  cm in non-survived group. Defect size  $\leq 4$  cm was significantly smaller in survived patients ( $P=0.041$ ). The hernia sac was present in the 9 cases. Postoperative death occurred in 9 (42.85%) patients without hernia sac. Results showed that none of the cases with hernia sac expired ( $P=0.035$ ). The frequency of prognostic factors and survived and non-survived groups are illustrated in Table 3. The percentage of prognostic factors in survived and non-survived groups are shown in Figure 1. Mean gestational age was  $37.12 \pm 1.54$  weeks in the presence of hernia sac and  $38.15 \pm 1.27$  in the absence of hernia sac ( $P=0.336$ ).

Mean days on mechanical ventilation was  $6.43 \pm 8.81$  days, mean days of mechanical ventilation in survived patients was  $7.66 \pm 9.91$  days. Three patients were extubated after surgery and did not undergo mechanical ventilation. One patient was reoperated due to bowel perforation, no case of recurrence was observed.

## Discussion

CDH is a complex congenital malformation with

**Table 1.** Characteristics and clinical findings in survived and non-survived group

Variable	Survived (n=11)	Non-survived(n=19)	P value
Age (day)	4.36±2.14	4.66±2.81	0.505
Gestational age (wk)	37.69±2.96	38.33±1.22	0.538
Birth weight (kg)	3.00±0.38	3.15±0.41	0.640
Preductal O <sub>2</sub> saturation during the first hour of birth (%)	89.05±5.14	86.66±6.04	0.512
Preoperative HCO <sub>3</sub>	26.77±6.07	21.25±6.93	0.069
Preoperative PCO <sub>2</sub>	43.72±5.23	57.51±23.41	0.050
Preoperative blood pH	7.35±.07	7.28±0.8	0.025

**Table 2.** Herniated organs into the thoracic cavity

	Left-sided (%)	Right-sided (%)	Bilateral	Total (%)
Intestine	24	2	1	27
Spleen	24	0	1	25
Liver	12	2	1	15
Stomach	13	0	1	14
Colon	8	1	1	10
Kidney	2	0	0	2
Total cases	26	3	1	

challenging management. In the last decades, there was a great improvement in managing CDH according to advancements in neonatal care and selective usage of ECMO. One of the most important factors in the outcome of patients with CDH is the severity of pulmonary hypertension. Currently, it is estimated that about 30% of mortality in CDH is the consequence of lung hypoplasia and/or pulmonary hypertension.<sup>10</sup> However, pulmonary hypertension is not the only issue that determines the outcome.

Traditionally, liver herniation is known as a bad prognostic factor in the surgical outcome of patients with CDH. In our study, mortality rate in cases with liver herniation was 77.77% versus 22.23% in cases without liver herniation ( $P=0.045$ ). It seems that liver herniation which is common in right-sided CDH is one of the prognostic factors in CDH, but it should be evaluated separately in right- and left-sided hernia. We suggest that the presence of the liver in the thoracic cavity in left-sided CDH mostly indicates a large defect in the diaphragm with the early herniation of abdominal viscera that may result in severe

pulmonary hypoplasia and poor outcome.

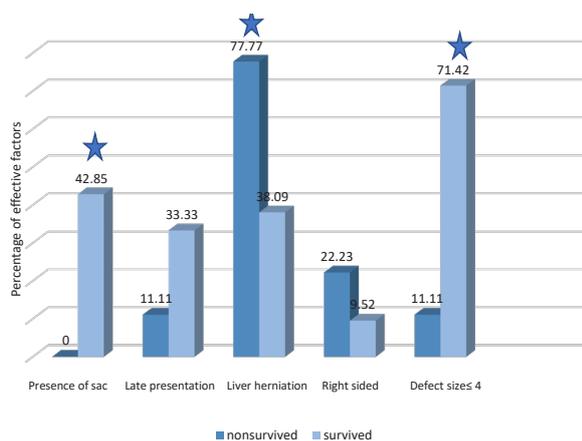
Our study demonstrated a better prognosis in smaller hernia defect size as Congenital Diaphragmatic Hernia Study Group was reported that the size of diaphragmatic defect is the major factor influencing outcome in infants with CDH.<sup>11</sup> That is why the defect-diaphragmatic ratio is becoming a new parameter for the assessment of CDH.<sup>12</sup>

