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Research Article

Factors Influencing Morbimortality in Patients with Congenital Diaphragmatic Hernia at a Tertiary Pediatric Center in México

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Abstract

Introduction: Congenital diaphragmatic hernia (CDH) consists of a posterolateral defect of the diaphragm, generally located on the left side, that allows passage of the abdominal viscera into the thorax. This study aimed to analyze the factors that influence the morbidity and mortality of patients with congenital diaphragmatic hernia.

Methods: We conducted an observational, descriptive, cross-sectional, and retrospective study, analyzing electronic health records of neonates admitted to the neonatal intensive care unit at Hospital para el Niño Poblano from January 2010 to December 2019. Statistical analysis involved measures of central tendency, Chi-square tests for nominal variables, and risk assessments.

Results: The incidence of CDH was 4.4 cases per year, with a mortality rate of 32% and a survival rate of 68%. Left posterolateral diaphragmatic hernia predominated, and echocardiography revealed significant associations between patent ductus arteriosus (PDA) and increased mortality. Surgical complications occurred in 15% of patients, with mortality primarily resulting from severe pulmonary hypertension, cardiogenic shock, and septic shock.

Discussion: The study identified significant associations between mortality and factors such as mode of delivery, positive pressure ventilation at birth, PDA, and severe pulmonary hypertension. Survival rates showed an inverse correlation with the severity of pulmonary hypertension.

Conclusion: The persistence of patent ductus arteriosus and severe pulmonary hypertension emerged as primary factors associated with increased mortality. Despite challenges, Hospital para el Niño Poblano maintained a commendable survival rate, underscoring the importance of a dynamic, multidisciplinary approach in neonatal care for CDH patients.

Keywords: *Congenital Diaphragmatic Hernia; Neonatal Intensive Care; Pulmonary Hypertension; Neonatal Mortality*

Introduction

Congenital Diaphragmatic Hernia (CDH) consists of a posterolateral defect of the diaphragm, generally located on the left side (Bochdalek), that allows passage of the abdominal viscera into the thorax. The mediastinum is displaced to the contralateral side, the lungs are hypoplastic and their arterioles are abnormal causing pulmonary hypertension. Respiratory and cardiovascular functions are severely compromised at birth and this, together with the frequently associated malformations, cause considerable mortality and morbidity [1].

The CDH it accounts for 8% of congenital malformations, with an estimated prevalence of 1 to 4 in 10,000 live births. Approximately 60% of cases can be diagnosed through routine ultrasound between 18 - 22 weeks of gestation [2].

The medical management is in a neonatal intensive care unit (NICU) or pediatric intensive care unit (PICU). Given the complex medical and surgical nature of these infants, many collaboratives have sought to standardize management guidelines to decrease variation in care and improve overall outcomes. Surgery to correct the diaphragmatic defect is necessary, but the timing of the surgery is still controversial. Persistent pulmonary hypertension is the most serious post-surgical complication [2,3].

Objective of the Study

The main objective of this study is to analyze the factors that influence the morbidity and mortality of patients with congenital diaphragmatic hernia at the Hospital para el Niño Poblano.

Methods

We conducted an observational, descriptive, cross-sectional, and retrospective study, analyzing the electronic health records of patients diagnosed with congenital diaphragmatic hernia who were admitted to the neonatal intensive care unit at Hospital para el Niño Poblano from January 2010 to December 2019. Our inclusion criteria comprised records of newborns aged between 1 and 28 days who received treatment for CDH in the neonatal intensive care unit at Hospital para el Niño Poblano. Conversely, records of patients diagnosed with this condition beyond 28 days of age and those not admitted to the NICU were excluded from the analysis.

Statistical analysis involved using simple frequencies and percentages, along with measures of central tendency. Descriptive statistical elements were evaluated using the SPSS software. Nominal variables were analyzed through the Chi-square test, and a risk assessment was conducted. A value of $p < 0.05$ was deemed statistically significant.

