

# A Study Of The Epidemiology And Outcomes Of Patients With Congenital Diaphragmatic Hernia

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## Abstract

**Background and aim:** The incidence of congenital diaphragmatic hernia (CDH) was reported as high as 1 in 3000. Neonates with congenital diaphragmatic hernia have a poor prognosis, and the prediction of mortality remains difficult. The aim of this study was to investigate the incidence of infants born with congenital diaphragmatic hernia (CDH) and the influence of perinatal factors on mortality rate. **Patients and Methods:** This retrospective study was carried out on 34 neonates from birth to 1 month of age diagnosed with CDH from March, 2001 to March, 2008. **Results:** From the databases used, the incidence of CDH was 1 per 4696 live births. Overall hospital mortality rate was 41%. Bi-variate analysis showed increased risk of death in neonates with low birth weight, low gestational age, low 5-minute APGAR scores, low arterial pH levels, and neonates who had respiratory distress on births. Multivariate analysis found that 5-minute APGAR, gestational age and arterial pH levels were independent predictors of total mortality rate. When the gestational age was increased by one week, an 8% mortality rate reduction was found. Furthermore, increase in 5-minute APGAR by 1 unit, and increase in arterial pH level by 0.1 units, reduced the mortality rate by 36% and 37%, respectively. **Conclusion:** Avoiding preterm delivery and improving preoperative stabilization are the measures most likely to improve survival.

## INTRODUCTION AND AIM

Congenital diaphragmatic hernia (CDH) is one of the most common causes of mortality and morbidity in the neonatal period. Although there are several advanced therapeutic regimens for CDH cases, the rate of mortality remains high, especially in cases who became symptomatic in the first 6 hours of life. The incidence of CDH varied from 1/2000 to 1/5000 in different reports. The most common presenting symptoms are respiratory (43%), gastrointestinal (33%), and combined respiratory and GI problems (13%). In 11% of cases, patients remain asymptomatic. Associated anomaly, diagnosis before delivery, low APGAR score, low estimated age, and low birth weight will reduce life expectancy of newborns.

## PATIENTS AND METHODS

This retrospective study was carried out in Imam Khomeini Hospital and Abuzar Pediatric Center from March 2001 to March 2008. Normal distribution was evaluated by one-sample Kolmogorov-Smirnov test. Chi-square tests were used for comparison between proportions. ANOVA and

Independent Samples t-Test were used for comparison between means of numerical variables. Logistic regression was used for analysis of independent factors affecting mortality and morbidity.

## RESULTS

Thirty-four cases with diaphragmatic hernia, admitted between March, 2001 and March, 2008 in Imam Khomeini Hospital and Abuzar Pediatric Center, were included in this study. Of 34 cases, 7 cases were born in Imam Khomeini Hospital and other cases were referred from other hospitals to Imam Khomeini and Abuzar Hospital. The total of live newborns delivered vaginally or by cesarean section in Imam Khomeini hospital was 32876. Seven of 32876 live newborns had diaphragmatic hernia. The frequency of congenital diaphragmatic hernia was 2.12/10000 or 1 per 4696 live births. Demographic information of the patients is shown in table 1.

**Figure 1**

Table 1: Demographic features of patients with CDH

|                       |                                      |
|-----------------------|--------------------------------------|
| Death cases           | 14 (41.2%)                           |
| Sex                   | M: 17 (50%), F: 17 (50%)             |
| Side of involvement   | Left: 26 (76.5%)<br>Right: 8 (23.5%) |
| Associated anomalies  | 13 (38.2%)                           |
| BBW (Mean±SD)         | 2899±429.4 (Min=2100, Max=4100)      |
| EDC (Mean±SD)         | 37.84±2.25 (Min=32.00, Max=42.00)    |
| 1-min APGAR (Mean±SD) | 7.28±1.76 (Min=4.00, Max=9.00)       |
| 5-min APGAR (Mean±SD) | 8.48±1.87 (Min=4.00, Max=10.00)      |

As shown in table 1, the number of male cases was 17 (50%); of female cases it was 17 (50%) as well and there was no sex predominance (p=1.000). Birth weight (Mean±SE) was 2930±470 for males and 2779±400 for females. There was no significant difference for birth weight (p=0.334). Mean EDC was 37.7±2.5 for females and 37.6±2 for males and no significant difference was seen (p=0.908). There were no significant differences between males (7.3±1.8) and females (6.6±1.8) for 1-min APGAR and also for 5-min APGAR (8.5±1.9 for males and 7.9±2.1 for females, p=0.385). From all cases, 52.9% of male and 64.7% of female cases were alive. The sex had no significant effect on mortality (p=0.486). Associated anomalies were seen in 13 cases. The most common anomalies were cardiac anomalies (5 cases), followed by pulmonary (3 cases), skeletal (2 cases), genetic (1 case) and GI anomalies (1 case) as well as imperforate anus (1 case).

