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Outcome of Congenital Diaphragmatic Hernia: A Single Center Experience

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ABSTRACT

Background: Congenital diaphragmatic hernia (CDH) is a complex malformation with a challenging perioperative care. The outcome is still not very impressive in developing countries despite its remarkable improvement in developed countries.

Methods: We analyzed outcomes, and factors associated with morbidity and mortality of 120 newborns with CDH, managed at our institution.

Results: The overall survival was 73.4%. Chromosomal aberrations, pneumothorax within 24 hours, left ventricular hypoplasia, biventricular dysfunction, fetal lung to head ratio (LHR) <40, were considered as factors of poor prognosis.

Conclusion: This is the largest series of a retrospective cohort study of CDH reported in India. We have briefly reviewed the topic and the management guidelines along with prognostic markers derived from this study.

Key words: Congenital diaphragmatic hernia; Newborn; Outcome; Factors; Survival; Developing country

INTRODUCTION

Congenital diaphragmatic hernia (CDH) is a major congenital malformation with an incidence of approximately one in 2500-3000 deliveries.[1] The outcome has significantly improved owing to advances in the management. Therapeutic principles have changed from early surgery to pre-surgery hemodynamic stabilization with better understanding of the fetal lung parenchymal and vascular development.[2] Several variable predictors of poor outcome have been identified in various studies.[3-9] In this single center study, we have reviewed the outcome of newborns with CDH and attempted to identify predictors of outcome in our cohort.

MATERIALS AND METHODS

Data of 120 newborns with CDH admitted to the NICU at Amrita Institute of Medical Sciences, from 2013 to 2018 was reviewed for gestational age, birthweight, associated congenital anomalies, APGAR scores, antenatal diagnosis including LHR (lung to head ratio) and position of liver, initial pH, use of vasopressors, echocardiographic findings, ventilatory modality, age at surgery, presence of pneumothorax, surgery (open vs thoracoscopic), length of stay of survivors, time of death (postnatal age in hours), sepsis, and persistent pulmonary hypertension. Variables were compared statistically in survivor and non-survivors. Kaplan Meier survival curve was used to detect the time of death and the probability of survival at different postnatal age in days.

RESULTS

Demography:

Mean gestational age (GA) and birthweight were 37.5±2 weeks and 2806±580 grams, respectively. Antenatal diagnosis was made in 96 cases (80%) at a mean age of30.5 ±5.9 weeks gestation. Twenty-one (17.5%) newborns transferred to our NICU and 99 (82.5%) were inborn. Males were 67 (55.8%) and 53 (44.2%) females. Right sided diaphragmatic hernia was present among 7 babies; 2 babies had defects involving both sides and in the rest 111 babies

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(92.5%) the defect was on the left side. Thirty-six (30%) babies were born vaginally and the rest by C-section. (Table 1).

Table. 1. Demographics and selected variables

	Survivors (n=88)	Non-survivors (n=32)	P
Gest. Age	37.6±1.75	37.4±2.76	0.6
BW (gm)	2830± 550	2685± 670	0.2
Inborn:outborn	71%:86%	29%:14%	0.18
Male:Female	72%:81%	28%:19%	0.1
Anomalies	0	8	0.00
Left:Right lesions	75%:66%	25%:34%	0.3
Pneumothorax (≤ 24hr age)	9 (10.2%)	10 (31.25%)	0.009
Position of liver in thorax	20 (22.7%)	5 (15.6%)	0.3
PPHN	86.4%	100%	0.2
Ventricular Dysfunction	20%	80%	0.001
Fetal gest. at diagnosis (wk)	29±5.7	33±5.5	0.13
LHR <40	25%	75%	0.02

Gest: gestational; BW: Birth weight; PPHN: Persistent pulmonary hypertension; wk: weeks

Management:

Sixty-three infants (52.5%) were treated with only conventional mechanical ventilation. The mean duration of ventilation (pre/post-surgery) was 11.8±12 days. Fifty-seven infants (47.5%) were treated with HFOV when clinical condition deteriorated on conventional ventilation. The indication for HFOV was hypercarbia (PCO2 >65 mm Hg) in 42% of patients, and hypoxia in 58% of cases. Sixty-five (74%) infants had open (laparotomy) surgery and 23 infants (26%) had thoracoscopic/laparoscopic surgery.

