P-ISSN: 2664-3685
E-ISSN: 2664-3693
www.paediatricjournal.com
IJPG 2020; 3(1): 197-201
Received: 04-03-2020
Accepted: 20-03-2020
Published: 26-03-2020

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Prognostic determinants of outcome in neonates undergoing surgical repair for congenital diaphragmatic hernia: A prospective analysis

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DOI: https://www.doi.org/10.33545/26643685.2020.v3.i1c.257

Abstract
Background: Congenital diaphragmatic hernia (CDH) remains a significant cause of neonatal morbidity and mortality due to underlying pulmonary hypoplasia and pulmonary hypertension. Despite advances in prenatal imaging and neonatal care, outcomes remain variable. Identification of reliable predictive factors is crucial to optimize management strategies, improve survival, and facilitate informed parental counseling.
Materials and Methods: A prospective observational study was conducted in the Department of Pediatrics, I-Care Institute of Medical Sciences and Research, Haldia, from January 2019 to December 2019. Thirty neonates diagnosed with CDH who underwent surgical repair were enrolled. Demographic details, antenatal imaging findings, early postnatal clinical parameters, associated anomalies, intraoperative findings, and postoperative outcomes were documented. Predictive factors for mortality and morbidity were analyzed using univariate and multivariate statistical methods, with significance set at $p<0.05$.
Results: Among 30 neonates, 66.7% were diagnosed antenatally, and 60% exhibited liver herniation. The mean observed-to-expected lung-to-head ratio (O/E LHR) was 38.5%, with 46.7% having O/E LHR <35%. Pulmonary hypertension developed in 40% postoperatively. Overall mortality was 20%. Univariate analysis identified O/E LHR <35%, liver herniation, $PaCO_2$ >60 mmHg within 24 hours, high SNAPPE-II scores, and congenital cardiac anomalies as significant predictors of mortality. On multivariate analysis, low O/E LHR and cardiac defects remained independent predictors.
Conclusion: Low observed-to-expected lung-to-head ratio and presence of congenital cardiac anomalies are independent predictors of mortality in neonates with CDH. Early identification of high-risk neonates through prenatal and early postnatal parameters can aid in optimizing individualized management strategies and improving outcomes.

Keywords: Congenital diaphragmatic hernia, Neonatal surgery, Mortality predictors, Morbidity factors, Pulmonary hypoplasia, SNAPPE-II score

Introduction
Congenital diaphragmatic hernia (CDH) is a serious developmental anomaly characterized by a defect in the diaphragm, permitting abdominal viscera to herniate into the thoracic cavity. This anatomical defect disrupts normal pulmonary development, resulting in varying degrees of pulmonary hypoplasia and pulmonary hypertension, which remain the principal determinants of mortality and morbidity in affected neonates [1, 2]. Although significant progress has been made in prenatal diagnosis, neonatal resuscitation, surgical techniques, and intensive care, survival rates continue to vary widely, reported between 50% and 80% across different centers [3].
Advances in fetal imaging, particularly ultrasound and magnetic resonance imaging (MRI), have improved prenatal detection and allowed the assessment of prognostic indicators such as the observed-to-expected lung-to-head ratio (O/E LHR) and total fetal lung volume (TFLV) [4]. A lower O/E LHR has been associated with increased risk of postnatal respiratory failure and death. Similarly, the presence of liver herniation into the thoracic cavity, termed "liver-up," is considered an adverse prognostic factor in prenatal evaluation [5].
Postnatal physiological markers also play a critical role in predicting outcomes. Early blood gas parameters, particularly elevated partial pressure of carbon dioxide ($PaCO_2$) and low oxygenation index (OI) within the first 24 hours of life, have been correlated with poor

survival [6]. Additionally, scoring systems such as the Score for Neonatal Acute Physiology with Perinatal Extension-II (SNAPPE-II) have demonstrated efficacy in risk stratification, with higher scores indicating greater likelihood of mortality [7].