Anomalies were present in 7 males (10 cases without anomaly), and in 6 females (11 without anomaly); there was no significant difference (p=0.724). There was no relationship between mortality and absence or presence of anomaly (Table 3).

Twenty-six cases had symptoms during the first 6 hours of delivery. In 2 cases, onset of symptoms was between the 1<sup>st</sup> and 2<sup>nd</sup> day. In 9 cases, onset of symptoms was after 48 hours. Eight cases were diagnosed incidentally. In table 3, onset of symptoms and mortality are shown. As seen in table 3, most of the cases were symptomatic in the first 6 hours after birth. Of the cases with symptoms after 6 hours, 25% died. There was no significant difference between the two groups for mortality (p=0.288). Some signs and symptoms were evaluated for possible relationship with mortality. The results of this evaluation are listed in table 3.

There are no significant differences between expired and survived neonates for the type of delivery (live, cesarean section: 6, vaginal delivery: 11; died, cesarean section: 5, vaginal delivery: 8; p=0.858). In table 2, visceral organs that entered the thorax and relation with outcome are shown.

**Figure 2**

Table 2: Relationship between herniated visceral organ and outcome

|                 | Survived          |                    | Expired           |                    | P-value |
|-----------------|-------------------|--------------------|-------------------|--------------------|---------|
|                 | Inside the thorax | Outside the thorax | Inside the thorax | Outside the thorax |         |
| Stomach         | 6                 | 10                 | 5                 | 1                  | 0.074   |
| Small intestine | 14                | 2                  | 5                 | 1                  | 0.636   |
| Large intestine | 14                | 2                  | 6                 | 0                  | 0.519   |
| Spleen          | 8                 | 8                  | 3                 | 3                  | 0.682   |
| Liver           | 1                 | 15                 | 2                 | 4                  | 0.169   |
| Kidney          | 3                 | 13                 | 6                 | 0                  | 0.364   |

Rate of mortality had no significant relationship with type of organ entered to the thorax. Twenty-three cases underwent laparotomy, primary repair and reduction of visceral organs. Two cases underwent laparotomy and herniorrhaphy. Seven cases died before surgery. Of 25 cases that underwent surgery, 18 cases are alive and the remainder died. Patients were classified according to time of surgery and outcome (Table 3). The hernia was located on the left side in 26 cases and on the right side in 8 cases. Table 3 shows side of hernia and final outcome. Side of hernia was not related to mortality (p=0.278). Mean of birth weight ±SD for newborns who survived was 2948±499 and for died newborns it was 2719±293 (p=0.151). The rate of mortality in cases with BBW<2850 was significantly higher than in cases with BBW>2850 (p=0.036). (Table 3)

Mean of 1-min, and 5-min APGAR score for expired and survived neonate were as follows: 1-min APGAR score: Survived: 7.5±1.1, expired:6.5±2; 5-min APGAR score: Survived: 9±1.5, expired:7.5±2. There was no significant difference between the two groups for 1-min APGAR score, but a significant difference for 5-min APGAR score (p=0.033). The rate of mortality in cases with 5-min APGAR<7 was significantly higher than in cases with 5-min APGAR>7 (5-min APGAR<=7: live=2, expired=6; 5-min APGAR>7: live=16, expired=7). EDC of cases with diaphragmatic hernia was 37.6±2.3 (p>0.05). Mean of EDC in survived newborns was 38.4±2.1 and in died cases 36.6±2.1. There was a significant difference between the two groups (p=0.037). Rate of mortality in cases with GA<37weeks was significantly higher than in those with GA>37weeks.

