

## Original Article

# Factors Influencing Outcome of Congenital Diaphragmatic Hernia

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Kuwait Medical Journal 2006, 38 (4): 287-291

**ABSTRACT**

**Objective:** To assess the presentation of congenital diaphragmatic hernia and to analyze the outcome of such babies according to the prognostic indicators in a neonatal intensive care unit

**Design:** Retrospective

**Material and Method:** All cases of congenital diaphragmatic hernia admitted to the neonatal intensive care unit at Khoula Hospital, Muscat, Sultanate of Oman from February 1994 to February 2001 were included in the study. The antenatal factors, presentation, resuscitation and the management of these babies were reviewed and their survival according to prognostic indicators compared with similar cases in literature.

**Results:** A total of 10 cases of congenital diaphragmatic hernia were admitted during this seven year period with an overall mortality of 80%.

Gestational age ranged from 33 weeks to full term. Eight (80%) babies had severe birth asphyxia needing intubation and ventilation soon after birth and had 100% mortality.

Two (20%) babies had mild birth asphyxia and presented after eight hours of life and had 100% survival. Five (50%) had polyhydramnios and three (30%) had associated anomalies. Ventilation index was < 1000 in three (30%) babies with a mortality of 33.3% and > 1000 in seven (70%) babies with 100% mortality.

Two (20%) babies operated after five days had 100% survival. Severe birth asphyxia, metabolic acidosis, hypoxia, hypercarbia and early presentation of diaphragmatic hernia had high mortality. Associated persistent pulmonary hypertension (PPHN) and pneumothorax had 100% mortality. Survival was seen in those two babies who had good prognostic factors and were operated after stabilization.

**Conclusion:** Compared to other neonatal intensive care units, mortality rate in our unit remains high in neonates presenting with congenital diaphragmatic hernia. This is due to lack of newer modes of ventilation, nitric oxide therapy and extracorporeal membrane oxygenation (ECMO).

KEY WORDS: congenital diaphragmatic hernia, prognostic indicators, ventilation index

**INTRODUCTION**

Congenital diaphragmatic hernia (CDH) is a disorder characterized by failure of the pleural and peritoneal canal to close approximately at eight week of gestation. This leads to displacement of the abdominal contents into the thoracic cavity resulting in pulmonary hypoplasia due to compression of the developing lungs by the viscera. Hernias through the posterolateral aspect of the diaphragm (Foramen of Bochdalek) account for approximately 80% of hernias, and hernias on the left side are five times more common than on the right side.

With the increased use of obstetric ultrasound, prenatal diagnosis of these hernias is common. Neonates present with asphyxia, respiratory distress, cyanosis and scaphoid abdomen. Those who develop respiratory failure within the first six

hours of life have the highest mortality. Despite the advances in neonatal intensive care and ventilation the mortality remains frustratingly high.

Various prognostic indicators have been suggested for survival of babies with CDH. These include birth weight, APGAR scores, age of presentation, associated congenital anomaly and ventilatory parameters like ventilation index, pCO<sub>2</sub>, pO<sub>2</sub> and oxygenation index. Other indicators are complications like pneumothorax, persistent pulmonary hypertension (PPHN) and also types of therapies used like hyperventilation, drugs and extracorporeal membrane oxygenation (ECMO).

In the past, babies with CDH were rushed immediately to the operating room without stabilization, but all the recent practice is to stabilize these patients first especially with the use of ECMO which has led to significant improvement

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**Table 1:** Antenatal and perinatal factors affecting mortality in babies born with CDH

	No. of Babies n (%)	Mortality n (%)
1. Type of delivery		
Spontaneous vaginal delivery	8 (80)	6 (75)
Emergency LSCS	2 (20)	2 (100)
2. Sex		
Male	6 (60)	4 (66.6)
Female	4 (40)	4 (100)
3. Gestation		
Preterm	2 (20)	2 (100)
Term	8 (80)	6 (75)
4. Birth Weight		
< 2.5 kg	2 (20)	2 (100)
> 2.5 kg	8 (80)	6 (75)
5. Associated anomalies	3 (30)	3 (100)
6. Antenatal Ultrasound		
Polyhydramnios	5 (50)	5 (50)
Diaphragmatic hernia	3 (30)	3 (100)
Not done	2 (20)	1 (50)

in outcome. Now the emphasis is on ventilatory strategies that minimize airway pressure and reduce barotrauma to the severely hypoplastic lungs.

This retrospective analysis over a period of seven years of all babies with CDH born at Khoula Hospital Muscat, Sultanate of Oman was undertaken at a neonatal intensive care unit (NICU) where no ECMO or pediatric surgical facilities were available. The aim was to determine the presentation of congenital diaphragmatic hernia and its outcome in these babies.