Outcome:

Thirty-two babies (26.6%) died in this series. The mean age of death was 3.9±7 days (median: 1, and range=1-38). Twenty-eight babies in this group (87.5%) had not undergone surgery. Twenty-four babies (75%) died within 48 hours after birth (Table 2, Figure 1). Cause of death was severe PPHN and cardiac dysfunction. Two infants had undergone ECMO but died. Of the total group of non-survivors, 4 (12.5%) had undergone surgery and 2 died of sepsis and 2 died of other associated anomalies (TEF). These 4 infants had open surgery. The length of stay of survivors was 28±21 days (range: 14-170 days). Length of stay between open and minimally invasive method of surgery was not statistically significant (33±26 vs 23.5±9 days) (P=0.06). Infants who underwent minimally invasive surgery were not as unstable hemodynamically as the group who had open surgery and required less ventilatory support. There was no difference in the incidence of sepsis between infants who underwent open (38%) vs minimally invasive surgery (26%) (P=0.3).

Table 2. Kaplan Meier curve analysis, Estimates time-defined survival probabilities in cases

Time period (days)	n	Died	Survival probability	95% CI
1	120	20	0.83	0.75 – 0.89
2	100	4	0.8	0.71 – 0.86
7	96	4	0.76	0.67 – 0.83
30	92	3	0.74	0.65 – 0.81
60	89	1	0.73	0.64 – 0.80

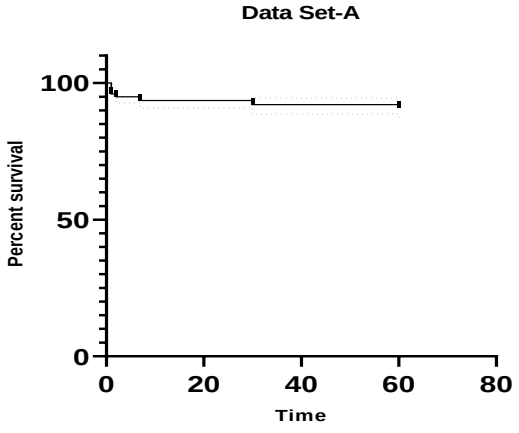

Figure. 1. Kaplan Meier Survival curve. The percent survival of CDH infants related to postnatal age. (x-axis is time in days). Eighty percent of mortality occurred within 3 days of birth and survival was not significantly affected afterwards.

Prognostic Factors:

Mean birthweight and gestational age of survivors and non-survivors were not proved as prognostic factors on univariate analysis. Similarly, side of the diaphragmatic defect, birth settings, gender ratio, position of liver in the abdomen or thorax, persistent pulmonary hypertension, surgery approach, and length of stay in open and minimal access groups, postoperative septicemia, mode of delivery, antenatal diagnosis and age at antenatal diagnosis were also not proved as factors of poor prognosis on univariate analysis (Table1).

In 43 cases, fetal LHR data was available from antenatal ultrasound examination. Mean LHR of survivors vs non-survivors was 49.8±12 and 43±10 (P=0.1), respectively. LHR of <40 was a significant poor prognostic factor on univariate analysis (OR: 6.66; CI 1.3 – 34) (P=0.02).

Nineteen infants developed pneumothorax within first 24 hours: 10 (52%) of these expired making it a poor prognostic factor (P=0.009). Similarly, associated congenital anomaly was a poor prognostic factor: all 8 infants who had associated congenital anomalies expired. These anomalies include tracheoesophageal atresia (2pts), Trisomy 21, Hypoplastic left heart syndrome, cerebral atrophy, renal anomalies, complex congenital cardiac malformation, duodenal web and hypoplastic aortic arch anomaly.

Nineteen (79%) of the 24 non-survivors without other congenital anomalies had moderate to severe ventricular dysfunction. Biventricular dysfunction was associated with 100% mortality. LV dysfunction contributed to more than 80% mortality.

DISCUSSION

CDH is a major anomaly that requires significant resources for successful outcome. Isolated CDH occurs in approximately 60-70% of the cases while in 30 to 40% of the cases, CDH is associated with anomalies of gastrointestinal, renal, cardiac, and nervous system. The outcome of newborns with CDH is poor if it is associated with other anomalies.[1] We also found that infants have poor prognosis if they have associated anomalies as none of them survived. With the advances in fetal diagnosis, intervention and neonatal intensive care, the reported survival from CDH has significantly increased and is currently around 75-80% in developed countries. Our study reveals that the survival outcome of CDH in our center is comparable to the data reported from developed countries.

