Congenital diaphragmatic hernia in a developing country

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ABSTRACT

Introduction: Outcome of neonates with congenital diaphragmatic hernia (CDH) varies widely and the data from developing countries is scanty. We aimed to study the management and outcome of CDH. We also aimed to ascertain prenatal and postnatal factors affecting the outcome.

Methods: A retrospective review of neonates with CDH admitted to a teaching hospital was conducted. Demographical data, prenatal and postnatal factors, birth details, management and outcomes were studied. Survival was the primary outcome.

Results: 16 live-born neonates with diaphragmatic hernia were admitted during the study period. All neonates had hernia on the left side. Mean (standard deviation) gestational age and birth weight were 38.6 (1.5) weeks and 2,616.6 (457) g, respectively. Polyhydramnios was associated in one patient, and additional anomalies in five patients (31.3 percent). Overall survival was 56.3 percent. The CDH was detected prenatally in four and postnatally in 12 patients. 12 neonates underwent surgery and nine survived. Prenatally-detected cases had significantly reduced survival to surgery, overall survival and lower Apgar scores at one minute (p-value is less than 0.04). Median age at surgery was 48 hours. Average duration of mechanical ventilation among survivors was 91.5 hours. Neonatal intensive care unit stay ranged from five to 27 (median nine) days. Six of seven deaths occurred within 72 hours of life. Non-survivors had significantly low Apgar scores and were symptomatic within 12 hours of life (p-value is less than 0.03).

Conclusion: Greater than 50 percent survival of neonates with CDH was observed in a centre with conventional ventilation. Poor outcome is likely in neonates who present within 12 hours of life.

Keywords: congenital diaphragmatic hernia, neonatal hernia, neonatal survival

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INTRODUCTION

Neonates born with congenital diaphragmatic hernia (CDH) suffer substantial morbidity and mortality. Modalities of treatment are said to influence outcome apart from prenatal and postnatal factors. Reports from developed countries describe improved survival with high frequency ventilation, inhaled nitric oxide (iNO) and extracorporeal membrane oxygenation (ECMO), apart from delayed surgical repair.[1,2] Many centres in developing countries lack these advanced facilities, and hence, the outcome is expected to be different. The overall mortality rate for CDH remains high, despite increased prenatal detection, transfer to tertiary institutions for delivery, and advances in neonatal care. Though many institutions have reported significant improvements in the survival rates for neonates with CDH in the past decade, researchers have considered that these reports refer invariably to select populations of patients and often impose dubious exclusion criteria.[3] The population-based studies found consistent mortality rates over the past 30 years, ranging from 66% in the 1970s to 62% in the 1990s.[4] Therefore, although specific subgroups of infants may show improved survival rates compared with their predecessors, the overall mortality rate for this condition remains static. A recent large study from Australia found no change in the survival rate for live-born infants over the 12 years studied.[5] In the present study, we aimed to study management and outcome of CDH over a three-year period. We also sought to ascertain the prenatal and postnatal factors associated with the morbidity and mortality in these neonates.

METHODS

All neonates with CDH admitted to the neonatal intensive care unit (NICU) of Kasturba Medical College Hospital, India, between May 2003 and April 2006, were included in the study. The centre has a level II NICU equipped with facilities for mechanical ventilation (conventional) and other supportive measures, but lacks high frequency ventilation, iNO and ECMO. It is also associated with a good paediatric surgery team. In neonates with CDH, detailed information including timing of detection (prenatal or postnatal) of diaphragmatic hernia, presence of polyhydramnios, place of birth, mode of

Table I. Perinatal characteristics (n = 16).

Characteristics	No. (%)
Gender	
Male	12 (75.00)
Female	4 (25.00)
Diagnosis	
Prenatal	4 (25.00)
Postnatal	12 (75.00)
Place of birth	
Inborn	5 (31.25)
Outborn	11 (68.75)
Mode of delivery	
Vaginal	11 (68.75)
LSCS	5 (31.25)
Other congenital anomalies	
Minor	4 (25.00)
Major	1 (6.25)
No anomalies	11 (68.75)
Age at presentation (hours)	
At birth	10 (62.50)
< 12	1 (6.25)
12–24	2 (12.50)
> 24	3 (18.75)

Table II. Outcomes of neonates with CDH.

Outcomes	No. (%)		
	All cases (n = 16)	Prenatally detected (n = 4)	Postnatally detected (n = 12)
Live born	16 (100)	4 (100)	12 (100)
Died at (hours)			
< 24	2 (12.50)	1 (25.00)	1 (8.33)
24–72	4 (25.00)	3 (75.00)	1 (8.33)
> 72	1 (6.25)	0	1 (8.33)
Survival to surgery	12 (75.00)	1 (25.00)	11 (91.67)
Survival > one year	9 (56.25)	0	9 (75.00)

delivery, gestational age, birth weight, Apgar scores, presence of associated anomalies, side of defect, age at surgery, contents and location of hernia, postoperative complications, durations of mechanical ventilation and hospital stay, were collected. Outcomes were classified as neonatal death before seven days and survival beyond one year of age. Treatment of neonates with CDH included elective intubation, sedation with or without muscle relaxation and ventilation, according to the clinical criteria. All neonates underwent surgery at our paediatric surgical centre. Univariate analyses of continuous and categorical variables were conducted with the Mann-Whitney U-test and chi-square test or Fisher's exact test, as applicable. Statistical analysis of data was performed with the Statistical Package for Social Sciences for Windows version 11.5 software (SPSS Inc, Chicago, IL, USA).