The side of herniation, herniated organs, and age at the time of surgery had no significant correlation with the outcome in this study. Hernia sac was observed in 30% of patients in our study. The reported incidence of hernia sac is approximately 20% in different studies ranging from 13% to 26% of CDH patients.<sup>9,13,15</sup> In our study, in the presence of hernia sac, there was not any observed death which was statistically higher than patients without sac ( $P=0.033$ ). Several studies corroborated hernia sac as a positive prognostic factor in the outcome of patients with CDH. They reported that the presence of a hernia sac in CDH was associated with a better outcome, especially survival at 6 months.<sup>9,14,15</sup> However, Levesque studied 71 patients with CDH and showed that mortality did not differ in presence or absence of hernia sac; nevertheless, the presence of a hernia was associated with decreased inhaled nitric oxide, vasoactive medication, and ventilator use.<sup>8</sup>

The exact impact of hernia sac in CDH is unknown. The sac was mentioned as a good prognostic factor that protects the lungs from being compressed, and it is suggested that the presence of sac in CDH is evidence of late herniation.<sup>9</sup> The difference in the outcome of patients with or without hernia sac could be somehow explained by the better development of lung in the size and volume

**Table 3.** Prognostic factors in survival of CDH

	Survived	Non-survived	Total	P value
Male gender	10 (47.61%)	5 (55.55%)	15	0.500
Presence of hernia sac	9 (42.85%)	0 (0%)	9	0.035
Defect size ≤4 cm	15 (71.42%)	1 (11.11%)	16	0.041
Right sided hernia	2 (9.52%)	2 (22.22%)	4	0.345
Presentation by hypoxia after birth	11 (52.38%)	5 (55.55%)	16	0.596
Late presentation	7 (33.33%)	1 (11.11%)	8	0.214
Liver herniation	8 (38.09%)	7 (77.77%)	15	0.045
Total	21	9	30	



**Figure 1.** The percentage of prognostic factors in survived and non survived groups

in the cases with hernia sac. This was reported by Oliver et al in 2019 studying 200 cases of unilateral CDH, which 46 (23%) had hernia sac with a higher mean lung-to-head ratio and a higher mean observed/expected LHR. Also, they had a higher mean observed/expected total lung volume on MRI (0.53 vs. 0.41;  $P < 0.01$ ). It seems that the length of stay in the hospital is positively affected by the presence of the sac.<sup>16</sup> Some studies reported the mean gestational age at diagnosis was higher in the presence of a hernia sac.<sup>9</sup> The limitations of this study were the inability to measure primary hypertension and the inability to evaluate the extent of pulmonary hypoplasia.

## Conclusion

In our study there was not any significant difference in gestational age between two groups. Future research efforts should be directed to accurately assess the degree of pulmonary hypoplasia related to defect size and in the presence of hernia sac. Prospective multicenter studies should be designed in order to perform a better evaluation of surgical prognostic factors that determine the survival rate in patients with CDH.

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## Authors' contribution

### Study Highlights

#### What is current knowledge?

- Congenital Diaphragmatic Hernia is congenital malformation with challenging management.

#### What is new here?

- The presence of hernia sac is good prognostic factor for CDH
- Large defect size is poor prognostic factor

DB and SA conceived of the presented idea. MJ developed the theory and performed the computations. NH and MG verified the analytical methods. DB and SA supervised the findings of this work. All authors discussed the results and contributed to the final manuscript.

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None.

## Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

## Conflict of Interest

Authors declare no conflict of interest in this study.