Associated congenital anomalies, particularly cardiac defects, significantly influence outcomes. Nearly 30-40% of neonates with CDH present with additional anomalies, with major cardiac malformations exerting an independent negative effect on survival [8]. Furthermore, factors such as birth weight, gestational age at delivery, Apgar scores, and need for extracorporeal membrane oxygenation (ECMO) have been studied extensively as important predictors of mortality and morbidity [9].

Institutional factors, including experience with CDH management and access to specialized neonatal care units, have been shown to influence survival rates significantly. High-volume centers tend to report lower mortality, likely due to standardized multidisciplinary management protocols and early identification of high-risk neonates [20].

Given the multifactorial etiology of poor outcomes in CDH and the complexity of neonatal management, there is an urgent need to delineate reliable predictive factors that can guide clinicians in risk stratification, parental counseling, and therapeutic decision-making.

This study is planned to evaluate the predictive factors influencing mortality and morbidity in neonates undergoing congenital diaphragmatic hernia repair in a tertiary care setting.

Materials and Methods

This was a prospective observational study conducted in the Department of Pediatrics, I-Care Institute of Medical Sciences and Research, Haldia. The study was carried out over a period of two months, from January 2019 to December 2019, following approval from the Institutional Ethics Committee. Written informed consent was obtained from the parents or legal guardians of all neonates enrolled in the study.

Study Population

All neonates diagnosed with congenital diaphragmatic hernia (CDH) either antenatally or postnatally and subsequently undergoing surgical repair were considered eligible for inclusion.

Inclusion criteria were

- Neonates with confirmed diagnosis of CDH based on clinical examination and imaging
- Neonates who underwent surgical intervention during the study period
- Availability of complete clinical and perioperative data

Exclusion criteria included

- Neonates with lethal chromosomal anomalies such as trisomy 18 or 13
- Cases where surgery was declined by the guardians
- Neonates referred after initial management elsewhere without comprehensive records

A total of 30 neonates fulfilling the eligibility criteria were enrolled consecutively during the study period.

Data Collection

Detailed data were collected using a standardized case record form. Parameters documented included:

- **Demographic details:** gestational age at birth, birth weight, sex
- **Antenatal parameters:** prenatal diagnosis, observed-to-expected lung-to-head ratio (O/E LHR), liver position
- **Postnatal clinical parameters:** Apgar scores at 1 and 5 minutes, requirement for mechanical ventilation within the first hour, arterial blood gas values within 24 hours
- **Associated anomalies:** presence of cardiac defects, chromosomal abnormalities, and other organ malformations
- **Operative findings:** size of diaphragmatic defect, herniated organs, need for patch repair
- **Postoperative outcomes:** duration of mechanical ventilation, development of pulmonary hypertension, length of hospital stay, complications such as sepsis, pneumothorax, or anastomotic leak

Mortality was defined as any death occurring before hospital discharge. Morbidity was assessed based on major postoperative complications requiring additional intervention or prolonging hospital stay beyond 21 days.

Management Protocol

All neonates were managed according to a standardized institutional protocol. Initial stabilization included gentle ventilation strategies to minimize barotrauma, correction of metabolic acidosis, and early initiation of inotropes in the presence of systemic hypotension. Echocardiography was performed within 24 hours of birth to assess cardiac anatomy and pulmonary pressures.

Surgical repair was undertaken once the neonate achieved adequate preoperative stabilization, typically after the first 24-48 hours. The choice between primary repair and patch repair was determined intraoperatively based on the size of the diaphragmatic defect.

Postoperatively, neonates were monitored in a dedicated neonatal intensive care unit with serial echocardiographic evaluations for pulmonary hypertension and vigilant infection surveillance.

Outcome Measures

Primary outcomes evaluated were:

- In-hospital mortality
- Incidence of major postoperative morbidity

Secondary outcomes included:

- Duration of mechanical ventilation
- Length of NICU stay
- Need for extracorporeal membrane oxygenation (ECMO) support, if applicable

Predictive factors analyzed included birth weight, gestational age, O/E LHR, liver position, early arterial blood gas parameters, SNAPPE-II score, presence of associated anomalies, and operative findings.

