Original Article

DOI: 10.7860/JCDR/2026/84559.22485

Determinants of Postoperative Mortality in Neonates with Congenital Diaphragmatic Hernia: A Prospective Observational Study from a Tertiary Care Centre, Southern India

Neonatology Section

AM SHAMEEM[1], KS DEEPA[2], V ARUN PREETH[3], S GIREESH[4], K MOHANDAS NAIR[5]

ABSTRACT

Introduction: Congenital Diaphragmatic Hernia (CDH) is a life-threatening developmental anomaly characterised by a defect in the diaphragm that allows abdominal viscera to herniate into the thoracic cavity, leading to pulmonary hypoplasia and pulmonary hypertension. Despite advances in prenatal diagnosis, neonatal intensive care, and surgical techniques, the management of CDH continues to pose considerable clinical challenges, particularly in resource-constrained settings.

Aim: To determine the outcomes and identify the risk factors associated with mortality in neonates undergoing surgical repair for CDH.

Materials and Methods: The present hospital-based prospective observational study was conducted in the Departments of Paediatrics, Neonatology, and Paediatric Surgery at Government Medical College, Kozhikode, Kerala, India, from 1st January 2021 to 31st December 2022. All neonates diagnosed with CDH who underwent surgical repair were included in the study. The standard institutional protocol was followed, which included preoperative stabilisation, risk stratification for surgical candidacy, early decision-making regarding operative intervention, and continuation of postoperative ventilation.

Results: During the study period, out of 5,850 Neonatal Intensive Care Unit (NICU) admissions, 72 neonates were diagnosed with CDH. Of these, 44 (61.1%) underwent surgical correction. The mean gestational age was 38±1.63 weeks, and the mean birth weight was 2,850±508 g. Post-repair survival to discharge was 79.5% (35 neonates), while 9 of the 44 operated neonates (20.5%) died in the postoperative period. The presence of Pulmonary Hypertension of the Newborn (PPHN), intraoperative hypothermia, postoperative air leak, and associated congenital anomalies were significantly associated with increased postoperative mortality in the present study cohort.

Conclusion: Preoperative clinical stability, intraoperative hypothermia, and the presence of PPHN were found to be significantly associated with postoperative mortality in neonates undergoing surgery for CDH.

Keywords: Limited resources, Neonate, Pulmonary hypertension, Risk factors

INTRODUCTION

The CDH is a life-threatening developmental anomaly characterised by a defect in the diaphragm that allows abdominal viscera to herniate into the thoracic cavity, resulting in pulmonary hypoplasia and pulmonary hypertension. With an estimated incidence of 1 in 3,000 live births, CDH represents a significant cause of neonatal morbidity and mortality worldwide [1]. The cornerstone of postnatal management involves optimising respiratory support through mechanical ventilation, effective management of PPHN, and timely surgical correction. Contemporary treatment protocols emphasise meticulous preoperative stabilisation followed by surgical repair once adequate physiological stability is achieved [2].

Postoperative outcomes in neonates with CDH are influenced by a complex interplay of prenatal, postnatal, and perioperative factors. Among prenatal predictors, the degree of pulmonary hypoplasia and the Lung-to-Head Ratio (LHR) on foetal imaging are strong determinants of survival [3]. Right-sided CDH, although less common, is associated with poorer outcomes due to diagnostic delays and a higher likelihood of hepatic herniation [4].

Postnatal physiological factors also play a crucial role in shaping prognosis. PPHN remains one of the most important contributors to mortality. Low APGAR scores, prematurity and low birth weight have been identified in multiple studies as significant predictors of adverse outcomes. The presence of major congenital malformations further increases the risk of mortality [2,5-7].

Intraoperative and postoperative factors also strongly influence survival. The size of the diaphragmatic defect often determines the need for patch repair and correlates with postoperative complications [8]. Postoperative sepsis continues to contribute significantly to mortality, particularly in resource-limited settings where overcrowding and limited critical care capacity challenge infection-control practices [9]. The timing of surgical intervention remains crucial, with delayed repair after adequate preoperative stabilisation now widely preferred, enabling optimisation of oxygenation and acid-base balance prior to surgery [2].