RESULTS

A total of 16 neonates with CDH were admitted during the study period. The perinatal characteristics and outcomes are shown in Tables I and II. All were singleton pregnancies, live-born and had hernia on the left side. Gestational age ranged from 34 to 42 (mean [SD] 38.6 [1.5], median 38) weeks and birth weight ranged from 1,700 to 3,080 (mean [SD] 2,616.6 [457], median 2,762.5) g. Polyhydramnios was present in one case (6.3%). Nine (56.3%) neonates survived beyond one year of age. Of the 16 neonates with CDH, five (31.3%) had other associated anomalies. These included trisomy 21 (bilateral cleft lip and palate, malformed left pinna, preauricular tag, nuchal fold and karyotype showing trisomy 21), urogenital anomalies (hypospadiasis, undescended testis with inguinal hernia), posterior cleft palate and natal teeth in one patient each. Another newborn had anomalies of pinna and segmentation anomalies of thoracic vertebrae. Contents of hernia included the intestine in all cases, spleen in ten cases, stomach in nine, kidney and liver in one case each.

11 of 16 neonates underwent prenatal ultrasonography. The diagnosis of CDH was made on the basis of prenatal ultrasonography findings in four (25%) cases. Of live-born infants with prenatally-detected CDH, one (25%) survived till surgery but the same infant died postoperatively. The remaining three neonates did not survive till surgery. They all died within 72 hours of life. Postnatal diagnosis occurred in 12 (75%) cases. Nine were diagnosed within 24 hours of birth and the remaining three were symptomatic between 24 and 48 hours of birth. 11 of them survived to surgery and nine (75%) survived beyond one year of age.

The comparisons of neonates with their timing of detection is shown in Table III. None of the prenatally-detected infants survived. On the other hand, 75% (9/12) of the postnatally-detected neonates survived. Neonates in whom the defect was detected prenatally had significantly reduced survival to surgery, compared to those postnatally detected (25% vs. 92%, $p < 0.03$). There was no statistically significant difference in gestational age at birth and birth weight between the two groups. All prenatally-detected infants were born in the centre, and two of them were born by caesarean section. Prenatally-detected cases had lower Apgar scores at one minute than postnatally-detected cases ($p < 0.04$). Three-quarters of neonates (12/16) with CDH survived till surgery. Among those who underwent surgery, 75% (9/12) survived. Average age at surgery was 80 (median 48, range 24–240) hours. Postoperative complications occurred in four neonates. They included wound dehiscence, ileus with conjugated hyperbilirubinaemia, pneumothorax requiring drainage, and Acinetobacter sepsis in one each.

Out of 16 cases which were born alive, nine survived beyond one year of age. Six of the seven deaths occurred within 72 hours of birth. Preoperative air leak was not observed in any of the cases. Factors associated with deaths are presented in Table IV. All the non-survivors were symptomatic within 12 hours of life and required

Table III. Comparison of neonates with their timing of detection.

Characteristics	No. (%)		p-value
	Prenatally detected (n = 4)	Postnatally detected (n = 12)	
Overall survival	0	9 (75.00)	0.019
Survival to surgery	1 (25.00)	11 (91.67)	0.026
Postop air leak	1 (25.00)	0	0.25
Other major anomaly	1 (25.00)	0	0.25
Gestation at birth (wk) §	39 (38–40)	38 (34–42)	0.67*
Birth weight (g) §	2,785 (2,180–3,000)	2,763 (1,700–3,130)	1.00*
Apgar score §			
1 min	3 (1–4)	5 (1–7)	0.039*
5 min	6 (3–8)	7 (3–9)	0.211*

§ Data is presented as median (range); * Mann-Whitney U test

Table IV. Predictors of mortality.

Characteristics	No. (%)		p-value
	Survivors (n = 9)	Non-survivors (n = 7)	
Other major anomalies	0	1 (14.29)	0.44
Prenatally detected	0	4 (57.14)	0.02
Inborn	0	5 (71.42)	0.005
Post op air leak	0	1 (14.29)	0.44
Age at presentation (hours)			
< 12	4 (44.44)	7 (100.00)	0.03
> 12	5 (55.56)	0 (0)	0.5
Timing of surgery (hours)			
< 24	1 (11.11)	0 (0)	0.56
> 24	8 (88.89)	3 (42.86)	0.07
Gestation at birth (wk) §	38 (38–42)	38 (34–40)	1.00*
Birth weight (g) §	2,900 (1,800–3,130)	2,250 (1,700–3,000)	0.12*
Apgar score §			
1 min	5 (3–7)	2 (1–7)	0.01*
5 min	8 (5–9)	6 (3–8)	0.03*

§ Data is presented as median (range); *Mann-Whitney U test

intubation at birth, followed by mechanical ventilation. They also had significantly low Apgar scores at one minute (p = 0.01) and five minutes (p = 0.05). Maturity and birth weight of non-survivors were comparable to survivors. The causes of death included persistent severe cyanosis and difficulty in oxygenation. Timing of surgery did not seem to have influenced the mortality. Duration of mechanical ventilation among survivors ranged from 40 hours to 288 hours, with an average of 91.5 (median 72) hours. Duration of NICU stay ranged from five to 27 days, with an average of 11.4 (median 9) days.