## References

1. Chandrasekharan PK, Rawat M, Madappa R, Rothstein DH, Lakshminrusimha S. Congenital diaphragmatic hernia-a review. *Matern Health Neonatol Perinatol.* 2017;3:6. doi: 10.1186/s40748-017-0045-1.
2. Puligandla PS, Skarsgard ED, Offringa M, Adatia I, Baird R, Bailey M, et al. Diagnosis and management of congenital diaphragmatic hernia: a clinical practice guideline. *CMAJ.* 2018;190(4):E103-E12. doi: 10.1503/cmaj.170206.
3. Dingeldein M. Congenital diaphragmatic hernia: management & outcomes. *Adv Pediatr.* 2018;65(1):241-7. doi: 10.1016/j.yapd.2018.05.001.
4. Pascall E, Tulloh Robert MR. Pulmonary hypertension in congenital heart disease. *Future Cardiology.* 2018;14(4): 343-353. doi: 10.2217/fca-2017-0065.
5. Kadir D, Lilja HE. Risk factors for postoperative mortality in congenital diaphragmatic hernia: a single-centre observational study. *Pediatr Surg Int.* 2017;33(3):317-23. doi: 10.1007/s00383-016-4032-9.
6. Kotecha S, Barbato A, Bush A, Claus F, Davenport M, Delacourt C, et al. Congenital diaphragmatic hernia. *Eur Respir J.* 2012;39(4):820-9. doi: 10.1183/09031936.00066511.
7. Fallahi M, Mohajerzadeh L, Borhani S, Kazemian M, Roozroukh M, Khaleghnejad-Tabari A, et al. Outcomes of congenital diaphragmatic hernia: an 8-year experience. *Iran J Pediatr.* 2017;27(2):e9144. doi: 10.5812/ijp.9144.
8. Levesque M, Derraugh G, Schantz D, Morris MI, Sawyer A, Lum Min SA, et al. The presence of a hernia sac in isolated congenital diaphragmatic hernia is associated with less disease severity: a retrospective cohort study. *J Pediatr Surg.* 2019;54(5):899-902. doi: 10.1016/j.jpedsurg.2019.01.016.
9. Aydin E, Lim FY, Kingma P, Haberman B, Rymeski B, Burns P, et al. Congenital diaphragmatic hernia: the good, the bad, and the tough. *Pediatr Surg Int.* 2019;35(3):303-13. doi: 10.1007/s00383-019-04442-z.
10. Gucciardo L, Deprest J, Done E, Van Mieghem T, Van de Velde M, Gratacos E, et al. Prediction of outcome in isolated congenital diaphragmatic hernia and its consequences for fetal therapy. *Best Pract Res Clin Obstet Gynaecol.* 2008;22(1):123-38. doi: 10.1016/j.bpobgyn.2007.08.006.
11. Lally KP, Lally PA, Lasky RE, Tibboel D, Jaksic T, Wilson JM, et al. Defect size determines survival in infants with congenital diaphragmatic hernia. *Pediatrics.* 2007;120(3):e651-7. doi: 10.1542/peds.2006-3040.
12. Rygl M, Kuklova P, Zemkova D, Slaby K, Pycha K, Stranak Z, et al. Defect-diaphragmatic ratio: a new parameter for assessment of defect size in neonates with congenital diaphragmatic hernia. *Pediatr Surg Int.* 2012;28(10):971-6.

- doi: 10.1007/s00383-012-3113-7.
13. Bouchghoul H, Marty O, Fouquet V, Cordier AG, Senat MV, Saada J, et al. Congenital diaphragmatic hernia has a better prognosis when associated with a hernia sac. *Prenat Diagn.* 2018;38(9):638-44. doi: 10.1002/pd.5326.
  14. Panda SS, Bajpai M, Srinivas M. Presence of hernia sac in prediction of postoperative outcome in congenital diaphragmatic hernia. *Indian Pediatr.* 2013;50(11):1041-3. doi: 10.1007/s13312-013-0276-9.
  15. Spaggiari E, Stirnemann J, Bernard JP, De Saint Blanquat L, Beaudoin S, Ville Y. Prognostic value of a hernia sac in congenital diaphragmatic hernia. *Ultrasound Obstet Gynecol.* 2013;41(3):286-90. doi: 10.1002/uog.11189.
  16. Oliver ER, DeBari SE, Adams SE, Didier RA, Horii SC, Victoria T, et al. Congenital diaphragmatic hernia sacs: prenatal imaging and associated postnatal outcomes. *Pediatr Radiol.* 2019;49(5):593-9. doi: 10.1007/s00247-018-04334-9.