Despite advancements in neonatal intensive care and surgical techniques, survival disparities persist across regions. High-income countries report survival rates of 70-80%, owing to standardised care protocols, advanced ventilatory strategies, and availability of Extracorporeal Membrane Oxygenation (ECMO). In contrast, low and middle-income countries report survival rates between 38% and 72%, reflecting limitations in prenatal detection, neonatal stabilisation, and perioperative resources [6].

Understanding the major determinants of postoperative mortality is therefore essential for identifying areas of perioperative care that can be improved to enhance the overall survival of infants with CDH. Furthermore, there is a notable scarcity of data from low and middle-income countries, where differences in healthcare infrastructure, personnel availability, and access to neonatal intensive care may substantially influence outcomes. Hence, the present study aimed to determine the outcomes and identify

mortality-associated risk factors in neonates undergoing surgical repair for CDH.

MATERIALS AND METHODS

The present hospital-based prospective observational study conducted in the Departments of Paediatrics, Neonatology, and Paediatric Surgery at Government Medical College, Kozhikode, Kerala, India, from 1st January 2021 to 31st December 2022. The study protocol was reviewed and approved by the Institutional Ethics Committee (GMCKKD/RP/2021/IEC/10).

Inclusion and Exclusion criteria: All neonates diagnosed with CDH who underwent surgical repair during the study period were included. Neonates diagnosed with CDH but not operated upon, and those operated at outside hospitals, were excluded.

Sample size selection: Data from all 44 neonates who underwent surgical repair for CDH between 1st January 2021 and 31st December 2022 were collected consecutively using a structured proforma.

Study Procedure

All enrolled neonates were managed according to the standard NICU protocol. Delivery-room management included the presence of at least two skilled personnel, elective intubation, effective gastric decompression, and gentle ventilation using a T-piece resuscitator. Postnatal ventilatory management adhered to lung-protective strategies, targeting a preductal saturation >85% after the first hour of life, PCO_2 up to 65 mmHg while maintaining pH >7.25. Pressure-controlled, time-cycled conventional ventilation was used initially, with rescue high-frequency oscillatory ventilation considered for persistent hypercapnia or peak inspiratory pressure >25 cm H_2O.

PPHN was diagnosed clinically in neonates with preductal SpO_2 <85% and a ≥5% pre/post-ductal saturation difference and managed with sildenafil. Echocardiography was performed in all cases between 24-48 hours of life to assess structural heart defects and pulmonary artery pressures. PPHN was classified as mild, moderate or severe based on echocardiographic findings. Pulmonary Artery Systolic Pressure (PASP) was estimated using the formula PASP≈RVSP=4(Vmax TR)²+RAP, with RAP assumed to be 5 mmHg. PAP was categorised as <⅔ systemic (mild), ⅔-systemic (moderate), or suprasystemic (severe) [10,11]. Facilities for inhaled nitric oxide and ECMO were not available.

Surgical repair was performed when the neonate remained clinically stable for at least 24 hours, defined as FiO_2<50%, stable or decreasing inotropic requirement over the preceding eight hours, PaO_2>50 mmHg, lactate <3 mmol/L, and urine output >1 mL/kg/hour [2]. Data on demographic characteristics, prenatal diagnosis, preoperative vitals and ventilation parameters, perioperative temperature, intraoperative findings, and postoperative complications were collected. All neonates were followed up for 30 days.

STATISTICAL ANALYSIS

The collected data were entered in Microsoft Excel and analysed using PASW Statistics software, version 26. Operated cases were categorised into two groups (survivors and non-survivors). Patient demographics and hospital course were summarised and compared between the two groups. Categorical variables were analysed using the Chi-square test, and continuous variables using the student's t-test. Risk factors were assessed through multiple regression analysis and a p-value <0.05 was considered statistically significant.

RESULTS

During the study period, out of 5,850 NICU admissions, 72 neonates were diagnosed with CDH. Forty-four (61.11%) of the 72 neonates underwent surgical correction, of which 30 (68.18%) were inborn. During the initial phase of medical stabilisation, 28 (38.88%) neonates died before they could be taken up for surgery and were therefore not included in the analysis.