The clinical presentation of CDH depends upon developmental status of lungs and heart. Newborns with severely compromised development usually do not survive beyond the first few hours of life. Those with moderate to severe pulmonary hypoplasia and hypertension with or without cardiac and ventricular dysfunction, are the most common form of clinical presentation. A small group of newborns (5-10%) with mild pulmonary hypoplasia and no pulmonary hypertension may not have significant symptoms at birth and present later [20]. In our study cohort 24 (20%) infants had severe pulmonary hypertension (suprasystemic pulmonary artery pressure) with ventricular dysfunction and all of them expired before surgery. Moderate to severe pulmonary hypertension (pulmonary pressures 50 to 100% of systemic artery pressure) was present in 86 (71.6%) infants and the mortality in this group was 9.3%. Ten (8.3%) infants had mild to no pulmonary hypertension and all of them survived.

ECMO is rarely done for CDH in India. We performed ECMO in 2 patients, but they died of sepsis. The indication for ECMO is severe cardiac dysfunction and severe pulmonary hypoplasia with pulmonary hypertension not responsive to pulmonary vasodilator therapy.

Our study shows that most of the non-survivors (75%) died within 48 hours of life [Table 2]. Two infants who had undergone surgery soon after birth had associated tracheoesophageal atresia (TEF) and both expired. Infants who had major associated anomalies also died within 48 hours of birth.

The factors that did not affect the outcome included gender, place of birth (in-born/out-born), presence of antenatal diagnosis, thoracic position of liver or stomach, site of the lesion (left/right), mode of delivery, and development of sepsis. In this cohort, 30% of newborns developed late onset sepsis and 97% of them survived. Previous studies have reported that the predictor's of poor outcome included lung to head ratio <1.4, significantly elevated PCO2 (>90) in the first 24 hours, severe PPHN with cardiac dysfunction, hypoplastic left ventricle and liver and stomach herniation to thorax and prematurity.[5,6, 9-12] Our data concur with these markers but liver and stomach herniation were not poor outcome predictors.

Treatment guidelines are based on the clinical condition of the newborn. In our series, all infants were intubated in the delivery room and sedated. This was done to reduce the distension of the stomach from crying which might compromise lung function. All infants were started on Milrinone infusion prior to the echocardiogram. Milrinone was discontinued if echocardiogram revealed normal pulmonary artery pressures with good ventricular function. We managed infants with permissive hypercarbia to reduce lung injury. This has been reported to have better outcome in CDH with reduced mortality.[13] When there is supra-systemic pulmonary artery pressure we tried to maintain systemic arterial pressures equal to or higher than pulmonary artery pressure to reduce right to left shunting at the ductus arteriosus or foramen ovale levels. For vasopressor effects we have used dopamine, dobutamine, epinephrine and low dose vasopressin infusions. Low dose vasopressin has been reported to improve hemodynamic status in infants with CDH.[2, 3, 13-19] In one study, vasopressin improved the oxygenation index.[2] Newborns with CDH have also been reported to have adrenal insufficiency and we have used hydrocortisone in physiological replacement doses in all infants who required vasopressor drug infusions.[17] Infants underwent surgery only when there was hemodynamic stability with significant improvements in oxygenation and ventilatory requirements.

Total parenteral nutrition (TPN) was provided from day of birth onwards. None of the infants were fed enterally before surgery. Enteral feeds were begun usually by the 7th post-operative day or earlier depending the presence of bowel sounds.

Retrospective nature and outcome evaluated up to only 2 months of age, were the limitations of this study. The strengths of this study include that it is one of the largest series reported from a single center; 82.5% of the babies were inborn babies which will reduce the effect of hidden mortality of CDH on the overall outcome.

CONCLUSION

In summary, we have presented a single center experience of the outcome of CDH. Our overall survival was 73.4%. Such high survival rates in infants

with CDH have not been reported previously in India. The factors that led to this outcome might be because of term gestation, pre-operative stabilization, early recognition and treatment of pulmonary hypertension and application of gentle ventilation with permissive hypercapnia. Multiple regression analysis revealed that poor biventricular cardiac function associated with pulmonary hypertension and CDH associated congenital anomalies were the most significant poor prognostic factors. Pulmonary hypertension with good ventricular function, side of the lesion and position of the liver were not significant poor prognostic factors. The etiology of the poor cardiac function may be related to the development of the ventricles and not necessarily related to the pulmonary hypertension.

Consent: Authors declared that they have taken informed written consent, for publication clinical photographs/material (if any used), from the legal guardian of the patient with an under-standing that every effort will be made to conceal the identity of the patient however it cannot be guaranteed.

Author Contributions: All the authors contributed fully in concept, literature review, and drafting of the manuscript and approved the final version of this manuscript.

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