**Figure 3**

Table 3: Relationship between some factors and outcome (S: Survived, E: Expired). The exact values of GA of 6 cases and BBW of 3 cases were not available.

|                                   |                      |                       |                        |                       |         |
|-----------------------------------|----------------------|-----------------------|------------------------|-----------------------|---------|
| Respiratory distress              | Yes<br>S=12<br>E=13  | No<br>S=8<br>E=1      |                        |                       | P=0.033 |
| Vomiting                          | Yes<br>S=9<br>E=2    | No<br>S=11<br>E=12    |                        |                       | P=0.06  |
| Cyanosis                          | Yes<br>S=15<br>E=8   | No<br>S=5<br>E=6      |                        |                       | P=0.273 |
| Displaced location of PMI         | Yes<br>S=8<br>E=6    | No<br>S=12<br>E=8     |                        |                       | P=0.868 |
| Audible bowel sounds in the chest | Yes<br>S=4<br>E=6    | No<br>S=16<br>E=8     |                        |                       |         |
| Anomaly                           | Yes<br>S=7<br>E=6    | No<br>S=3<br>E=8      |                        |                       | P=0.307 |
| Onset of symptoms                 | 6hrs<br>S=14<br>E=12 | 6-24hrs<br>-          | 24-48hrs<br>S=6<br>E=2 | >48hrs<br>-           | P=0.288 |
| Time of surgery                   | 6hrs<br>S=0<br>E=1   | 6-24hrs<br>S=3<br>E=1 | 24-48hrs<br>S=0<br>E=0 | >48hrs<br>S=15<br>E=5 | P=0.436 |
| Side of Hernia                    | Right<br>S=6<br>E=2  | Left<br>S=14<br>E=12  |                        |                       | P=0.278 |
| BBW                               | <2850<br>S=7<br>E=10 | >2850<br>S=11<br>E=3  |                        |                       | P=0.036 |
| GA                                | <37wks<br>S=2<br>E=8 | >37wks<br>S=14<br>E=4 |                        |                       | P=0.005 |

**Figure 4**

Table 4: Blood gas analysis in the two groups

|              | Total     | Survived  | Expired   |
|--------------|-----------|-----------|-----------|
| pH (Mean±SE) | 7.17±0.2  | 7.23±0.16 | 7.07±0.23 |
| PaCO2        | 56.8±31.2 | 53.7±28.5 | 61.1±35.4 |
| HCO3         | 23.5±12.4 | 23.6±9.1  | 23.2±16.4 |

As shown in table 5, there was no significant difference between alive and died newborns for pH, PaCO2, and HCO3. Rate of mortality in cases with pH equal to or less than 7.18 was significantly higher than in cases with pH>7.18 (p=0.02).

**Figure 5**

Table 5: Significant correlation between pH

| Outcome | pH    |       | Total |
|---------|-------|-------|-------|
|         | <7.18 | >7.18 |       |
| Alive   | 4     | 11    | 15    |
| Death   | 8     | 3     | 11    |

(\* P<0.02)

**DISCUSSION**

The prevalence of associated anomaly with CDH was reported from 10% to 50% . In our study, the proportion of associated anomalies was 38%; left-sided and right-sided CDH were seen in 26 (76.5%) and 8 (23.5%) cases, respectively, similar to other studies . In the study by Gallot et al., associated anomalies were reported in 37%, right-sided defects in 20%, and bilateral congenital defects in 4% . There is some evidence that anomaly is associated with

higher rate of mortality<sup>2</sup>. In our study, there was no difference in mortality rate between cases with and without anomaly. Univariate analysis revealed that risk factors for mortality of CDH cases were respiratory distress at the time of admission, low body birth weight, estimated age of conception, low 5-min APGAR score, and low arterial pH. Increased mortality was associated with low estimated age of conception and decreased life expectancy was associated with low BBW<sup>4,7,8</sup>. A higher mortality rate with left CDH was reported if stomach and liver were herniated into the thorax, There is also a report of an ectopic intra-thoracic kidney in a case with CDH .

This study showed no significant relationship between mortality and sex, onset of disease, time of surgery, type of delivery, type of herniated viscus, associated anomaly, 1-min APGAR, arterial HCO3, and arterial pCO2. The multivariate analysis performed in this study showed that independent factors affecting mortality were EDC (p=0.037), 5-min APGAR (0.037), and arterial pH (p=0.043). With 1 week increment in age, 0.8 reduction in mortality was seen. With 1 score increment in 5-min APGAR, 36% reduction in mortality and with 0.1 increment in pH, 0.37 reduction in mortality was seen.

In our study, there are some limitations: This is a retrospective study; some treatment options such as ECMO and nitric oxide were not available in our hospital and our sample number is lower than in other large studies.

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