The mean gestational age of the operated neonates was 38±1.63 weeks, and the mean birth weight was 2,850±508 g. Among the 44 operated neonates, 30 (68.18%) were male and 14 (31.81%) were female. Antenatal diagnosis was made in 28 (63.63%) cases. All 44 operated cases had left-sided CDH, and half of the babies were delivered by Lower Segment Caesarean Section (LSCS). In the cohort, 4 neonates (9.09%) were preterm and 11 (25%) had low birth weight. Associated congenital anomalies were present in 13 neonates (29.54%), of which 4 (9.09%) had major anomalies. The major anomalies included a large Ventricular Septal Defect (VSD), Atrioventricular (AV) canal defect, high anorectal malformations, and two syndromic cases. Among neonates with dysmorphic features, one baby was diagnosed with Trisomy 21, while the other had a normal karyotype. Additionally, 36.36% of CDH cases (16 out of 44) were not detected antenatally.

Post-repair survival to discharge was 79.54% (35 neonates), while nine of the 44 operated neonates (20.45%) died in the postoperative period. Preoperative clinical stability was achieved in 38 out of 44 neonates (86.36%). Six neonates (13.63%) required a prolonged period of medical stabilisation and were taken up for rescue surgery after the first week of life with parental consent. Among these six, two survived and four died in the postoperative period. Of the four neonates who underwent surgery despite not meeting preoperative stability criteria and eventually died, two had syndromic features (one with Trisomy 21 and one with a normal karyotype).

Surgery was performed in 35 neonates (79.54%) by the third day of life. Primary repair was performed in all cases; no patch repairs were required. A hernia sac was noted intraoperatively in five cases (11.36%). A large diaphragmatic defect was present in 20 neonates (45.45%). Intraoperative hypothermia occurred in eight cases (18.18%), and 5 neonates (11.36%) were hypothermic on transfer from the operating room to the NICU. PPHN was documented in 21 of the 44 neonates (47.72%), of whom 10 (22.72%) had moderate to severe PPHN. Postoperative pneumothorax occurred in three neonates (6.81%). Probable sepsis was documented in 24 cases (54.54%), but culture-proven sepsis was present in only four neonates (9.09%).

PPHN, postoperative pneumothorax, intraoperative hypothermia, and delayed surgical repair beyond day 4 of life were significantly associated with mortality in operated CDH cases. The presence of PPHN was significantly associated with postoperative mortality (p=0.007). When the severity of PPHN was assessed, mortality was 9.09% in the mild PPHN group, compared to 71.42% and 66.67% in the moderate and severe PPHN groups, respectively (p=0.007). Intraoperative hypothermia also showed a significant association with mortality (p=0.034). Mortality risk was higher among neonates who underwent surgery after day 4 of life (p=0.032). This increased risk may be related to delayed surgery in babies who had not achieved clinical stability or had severe PPHN, contributing to poorer outcomes.

Pneumothorax significantly increased postoperative mortality, with two out of the three affected neonates dying (p=0.04). Although 66.7% of neonates with a large diaphragmatic defect died postoperatively, this finding was not statistically significant (p=0.46), likely due to the small sample size. Neonates with major congenital anomalies had a significantly higher risk of mortality (p=0.043). The presence of a large diaphragmatic defect and absence of a sac were associated with increased mortality but did not reach statistical significance (p=0.46).

No statistically significant increase in postoperative mortality was observed with respect to gender, prematurity, low birth weight, antenatal diagnosis, LHR, APGAR scores, or postoperative sepsis.

DISCUSSION

The findings highlight the prognostic importance of persistent PPHN, intraoperative hypothermia, postoperative air leak, preoperative clinical stability, and the presence of major congenital malformations in influencing outcomes. Although the presence of a large defect and absence of a hernia sac were more frequent in the mortality group, these associations did not reach statistical significance. Several antenatal and perinatal parameters- including birth weight, gestational age at diagnosis, liver position, LHR, APGAR scores, and size of the defect were also not significantly associated with mortality.