DISCUSSION

We presented an outcome of neonates with CDH admitted to a level II neonatal ICU that is equipped with conventional mechanical ventilation in a developing country. 11 of the 16 neonates were referred from outside institutions. 13 were symptomatic within 24 hours. Of the total, nearly a third had associated additional anomalies. One patient had a recognisable syndrome, trisomy 21. This is in agreement with previous reports. West et al reported associated anomalies in 33%,[2] and Colvin et al reported another anomaly in 32% of live-born infants.[5] The prenatal detection rate for CDH varies enormously in published studies, from 10%[6] to 79%,[7] reflecting differences in local protocols of prenatal care and variable ultrasonographical expertise. In our series, of a total of 16 neonates, 11 had prenatal ultrasonography. CDH was detected in 25% of cases. Two were detected at 24 weeks and another two at 28 weeks. Polyhydramnios was associated in one case. Colvin et al reported a 53% prenatal detection rate in their study of over 12 years.[5] Survival of neonates with CDH depends on many factors and varies widely. We observed an overall survival of 56.3%. Previously, a survival of 62% had been reported from the Indian literature.[8] A large population-based study from Western Australia reported a survival of 52% among the live-born infants with CDH.[5] In contrast, a much higher overall survival of 88% was reported by West et al in their series of 59 infants.[2] Harrison et al wrote that the reported mortality in retrospective studies varies from < 25% to > 75%.[9]

Wide variations in survival rates for different subsets of infants with CDH occur throughout the literature. Studies of cases with a prenatal diagnosis frequently report a high mortality rate. We also found a high mortality in prenatally-detected compared to postnatally-detected cases (100% vs. 25%, p < 0.02). However, the limitation

in our findings is that the prenatal ultrasonography was done at 20 weeks and further scans were done only based on indications. Previously, a mortality of 80% in the neonatal period was found by Adzick et al in their series of 94 cases, despite optimal conventional therapy among foetuses with detectable CDH.[10] In contrast, survival of 65% of prenatally-diagnosed CDH was found by Metkus et al in an ECMO centre. They further reported that survival was better if diagnosis was made after 25 weeks.[11] Harrison et al, in their prospective study, observed 58% mortality among CDH diagnosed before 24 weeks despite optimal postnatal care.[9] Colvin et al reported that prenatal diagnosis itself was an important predictor of mortality rates for live-born infants, with a 33% survival rate, compared with a 67% survival rate for postnatally-diagnosed infants. However, they did not find the gestational age at diagnosis affecting the survival rate for live-born infants.[5] In our series, all four neonates with prenatal detection died, irrespective of gestational age at diagnosis. One of them had associated polyhydramnios. Polyhydramnios, a prenatal predictor of poor clinical outcome with 80% mortality, has been reported by Adzick et al.[10] It is possible that prenatal diagnosis detects cases with a greater degree or longer duration of visceral herniation, and thus an associated increased severity of pulmonary hypoplasia.

Early presentations and severe symptoms have been identified as one of the predictors of mortality. Sawyer et al reported 100% survival in neonates with no or minimal distress at birth and had operative intervention when they were more than 24 hours of age, compared to 54% survival in those who required immediate intubation and ventilation followed by operative intervention at less than 12 hours of age.[1] From India, Jain et al reported death of all nine (out of a total of 13) neonates who presented within 24 hours, among whom four also underwent surgery.[12] We observed that all non-survivors presented within 12 hours of birth ($p = 0.03$). Inborn infants had significantly lower survival rates than outborn infants, which might be accounted for by the fact that all prenatally-detected infants were inborn. Prenatally-diagnosed neonates could have severe pulmonary hypoplasia. Nguyen et al established that lung hypoplasia is certainly a major factor in patients who were doing poorly.[13]

In our study, the survival-to-surgery rate was 75%. Survival rate of surgical patients was also 75%. Prenatally-detected cases had a reduced survival to surgery rate compared to postnatally-detected rates (25% vs. 92%). Previously, Colvin et al reported a survival-to-surgery rate of 56% and a survival rate of surgical patients of 92% among live-born infants, with acute postoperative complications in 45%.[5] We observed a lower rate (33%) of acute complications. One neonate with liver in the hernia died. Worse prognosis was reported in foetuses with CDH and liver herniated into the hemithorax compared to similarly-affected foetuses without liver herniation in Albanese et al's study.[14] We did not find the significance of the site of the stomach in the outcome of these neonates, unlike the study by Goodfellow et al.[15] In conclusion, more than 50% survival of neonates with CDH was observed in a centre with conventional ventilation. Poor outcome is likely to be associated with neonates who manifest within 12 hours of birth.

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