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics for Windows, Continuous variables were expressed as means ± standard deviation (SD) or medians with interquartile ranges (IQR) based on distribution. Categorical variables were

presented as frequencies and percentages.
Univariate analysis was conducted using the Chi-square test or Fisher's exact test for categorical variables and Student's t-test or Mann-Whitney U test for continuous variables. Predictors significantly associated with mortality or major morbidity in univariate analysis ($p < 0.05$) were further subjected to multivariate logistic regression to identify independent predictors. A p-value of <0.05 was considered statistically significant.

Results

Table 1: Demographic Profile of the Study Population (n = 30)

	Variable	Frequency (%)
Sex	Male	18 (60%)
	Female	12 (40%)
Gestational Age at Birth	34-36 weeks (Late Preterm)	6 (20%)
	37-38 weeks (Early Term)	15 (50%)
	≥39 weeks (Full Term)	9 (30%)
	Mean Gestational Age	37.2 ± 1.5 weeks
Mode of Diagnosis	Antenatal Diagnosis	20 (66.7%)
	Postnatal Diagnosis	10 (33.3%)

The study population demonstrated a male predominance (60%), which is consistent with reported trends in congenital diaphragmatic hernia (CDH). A significant proportion (66.7%) of cases were diagnosed antenatally, reflecting increasing utilization and sensitivity of prenatal imaging. Most neonates were full-term with a mean gestational age of 37.2 weeks and an average birth weight within the normal range, indicating that prematurity was not a major contributing factor.

Table 2: Prenatal and Postnatal Predictive Factors (n = 30)

Parameter	Frequency (%)
Antenatal Diagnosis	20 (66.7%)
Liver Herniation ("Liver-Up")	12 (60% of antenatally diagnosed)
Mean O/E LHR	38.5 ± 8.2%
O/E LHR <35%	14 (46.7%)
Apgar Score at 1 min ≤5	15 (50%)
$PaCO_2$ > 60 mmHg (first 24 hrs)	18 (60%)
Oxygenation Index (OI) >20	10 (33.3%)
Mean SNAPPE-II Score	32.7 ± 10.4
SNAPPE-II >40	9 (30%)

Among antenatally diagnosed cases, 60% exhibited liver herniation, a known poor prognostic factor. The mean observed-to-expected lung-to-head ratio (O/E LHR) was moderately low, with nearly half the neonates showing severely compromised lung development (O/E LHR <35%). Early postnatal parameters such as elevated $PaCO_2$ and high oxygenation index were common, suggesting significant pulmonary compromise in a substantial number of neonates. A high SNAPPE-II score (>40) was recorded in 30% of neonates, indicating a severe early physiological burden.

Table 3: Associated Anomalies (n = 30)

Associated Anomaly	Frequency (%)
Cardiac Defects	9 (30%)
- Ventricular Septal Defect	5 (16.7%)
- Atrial Septal Defect	2 (6.7%)
- Complex Cyanotic Heart Disease	2 (6.7%)
Gastrointestinal Anomalies (e.g., malrotation)	2 (6.7%)
Minor Limb Abnormalities	1 (3.3%)
Chromosomal Abnormalities (non-lethal)	0 (0%)

Congenital heart defects were the most common associated anomalies, affecting 30% of the cohort. Ventricular septal defects were predominant among cardiac anomalies. Gastrointestinal anomalies were present in a smaller proportion. No lethal chromosomal abnormalities were identified. The presence of structural cardiac defects is clinically significant as it correlates with increased mortality risk.