## METHODS

All babies born at Khoula Hospital from February 1994 to February 2001 with the diagnosis of CDH and admitted to the NICU were included in the study. Their case notes were retrieved and analyzed for the antenatal presentation and the postnatal outcomes.

All babies were ventilated with pressure controlled, timed cycled positive pressure ventilators (Bear Cub, Sechrist and Drager ventilators). The sex of the baby, gestation, type of delivery, antenatal ultrasound for congenital anomalies, initial APGAR, the need for resuscitation and their anthropometric measurements were noted.

All the babies were shifted soon after birth to the NICU and the age of presentation of the diaphragmatic hernia was noted. Oxygen needs and ventilatory requirements like maximum pressure, oxygen and ventilation index was calculated.

Arterial blood was collected and analyzed by Blood gas analyzer for initial pH, pO<sub>2</sub>, pCO<sub>2</sub> and base excess. Ventilation and electrolytes monitoring

**Table 2:** Factors influencing mortality in diaphragmatic hernia

	No. of Babies n (%)	Mortality n (%)
1. Birth Asphyxia		
Severe	8 (80)	8 (100)
Mild	2 (20)	0 (0)
2. Time of presentation		
Soon after birth	8 (80)	8 (100)
> 8 hours after birth	2 (20)	Nil (0)
3. Site of hernia		
Left	8 (80)	7 (87)
Right	2 (20)	1 (50)
4. Associated PPHN	8 (80)	8 (100)
5. Pneumothorax	3 (30)	3 (100)

of all these babies during their stay in the NICU was done according to the unit protocols. The criteria for conventional ventilation included severe persistent metabolic acidosis, pO<sub>2</sub> < 60 mmHg and progressively rising pCO<sub>2</sub> > 60 mmHg. All babies had a peripheral arterial line for blood sampling. Monitoring of these babies was done by continuous recording of heart rate, temperature, pulse oximetry, respiratory rate and blood pressure recordings on a Hewlett Packard cardiac monitor. Repeated blood gas analysis according to the changes in ventilation and complete blood counts, electrolyte and blood sugar monitoring was done. Additional management of some babies with PPHN consisted of applying modalities like use of drugs such as tolazoline and prostacyclin. The response to treatment and complications of ventilation like associated pneumothorax was noted and final outcome was analyzed.

As the NICU at Khoula Hospital had no facilities for pediatric surgery, the neonates were stabilized and then shifted on a transport ventilator (Drager) to a tertiary care NICU at the Royal Hospital where they were managed by a team of pediatric surgeons and neonatologists. The time of transfer, operative management and associated mortality was also assessed.

All these data was analyzed for the incidence of CDH during these seven years, its presentation and outcome.

## RESULTS

During the seven year period from February 1994 to February 2001, there were a total of 30,157 live-born babies at Khoula hospital out of which ten had CDH. Six (60%) were female and four (40%) male. Gestational ages of these babies ranged from 33 weeks to full term. Two out of them were preterm.

Eight (80%) babies were born by normal vaginal delivery and two (20%) by emergency LSCS. Polyhydramnios was noted in five (50%),

**Table 3:** Initial blood gas parameter and mortality in congenital diaphragmatic hernia

	No. of Babies n (%)	Mortality n (%)
1. pH		
< 7	7 (70)	7 (100)
7 - 7.2	2 (20)	1 (50)
> 7.2	1 (10)	Nil (0)
2. pO <sub>2</sub>		
30-60 mm of Hg	8 (80)	8 (100)
> 60 mm of Hg	2 (20)	Nil (0)
3. pCO <sub>2</sub>		
> 60 mm of Hg	6 (60)	6 (100)
< 60 mm of Hg	4 (40)	2 (50)
4. Severe metabolic acidosis	8 (80)	8 (80)
5. Ventilation Index (MAPx Respiratory rate)		
< 1000	3 (30)	1 (33.3)
> 1000	7 (70)	7 (100)

diaphragmatic hernia noted antenatally in three (30%) and associated anomalies in the form of dysmorphic features and cardiovascular anomalies in three (30%) babies (Table 1).

Eight (80%) babies had severe birth asphyxia needing intubation and ventilation soon after birth with 100% mortality. Two (20%) babies had mild birth asphyxia and presented late (after 8 hours) and had 100% survival.

Left sided hernia was seen in eight (80%) cases out of which seven (87%) died and right sided hernia in two cases out of which one (50%) died. PPHN was present in eight (80%) cases with 100% mortality and pneumothorax in three cases with 100% mortality (Table 2).