Results

A total of 47 records of neonates diagnosed with congenital diaphragmatic hernia were identified from our database from January 2010 to December 2019. Three records were excluded as the patients were not admitted to the neonatal intensive care unit. Subsequently, a comprehensive analysis was conducted on the remaining 44 records.

The incidence rate of cases of patients diagnosed with congenital diaphragmatic hernia was approximately 4.4 admissions per year, with a total of 44 patients admitted to the neonatal intensive care unit during the period of this study.

Table 1 presents the main characteristics of newborns admitted to the NICU, revealing a higher frequency among males, comprising 29 patients (66%), in contrast to 15 females (34%).

	Frequency	Percentage (%)
Female	15	34
Male	26	66
	Average	Range
Gestational Age (Weeks)	38	29-42
Age at Admission to NICU (Days)	3	1-14
Age at Surgery (Days)	5	1-17
Birth Weight	2.9	1.115-4.45

Table 1: *General characteristics of newborns.*

All patients were referred from other hospitals to our unit and had an average age at admission of 3 days, as specified in table 1. Birth conditions and details of neonatal resuscitation are provided in table 2.

	Frequency	Range
Apgar at 5 Minutes	8	6-9
	Frequency	Range
Intubation at Birth	10	22.7%
Use of Positive Pressure Ventilation	17	38.6%
Use of CPAP after Resuscitation	10	22.7%

Table 2: *Birth conditions and during resuscitation.*

The primary characteristics of congenital diaphragmatic hernia are detailed in table 3. The most common location was on the left posterolateral side, observed in 39 cases (88.6%), while the location on the right posterolateral side was noted in 5 patients (11.4%). Liver herniation was identified in 11 patients, constituting 27.5% of the cases, and the presence of a hernia sac was recorded in 16 patients, representing 40% of the sample. Pulmonary hypoplasia was reported in 71% of the patients.

Characteristics	Frequency	Percentage
Left posterolateral location	39	88.6%
Right posterolateral location	5	11.4%
Liver Herniation	11	27.5%
Presence of Hernia Sac	16	40%
	Average	Range
Pulmonary Hypoplasia	71%	0-95%

Table 3: *Main characteristics of congenital diaphragmatic hernia.*

Echocardiography was performed upon admission. Table 4 provides an overview of the observed findings. A total of 21 patients (47.7%) showed no association with congenital heart disease. The most prevalent congenital heart condition was patent ductus arteriosus, present in 12 patients (27.2%). The remaining cases exhibited alterations in the atrial and ventricular septa.

	Frequency	Average
Without congenital heart disease.	26	60%
Patent ductus arteriosus.	12	27.7%
Atrial Septal Defects.	3	6.8%
Ventricular Septal Defects.	2	3.3%
Atrial Septal Defects and Ventricular Septal Defects.	1	2.2%

Table 4: *The association of congenital diaphragmatic hernia with congenital heart disease.*

Surgery was conducted on 40 out of the 44 patients diagnosed with congenital diaphragmatic hernia, with 4 deaths recorded prior to the surgical intervention. Among the patients undergoing surgery, postoperative complications were observed in 15% (n = 6). These complications included volvulus in 5% (n = 2), re-herniation of the defect, also in 5% (n = 2), intestinal perforation in 2.5% (n = 1), and chylothorax in 2.5% (n = 1).

The mortality of patients with Congenital Diaphragmatic Hernia from 2010 to 2019 was 32%, with a survival rate of 68% (Table 5). Figure 1 illustrates the annual mortality.