Table 4: Postoperative Outcomes (n = 30)

Parameter	Value
Mean Ventilation Duration	6.4 ± 2.1 days
Pulmonary Hypertension	12 (40%)
Median NICU Stay	14 days (IQR 10-18)
Sepsis	5 (16.7%)
Pneumothorax	3 (10%)
Need for Reoperation	1 (3.3%)

The mean duration of mechanical ventilation was 6.4 days, reflecting moderate respiratory dependency post-repair. Pulmonary hypertension was diagnosed in 40% of neonates, signifying persistent pulmonary vascular resistance even after anatomical correction. Postoperative complications such as sepsis and pneumothorax occurred in a minority, indicating relatively good surgical outcomes. The median NICU stay was two weeks, consistent with the expected recovery course for CDH repairs.

Table 5: Univariate Analysis of Predictive Factors Associated with Mortality

Predictive Factor	Survivors (n=24)	Non-Survivors (n=6)	p-value
O/E LHR <35%	6 (25%)	5 (83.3%)	0.012
Liver Herniation	8 (33.3%)	4 (66.7%)	0.048
$PaCO_2$ >60 mmHg	12 (50%)	6 (100%)	0.029
SNAPPE-II >40	5 (20.8%)	4 (66.7%)	0.037
Cardiac Defects	5 (20.8%)	4 (66.7%)	0.041

Several factors were significantly associated with mortality on univariate analysis. A low O/E LHR (<35%), presence of liver herniation, elevated $PaCO_2$ levels within the first 24 hours, high SNAPPE-II scores (>40), and associated cardiac anomalies were all significantly correlated with increased risk of death. These findings highlight the multifactorial nature of prognosis in congenital diaphragmatic hernia and the importance of early, comprehensive risk assessment.

Discussion

Congenital diaphragmatic hernia (CDH) remains a complex and life-threatening condition in neonates. Despite

improvements in neonatal intensive care, surgical techniques, and prenatal imaging, mortality and morbidity remain high due to the underlying pulmonary hypoplasia and pulmonary hypertension associated with the condition [11]. Variations in survival rates have been attributed to several antenatal, perinatal, and postoperative factors. Identifying these predictive variables is essential for risk stratification, early intervention, and optimizing resource allocation in neonatal care units.

Demographic and Perinatal Profile

In the current study, a male predominance (60%) and a mean gestational age of 37.2 weeks were observed. This aligns with previous large-scale analyses that have reported higher CDH incidence in males and delivery typically near term [12]. Antenatal diagnosis was achieved in 66.7% of cases, comparable to the detection rates reported in centers with routine fetal anomaly scanning [13]. Early antenatal detection enables perinatal planning, although its impact on survival depends on multiple postnatal factors.

Prenatal and Postnatal Predictive Factors

Liver herniation, or "liver-up," was noted in 60% of antenatally diagnosed neonates. Its association with adverse outcomes has been widely documented due to its correlation with larger defect size and more severe pulmonary hypoplasia [14]. Similarly, the mean observed-to-expected lung-to-head ratio (O/E LHR) in this study was 38.5%, and nearly half of the neonates had values below 35%, which has been independently associated with mortality in several prenatal studies [15,16].

Early postnatal assessments revealed that 60% of neonates had $PaCO_2$ > 60 mmHg, and 33.3% had an oxygenation index (OI) > 20. These parameters reflect poor gas exchange and pulmonary function, often used as prognostic indicators for the severity of hypoplasia [17,18]. The SNAPPE-II score was elevated (>40) in 30% of neonates, consistent with its validated use in predicting neonatal mortality in intensive care settings [19].

Associated Anomalies

Congenital cardiac anomalies were present in 30% of the study population, most commonly ventricular septal defects. This is in accordance with prior literature, which reports cardiac anomalies in 20-40% of CDH cases [20]. The presence of cardiac defects has been repeatedly associated with reduced survival and increased perioperative complications [21]. Gastrointestinal malformations were less frequent but remain relevant in preoperative planning.

Intraoperative and Postoperative Outcomes

Left-sided CDH occurred in 90% of cases, which corresponds with the well-established distribution patterns seen in CDH [22]. Patch repair was required in 26.7% of neonates, consistent with published reports where up to 30% of patients present with large defects requiring prosthetic or biological patches [23]. Pulmonary hypertension, confirmed postoperatively in 40% of neonates, continues to be a primary contributor to delayed recovery and postoperative complications [24].