Conventional ventilation was used in all babies using Bear Cub, Sechrist or Drager ventilators and drugs like tolazoline and prostacyclin were used in four (40%) babies with 100% mortality.

Blood gas analysis showed that seven (70%) babies with an initial pH < 7 had 100% mortality. Two babies (20%) had a pH between 7-7.2 with 50% mortality and one baby (10%) with a pH > 7.2 survived. Eight babies (80%) with an initial pO<sub>2</sub> of 30-60 mmHg had 100% mortality. Those with a pO<sub>2</sub> > 60 mmHg (2 babies, 20%) survived. Six babies (60%) with a pCO<sub>2</sub> > 60 mmHg died whereas four babies (40%) with a pCO<sub>2</sub> < 60 mmHg showed a 50% mortality. Severe metabolic acidosis with base excess of more than -15 was seen in eight (80%) cases with 100% mortality. Ventilation Index, a ratio of mean airway pressure x respiratory rate was < 1000 in three (30%) babies with a mortality of 33.3% and > 1000 in seven (70%) cases with a mortality of 100% (Table 3).

Six (60%) babies were stabilized and transferred to a tertiary care unit with a pediatric surgical service and four (40%) were operated. Two (20%)

**Table 4:** Interventions and mortality in diaphragmatic hernia

	No. of Babies n (%)	Mortality n (%)
1. Age at ventilation		
Soon after birth	8 (80)	8 (100)
> 8 hrs after birth	2 (20)	Nil (0)
2. Type of ventilation		
Conventional	10 (100)	8 (80)
Conventional with tolazoline/ prostacyclin	4 (40)	4 (100)
3. Transfer to tertiary care hospital		
Transferred	6 (60)	4 (66.6)
Not transferred	4 (40)	4 (100)
4. Operated	4 (40)	2 (50)
5. Age of surgery		
< 5 days	2 (20)	2 (100)
> 5 days	2 (20)	Nil (100)
Overall Mortality	10 (100)	8 (80)

were operated within five days of birth and both died while the other two operated later survived. Four (40%) babies could not be transferred as they could not be stabilized and died at Khoula Hospital. PPHN was present in eight (80%) cases with 100% mortality and pneumothorax in three (30%) cases with 100% mortality. Conventional ventilation was used in all babies and drugs like tolazoline and prostacyclin were used in four (40%) cases with 100% mortality. The overall mortality was eight (80%) and those who survived presented late and were operated upon after the 1st week of life (Table 4).

## DISCUSSION

The infant born with CDH presents a challenge and remains one of the most complex patients to manage. Pulmonary hypoplasia and immaturity of the lung are well-recognized definitive limitations leading to high mortality rates<sup>[1]</sup>. Congenital diaphragmatic hernia is a well-known condition for almost 200 years but its treatment strategy has changed during the past few decades. Despite these improvements the mortality rates remain frustratingly high (> 50%), especially for those presenting in the first six hours of birth<sup>[2,3]</sup>.

We analyzed our experience with this condition over the last seven years in our NICU where no facilities for high frequency ventilation or ECMO were available. After the initial ventilation and stabilization these babies had to be transferred to a pediatric surgical unit in other hospital.

The incidence of congenital diaphragmatic hernia in our unit was 1:3000 live births which correlates well to that reported in the literature. National Maternity Hospital in Dublin, Ireland reported an incidence of 1:2107 after a review of

99,000 patients<sup>[4]</sup>. Left sided hernia was seen in 80% cases which is similar to our findings<sup>[5]</sup>. Gestational age analysis revealed that most of our babies (80%) were term babies. Polyhydramnios was seen in 50% cases. Three of our babies were diagnosed antenatally as cases of CDH and were referred for delivery to a center with pediatric surgical facilities. But they came in labor at our institute and the babies had 100% mortality. In most centers, antenatal diagnosis with sonography is accurate in 88-94% cases as reported by Bell *et al* who also found polyhydramnios in most of their cases<sup>[6]</sup>.

Three (30%) babies had associated anomalies in the form of dysmorphic features of Trisomy 18, hydrocephalus and ventricular septal defect with 100% mortality in this group. Associated anomalies are present in 35% of cases out of which cardiac lesions predominate and infants with associated anomalies have a low APGAR, lower pO<sub>2</sub> and poor prognosis<sup>[7]</sup>. The Iowa city birth defects registry noted that 28% of babies with CDH had associated anomalies like meningocele, encephalocele, hydrocephalus, ventricular septal defect, vascular rings, trisomy 13 and 18, omphalocele and had poor survival rates (5%)<sup>[8]</sup>.