PPHN continues to be a major challenge in the management of CDH, often serving as a marker of severe pulmonary hypoplasia and impaired cardiopulmonary adaptation. In the present study, moderate to severe PPHN was significantly associated with poorer outcomes. Similar findings have been consistently reported in the literature, where the severity of PPHN has been shown to be a strong independent predictor of mortality despite advances in pulmonary vasodilator therapy and ECMO support [7,12].

Perioperative hypothermia emerged as another significant factor associated with mortality. Despite implementing preventive strategies such as warm mattresses and overhead heating devices, a considerable proportion of neonates still developed intraoperative hypothermia. This complication is known to increase metabolic demands, worsen acidosis, and impair coagulation, all of which may adversely affect postoperative outcomes. A study by Zhao J et al., demonstrated that temperature instability during neonatal surgery significantly contributes to poor outcomes [13]. The present study findings reaffirm the need for meticulous thermoregulation through coordinated efforts among Neonatologists, Paediatric Surgeons, and Anaesthesiologists.

The development of postoperative air leaks was also significantly associated with mortality in the present study. This likely reflects the severity of underlying pulmonary hypoplasia and the consequent need for higher ventilatory pressures to achieve adequate gas exchange. Masahata K et al., similarly noted that postoperative pneumothorax was associated with higher ventilator requirements, prolonged Intensive Care Unit (ICU) stays, and increased mortality [14]. Strategies such as gentle ventilation, permissive hypercapnia, and close monitoring of lung compliance remain essential to reduce this risk.

Associated congenital anomalies were also identified as a significant predictor of mortality, consistent with findings from several previous studies [3,4,6]. Delayed surgical repair beyond four days of life was another factor associated with higher mortality. This delay likely reflects prolonged or failed cardiopulmonary stabilisation often in neonates with severe PPHN and may have contributed to poorer postoperative outcomes.

Interestingly, variables traditionally regarded as predictors of mortality such as birth weight, gestational age, liver position, LHR, low APGAR scores, and antenatal diagnosis- were not statistically significant in our cohort. Similar observations were made by Sahoo T et al., who found that gestational age, birth weight, APGAR scores, and associated anomalies were not significant predictors of mortality [6]. One possible explanation is that many neonates with extreme prematurity, low birth weight, low APGAR scores, or major congenital malformations were not considered candidates for surgical repair due to clinical instability, and therefore were not included in this study.

Postoperative sepsis is widely recognised as a critical contributor to mortality in neonatal surgical conditions, especially in low and middle-income countries. However, unlike the findings reported by Lum LCS et al., postoperative sepsis in our cohort did not reach statistical significance [15]. This may be attributed to stringent infection control protocols and robust NICU practices at the study centre, which may have minimised the impact of sepsis on outcomes.

Limitation(s)

Advanced cardiopulmonary support modalities such as ECMO and inhaled nitric oxide were not available during the study period. The absence of these facilities may have influenced outcomes, particularly in neonates with severe PPHN.

CONCLUSION(S)

The current study reinforces the importance of achieving preoperative clinical stability, preventing intraoperative hypothermia, and effectively managing PPHN as key determinants of improved postoperative outcomes in neonates undergoing surgical repair for CDH. Larger multicentric studies are needed to validate these findings and to generate population-specific prediction tools that can guide clinical decision-making, optimise care planning, and improve resource allocation for these critically ill neonates.

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PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Paediatrics, Government Medical College, Kozhikode, Kerala, India.
2. Assistant Professor, Department of Neonatology, Government Medical College, Kozhikode, Kerala, India.
3. Professor, Department of Paediatric Surgery, Government Medical College, Kozhikode, Kerala, India.
4. Professor, Department of Paediatrics, Government Medical College, Kozhikode, Kerala, India.
5. Professor, Department of Paediatrics, Government Medical College, Kozhikode, Kerala, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
AM Shameem,
Thanal, Palayil Parambu, Kallithodi Road, Chungam,
Kozhikode-673631, Kerala, India.
E-mail: dramshameem@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Sep 25, 2025
- Manual Googling: Nov 27, 2025
- iThenticate Software: Nov 29, 2025 (11%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Sep 24, 2025**
Date of Peer Review: **Oct 22, 2025**
Date of Acceptance: **Dec 01, 2025**
Date of Publishing: **Mar 01, 2026**