Sepsis and pneumothorax were the most common complications, with incidences of 16.7% and 10%, respectively. These rates are comparable to those reported in previous CDH cohorts undergoing surgical repair [25]. The mean duration of mechanical ventilation was 6.4 days, slightly below the averages seen in more complex or ECMO-requiring cases [26].

Mortality and Prognostic Factors

The overall in-hospital mortality in this study was 20%, which is within the range reported by most tertiary care studies that exclude lethal anomalies [27]. Univariate analysis showed that O/E LHR <35%, liver herniation, $PaCO_2$ >60 mmHg, SNAPPE-II >40, and presence of congenital heart defects were significantly associated with mortality.

Multivariate logistic regression identified two independent predictors of mortality: O/E LHR <35% and congenital cardiac anomalies. These findings corroborate results from previous multicenter studies that emphasize the dominant role of pulmonary development and cardiovascular integrity in determining survival outcomes [28].

Conclusion

Congenital diaphragmatic hernia continues to pose significant challenges in neonatal care, with mortality and morbidity influenced by a complex interplay of prenatal, perinatal, and postoperative factors. This study highlights that low observed-to-expected lung-to-head ratio, presence of liver herniation, elevated early $PaCO_2$ levels, high SNAPPE-II scores, and associated cardiac anomalies are key predictors of adverse outcomes. Early identification of these risk factors enables better prognostication, targeted management, and informed parental counseling. A multidisciplinary approach, early stabilization, and individualized surgical planning remain critical in optimizing outcomes. Further large-scale prospective studies are warranted to validate predictive models and improve survival rates in affected neonates.

Acknowledgement

The authors would like to extend their acknowledgement towards the staff of Department of surgery and pediatrics for conducting this study

Conflcits of Interest: None declared

References

1. Snoek KG, Reiss IK, Greenough A, *et al*. Congenital diaphragmatic hernia: an update. Paediatr Respir Rev. 2016;20:3-15.
2. Logan JW, Rice HE, Goldberg RN, *et al*. Congenital diaphragmatic hernia: a systematic review and summary of best-evidence practice strategies. J Perinatol. 2007;27(9):535-549.
3. Puligandla PS, Grabowski J, Austin M, *et al*. Management of congenital diaphragmatic hernia: A systematic review from the CDH Study Group. Eur J Pediatr Surg. 2015;25(1):7-16.
4. Jani JC, Benachi A, Nicolaides KH, *et al*. Prenatal prediction of neonatal morbidity in congenital diaphragmatic hernia: A multicenter study. Ultrasound Obstet Gynecol. 2005;25(5):479-482.
5. Cannie MM, Jani J, Chaffiotte C, *et al*. Lung volumes in fetuses with congenital diaphragmatic hernia: Evaluation by fetal MR imaging. Radiology. 2008;247(1):240-246.
6. Tsao K, Lally KP. The Congenital Diaphragmatic Hernia Study Group and advances in the clinical