Eight (80%) babies presented soon after birth and had severe birth asphyxia needing intubation. They were ventilated soon after birth with conventional ventilation at high parameters. This group with early presentation and low APGAR had 100% mortality. Two (20%) babies presented after eight hours and survived. The CDH study group from the department of surgery, University of Texas, Houston estimated the disease severity in first five minutes of life. Survival data on 322 consecutive live-born infants with CDH were collected from 71 institutions and factors associated with the outcome like birth-weight, APGAR score, gestational age, age at presentation and associated cardiac anomaly was analyzed. In their study APGAR score was found to be the most useful predictive equation which correlated well with the poor outcome<sup>[9]</sup>.

Blood gas analysis was done on all babies soon after birth and an initial pH < 7 was seen in seven (70%) babies with 100% mortality. Mishalany *et al* analysed 55 patients with CDH and found that those with uncorrected pH of < 7 had 100% mortality in their series whereas those with a pH between 7 - 7.2 had 50% mortality. Early surgery and correction of acidosis did not improve the survival. They concluded that initial pH was of great prognostic importance<sup>[10]</sup>. Initial pO<sub>2</sub> of < 60 mmHg was seen in eight (80%) of our babies with 100% mortality and > 60 mmHg in two babies who survived.

Several reports documented the fact that an initial pCO<sub>2</sub> of > 40 mmHg is associated with high mortality rate (between 75-100%)<sup>[11,12,13]</sup>. The outcome of CDH presenting in first six hours of life correlates to the degree of pulmonary hypoplasia as indicated by preoperative index of ventilation which if >1000 indicates a very high mortality. Ventilation index, a ratio of mean airway pressure x respiratory rate was < 1000 in three (30%) cases with 33.3% mortality and > 1000 in seven (70%) cases with 100% mortality. Bohn *et al* observed that when ventilation index in their series of 66 infants was > 1000 the mortality was 50%. Associated PPHN was seen in eight (80%) babies from our series with 100% mortality. Three (30%) babies developed pneumothorax with 100% mortality. Chou *et al* in their review of 32 babies found very high mortality rates with associated pneumothorax and PPHN.

Due to lack of facilities of hyperventilation and ECMO in our unit all the babies were put on conventional ventilation. Drugs like tolazoline and prostacyclin, which are thought to reduce PPHN, were tried in four (40%) cases with 100% mortality. In a study by Bos *et al*, in 52 high risk babies with CDH who needed ventilation within six hours with documented PPHN in 21 (46%) cases, tolazoline did not reduce the oxygen index or alveolar arterial oxygen difference<sup>[14]</sup>.

Out of six babies who were transferred, four (40%) were operated upon. Two (20%) were less than five days old and had 100% mortality while the other two babies (20%) were more than five days old and survived. The primary problem in these babies is respiratory failure not due to lung compression by the herniated viscera but due to pulmonary hypoplasia and associated pulmonary hypertension. Weber *et al* compared the survival rates of the three eras of management of CDH on 203 neonates. In era 1 with immediate repair the survival was 42% as compared to era 3 in which there was delayed repair of CDH with ECMO where the survival rate was 96%<sup>[13]</sup>. David *et al* evaluated the impact of non-standard ventilatory strategy on survival in CDH and concluded that hyperventilation with alkalinisation had a detrimental effect and should be abandoned and that the survival rates of delayed surgery and ECMO were significantly higher<sup>[15]</sup>.

Ventilatory strategies that minimize airway pressure reduce the barotrauma and lung injury to the severely hypoplastic lungs, thereby improving survival of babies with CDH. Gentle ventilation which allows arterial pCO<sub>2</sub> to be slightly higher than normal (permissive hypercapnia) and marginal post-ductal oxygenation are associated with higher survival rates than conventional ventilation. ECMO is most successful when used

for reversible pulmonary diseases like PPHN, meconium aspiration or PFC. In diaphragmatic hernia, ECMO has been used successfully to prevent barotrauma from mechanical ventilation and allow vasculature remodeling and thereby stabilize the baby before surgical repair. Due to underlying pulmonary hypoplasia in diaphragmatic hernia, the gain by ECMO is not substantial as compared to that in meconium aspiration syndrome. Comparative data by Ann Arbor, Michigan ECMO organization study in 1997 indicated that out of 4519 babies treated with ECMO for meconium aspiration, 94% survived as compared with only 54% survival out of 2627 babies treated for diaphragmatic hernia.

### CONCLUSION

CDH due to its fundamental complex problems of pulmonary hypoplasia and hypertension still remains a management challenge with its high mortality. As compared to other studies the mortality rates in our study was quite high due to non-availability of newer modes of ventilation and ECMO and delay in stabilization and transfer of such neonates.

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