Mortality	14	32%
Survival Rate	30	68%

Table 5: *Mortality of patients with congenital diaphragmatic hernia in the neonatal intensive care unit (NICU) of the HNP.*

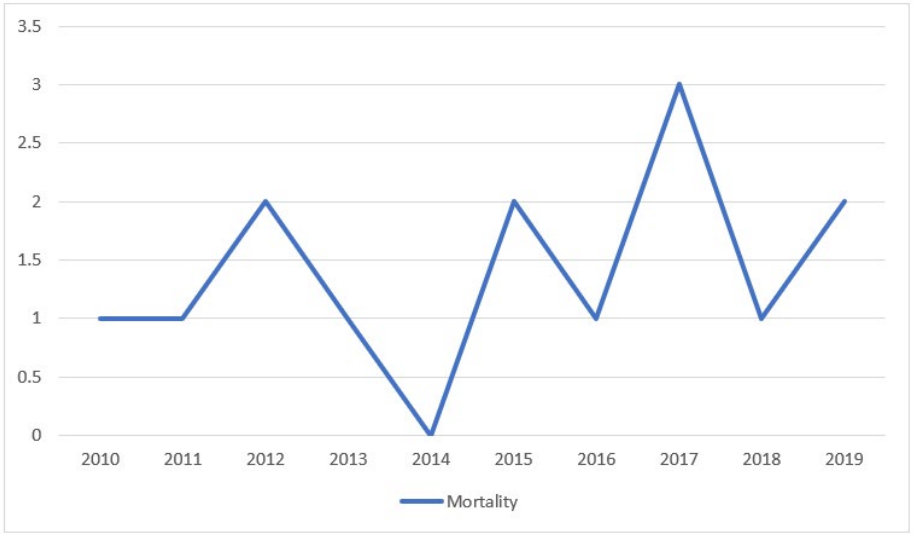

Figure 1: *Mortality by year in patients with congenital diaphragmatic hernia in the NICU of the HNP.*

A descriptive analysis of variables was undertaken, assessing risk factors through Chi-square analysis, and exploring associated risks for each variable. We assessed conditions at birth, resuscitation maneuvers, and various factors influencing patient outcomes, such as persistent ductus arteriosus, the severity of pulmonary hypertension, high frequency ventilatory therapy, and congenital diaphragmatic hernia characteristics.

Table 6 offers a detailed overview of birth conditions and the assessment of mortality risk in patients with prenatal diagnoses. On the other hand, nine patients were delivered by cesarean section, showing a significant association with a p-value of 0.009, suggesting an increased risk of mortality associated with cesarean delivery. However, no significant results were found concerning gestational weeks, birth weight less than 2500 grams, or prenatal diagnosis.

	N = 44	*p	OR	IC de 95%
Birth weight < 2500 grams.	3	0.913	1.09	0.23 - 5.1
Preterm product (<37 weeks of gestational age).	2	0.84	0.85	0.18 - 3.8
Cesarean section (C-section).	9	0.009	2.30	1.3 - 4.4
Prenatal diagnosis.	0	0.22	1.1	0.98 - 1.25

Table 6: *Birth conditions.*

We examined the newborn's conditions at the time of delivery, assessing cases that required intubation from birth, as well as those needing positive pressure ventilation or the use of nasal CPAP in the first hours of life. A significant result was only observed in patients who received positive pressure ventilation (PPV) at birth (Table 7).

	N = 44	*p	OR	IC de 95%
APGAR score < 7 at 5 minutes.	3	0.82	1.1	0.3 - 3.7
Intubation at birth.	4	0.52	1.4	0.47 - 4.2
Positive Pressure Ventilation.	11	0.001	3.9	1.8 - 8.4
Use of CPAP.	4	0.3	1.7	0.6 - 5.22

Table 7: *Evaluation of the newborn at the moment of birth.*

The patient's comorbidities and alterations were examined, including the association with patent ductus arteriosus, the presence of severe pulmonary hypertension, the time elapsed until defect correction, and the treatment used, including the use of pulmonary vasodilators. A statistically significant result was observed only in the association with patent ductus arteriosus and those with severe pulmonary hypertension (Table 8).