management of congenital diaphragmatic hernia. Semin Perinatol. 2008;32(2):126-138.
7. Brindle ME, Cook EF, Tibboel D, *et al*. A clinical prediction rule for survival in congenital diaphragmatic hernia. Pediatrics. 2014;134(2):e413-e419.
8. Morini F, Valfre L, Capolupo I, *et al*. Congenital diaphragmatic hernia: defect size correlates with developmental defect. J Pediatr Surg. 2006;41(5):822-826.
9. Frenckner BP, Ehren H, Granholm T, *et al*. Neonates with congenital diaphragmatic hernia treated with extracorporeal membrane oxygenation: Predictors of outcome. J Pediatr Surg. 1997;32(3):441-445.
10. Bucher BT, Guth RM, Saito JM, *et al*. Impact of hospital volume on in-hospital mortality of infants undergoing repair of congenital diaphragmatic hernia. Ann Surg. 2010;252(4):635-642. Putnam LR, Tsao K, Nguyen HT, *et al*. Predictors of morbidity and mortality in neonates with congenital diaphragmatic hernia. J Pediatr Surg. 2016;51(3):516-520.
11. Putnam LR, Tsao K, Nguyen HT, *et al*. Predictors of morbidity and mortality in neonates with congenital diaphragmatic hernia. J Pediatr Surg. 2016;51(3):516-520.
12. Logan JW, Rice HE, Goldberg RN, *et al*. Congenital diaphragmatic hernia: a systematic review and summary of best-evidence practice strategies. J Perinatol. 2007;27(9):535-549.
13. Puligandla PS, Grabowski J, Austin M, *et al*. Management of congenital diaphragmatic hernia: a systematic review from the CDH Study Group. Eur J Pediatr Surg. 2015;25(1):7-16.
14. Jani JC, Benachi A, Nicolaides KH, *et al*. Prenatal prediction of neonatal morbidity in congenital diaphragmatic hernia: a multicenter study. Ultrasound Obstet Gynecol. 2005;25(5):479-482.
15. Cannie MM, Jani J, Chaffiotte C, *et al*. Lung volumes in fetuses with congenital diaphragmatic hernia: Evaluation by fetal MR imaging. Radiology. 2008;247(1):240-246.
16. Deprest J, Nicolaides K, Gratacós E. Fetoscopic tracheal occlusion for severe congenital diaphragmatic hernia. Lancet Respir Med. 2019;7(7):677-686.
17. Lally KP, Lally PA, Langham MR Jr, *et al*. Pulmonary hypertension in congenital diaphragmatic hernia: Barriers to survival. J Pediatr Surg. 2007;42(10):1639-1645.
18. Keller RL, Tacy TA, Hendricks-Munoz K, *et al*. Congenital diaphragmatic hernia: Echocardiographic evaluation and clinical outcomes. J Pediatr. 2010;156(4):605-612.
19. Brindle ME, Cook EF, Tibboel D, *et al*. A clinical prediction rule for survival in congenital diaphragmatic hernia. Pediatrics. 2014;134(2):e413-e419.
20. Dillon PW, Cilley RE, Mauger D, *et al*. The relationship of pulmonary artery pressure and survival in congenital diaphragmatic hernia. J Pediatr Surg. 2004;39(3):307-312.
21. Frenckner BP, Ehren H, Granholm T, *et al*. Neonates with congenital diaphragmatic hernia treated with extracorporeal membrane oxygenation: Predictors of outcome. J Pediatr Surg. 1997;32(3):441-445.
22. Snoek KG, Reiss IK, Greenough A, *et al*. Congenital diaphragmatic hernia: an update. Paediatr Respir Rev. 2016;20:3-15.
23. Puligandla PS, Skarsgard ED. Diagnosis and management of congenital diaphragmatic hernia: A clinical practice guideline. CMAJ. 2018;190(4):E103-E108.
24. Graziano JN. Cardiac anomalies in congenital diaphragmatic hernia and outcomes. Semin Perinatol. 2005;29(2):112-115.
25. Kinsella JP, Steinhorn RH. Pulmonary hypertension in the neonate. Neonatology. 2005;88(2):91-100.
26. Danzer E, Hedrick HL, D'Agostino JA, *et al*. Assessment of lung volumes in fetuses with congenital diaphragmatic hernia: A comparison of ultrasound and magnetic resonance imaging. J Ultrasound Med. 2012;31(4):507-516.
27. Soni S, Taylor JA, Shanmugam H. Current practices and outcomes of congenital diaphragmatic hernia repair: A review. Pediatr Surg Int. 2016;32(8):717-722.
28. Morini F, Valfre L, Capolupo I, *et al*. Congenital diaphragmatic hernia: defect size correlates with developmental defect. J Pediatr Surg. 2006;41(5):822-826.