	N=44	*p	OR	IC de 95%
Association with Patent Ductus Arteriosus.	7	0.005	3.7	1.46 - 9.5
Pulmonary pressure > 60 mmHg.	7	0.033	3.3	1 - 10
Surgical intervention after 3 days of life.	6	0.692	1.12	0.65 1.9
Use of High-Frequency Oscillatory Ventilation.	1	0.69	0.66	0.083 - 5.3
Requires management of Persistant Pulmonary Hypertension	5	0.4	1.4	0.6 - 3.4

Table 8: *Conditions influencing the evolution and management of the patient.*

In the analysis of congenital diaphragmatic hernia characteristics, no statistically significant values were identified that would elevate mortality risk in relation to the degree of pulmonary hypoplasia, herniation of the liver, or the absence of a hernia sac.

The management of pulmonary hypertension in patients with congenital diaphragmatic hernia at our hospital includes the administration of pulmonary vasodilators, such as nitric oxide, sildenafil, milrinone, and prostaglandin E. Table 9 provides details on the

evaluation of mortality concerning the severity of pulmonary hypertension. Among patients without pulmonary hypertension (PAH), the mortality rate was low, at 7.1%. As pulmonary arterial pressure increased, a progressive escalation in mortality rates became apparent. In the subgroup with PAH ranging from 25 to 45 mmHg, the mortality rate was 14.3%, whereas in the 45 - 60 mmHg range, it escalated to 28.6%. PAH surpassing 60 mmHg correlated with a mortality rate of 50%. Conversely, when analyzing survival outcomes, an inverse correlation was found. Patients without PAH exhibited an 83.3% survival rate, which declined with increasing PAH. In the subgroup with PAH ranging from 25 to 45 mmHg, survival dropped to 46.7%, in the 45 - 60 mmHg range it reduced to 30%, and among those with PAH exceeding 60 mmHg, survival was only 6.6%.

	No PAH	25 - 45 mmHg	45 - 60 mmHg	> 60 mmHg
Deceased (n = 14)	1	2	4	7
Percentage	7.1%	14.3%	28.6%	50%
Survival (n = 30)	16.7%	46.7%	30%	6.6%

Table 9: *Pulmonary hypertension and mortality.*

Out of the 40 patients undergoing surgical intervention, 10 died in the postoperative period, with an average of 3.3 days after surgery, of which 40% passed away within the first 48 hours following the surgical procedure. The primary causes of death included severe pulmonary hypertension in 7 patients, cardiogenic shock in 4 patients, and septic shock in 3 patients, with a total of 14 reported fatalities.

The overall survival of patients with CDH hospitalized in the neonatal intensive care unit between 2010 and 2019 was 68% (30 patients), with an average hospital stay of 30.7 days and an average gestational age of 38 weeks. Mortality was 32% (14 patients), with 22.7% dying in the immediate postoperative period and 9.3% before surgical intervention. Table 10 provides detailed information on the main characteristics of the surviving patients.

Overall Survival	68%
Average Gestational Age	38 weeks
Without Prenatal Diagnosis	93%
Average Age at Repair	5 days
Days of Mechanical Ventilation	15.3 days
Days of Parenteral Nutrition	16 days
Days of In-Hospital Stay	30.7 days
Post-Surgical Complications	15%

Table 10: *Characteristics of surviving patients with CDH.*

Discussion

The Hospital para el Niño Poblano is a tertiary-level healthcare facility, that has a neonatal intensive care unit (NICU), which receives patients with complex surgical conditions, including patients with congenital diaphragmatic hernia, who are initially treated in second-level hospitals, most do not have a prenatal diagnosis, so the management is even more complex. In our study, only 3 patients had a prenatal diagnosis, but without assessing mortality or morbidity factors described in the literature.

In the study period (January 2010 to December 2019) an incidence of 4.4 cases per year was found, with a mortality of 32% and a survival of 68% of these patients, compared to that reported by Canadian Pediatric Surgery Network (CAPSNet) 80%.

The variables that occurred most frequently were male sex, an average age of 38 gestational weeks, a weight of 2900 grams, and an age of 3 days. However, these variables did not show a significant relationship that would increase the risk of mortality.

The left posterolateral diaphragmatic hernia was the most observed, consistent with the information mentioned in all the cited literature. Of these, 27.5% (11 patients) had liver herniation, and 40% (10 patients) had a hernia sac. However, these clinical aspects were not significant as factors related to higher mortality.

The echocardiogram is one of the diagnostic tools most frequently used for the comprehensive assessment of the patient. It is recommended to perform it in the first 48 hours of life to assess cardiac anatomy and function, the size of the pulmonary arteries (McGoon index), the severity of pulmonary hypertension and the presence and direction of both ductal and intracardiac shunts, ventricular function and to determine the presence of congenital heart disease [1,4], in the study carried out, no complex congenital heart diseases were identified. However, a significant result was observed in relation to the presence of Patent Ductus Arteriosus (PDA) and the increased mortality ($P < 0.05$). Additionally, there was an increase in mortality among those with severe pulmonary hypertension (> 60 mmHg) ($P < 0.05$), establishing a correlation with the consulted literature.

Severe pulmonary hypertension was the main complication and cause of mortality in patients admitted to the Neonatal Intensive Care Unit (NICU) of the Hospital para el Niño Poblano, as well as right and left ventricular dysfunction for which intensive aminergic management was required. The systematic administration of vasopressors is recommended in the presence of left ventricular dysfunction. Furthermore, the measurement of left ventricular mass is also an indicator of survival, as reduced mass is associated with a worse prognosis [5,6].

The pharmacological treatment used in these patients as part of the management of pulmonary hypertension, involving the use of pulmonary vasodilators, included the use of Milrinone, Sildenafil, and Nitric Oxide. Noori., *et al*. reviewed 7 CDH patients with pulmonary hypertension noting improvement in cardiac output due to acute decrease in pulmonary arterial pressures within 1 - 4 hours after administration of sildenafil, with improvement in oxygenation [7]. In the same way, prostaglandins were used to treat 2 patients with pulmonary arterial hypertension, which is a treatment that is used to provide ductus arteriosus patency may allow for right ventricular pressure relief, leading to improved right ventricular function and allowing time for pulmonary vascular relaxation.

Currently, the management of the CDH whit extracorporeal membrane oxygenation (ECMO), is controversial. According to the Extracorporeal Life Support Organization (ELSO), the survival rates reported by them have continued to drop in the modern era. However, systematic reviews regarding the benefit of ECMO in Congenital Diaphragmatic Hernia (CDH) did not find an advantage for ECMO [8].

Likewise, it has been demonstrated that the use of ECMO as a standard rescue therapy in isolated congenital diaphragmatic hernias, is undoubtedly an effective therapy in the management of severe pulmonary hypertension, whit survival reported from 50 to 70% in some centers and even exceed 80% in patients with poor prognostic factors [9]. Despite the fact that the use of ECMO is not yet standardized, it is considered an indispensable tool in our hospital that could greatly benefit our patients with this pathology.

The management of these patients with HDC is dynamic and multidisciplinary, where neonatologists must collaborate with other medical subspecialties to establish the degree of hypoplasia and pulmonary hypertension, as well as the degree of ventricular dysfunction. This involves providing appropriate treatment tailored to the patient's needs to improve the survival of HDC patients. Despite the lack of resources, new technologies, and the adoption of protocols from developed countries such as the use of ECMO, the Hospital para el Niño Poblano maintains a low mortality rate compared to other healthcare units.

Conclusion

From January 2010 to December 2019, there was an annual incidence of 4.4 patients diagnosed with congenital diaphragmatic hernia admitted to the Neonatal Intensive Care Unit. The mortality rate during these 10 years was 32%, while the survival rate was 68%. The persistence of the patent ductus arteriosus and the presence of severe pulmonary hypertension (> 60 mmHg) were identified as the primary factors associated with an increased risk of mortality. The leading causes of death included severe pulmonary hypertension and heart failure. Surgical complications occurred in 15% of the patients, encompassing issues such as intestinal volvulus, re-herniation, intestinal perforation, and chylothorax. Genetic studies were not conducted in these cases, and there was no association with other genetic syndromes.

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