

## Congenital Diaphragmatic Hernia: Risk Factors and Experience in Southwest Region of Saudi Arabia

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**ABSTRACT.** Congenital diaphragmatic hernia is a common surgical emergency in neonatal referral centres. Various pre- and post- operative radiologic, ventilatory, and clinical data parameters were studied as factors to predict the outcome of this condition. A total of 27 cases were admitted to King Fahad Hospital in Al Baha (Southwest region of Saudi Arabia) between October, 1981, and October, 1992 inclusive the gross mortality rate was 22% but when applied on patients presented within the first 6 hours of life, it was 40%. About 30 risk factors were studied and its statistical significance was drawn out when applied to each patient. In conclusion, we found the incidence of congenital diaphragmatic hernia in Southwest region of Saudi Arabia to be 1 : 2,320 live births. The major risk factors adversely affect survival were low birth weight, low PaO<sub>2</sub>, oxygenation index, and thoracic stomach position. Other risk factors affected the survival to lesser extent were high PaCO<sub>2</sub>, and alveolar-arterial oxygenation index. The details of the risk factors and the cases are presented.

**Keywords:** Congenital diaphragmatic hernia, Risk factors

### Introduction

Congenital diaphragmatic hernia (CDH) is a common surgical emergency in neonatal

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Accepted for publication: 05 July 2003. Received: 28 December 2002.

referral centres and is an anatomically simple defect that can easily corrected by replacing the herniated viscera from the chest into the abdomen and closing the diaphragm.

In the fetus with CDH, the pleuro-peritoneal canal fails to close by the time that the intestines return to the abdomen at 8 to 10 weeks of gestation.

Early diagnosis, efficient resuscitation and maximum cardiopulmonary support can considerably reduce the mortality of patients with even large congenital diaphragmatic hernia defect<sup>[1]</sup>.

Antenatally, CDH can be diagnosed by the use of ultrasound especially if there was polyhydramnios. Antenatal diagnosis of CDH did not lead to a significant drop in the mortality, contrary, if the diagnosis was made before 25 weeks gestation and associated with polyhydramnios, the outcome is dismal<sup>[2, 3]</sup>.

In general, the earlier the presentation, the higher the mortality rate. This is especially seen in patients presented younger than 6-hours old<sup>[4-6]</sup>.

Various attempts have been made to grade the severity of the CDH and predict the outcome on the basis of various clinical, radiological and ventilatory parameters, *e.g.*, pre- and post- operative pH, Alveolar-arterial oxygenation difference (A-a) DO<sub>2</sub>, Oxygenation Index, Pa CO<sub>2</sub>, Pa O<sub>2</sub>, ventilation index, stomach site on chest X-ray, severity of Dextrocardia, pneumothorax, associated congenital anomalies, and others<sup>[2, 6]</sup>.

To evaluate the effect of the mentioned risk factors, we applied it on all patients with the diagnosis of congenital diaphragmatic hernia seen in our hospital, retrospectively.

### Material and Methods

The records of all patients under the age of 15 years, admitted to King Fahd Hospital (KFH) in Al Baha between October, 1981 and October, 1992 inclusive with diagnosis of congenital diaphragmatic hernia were reviewed. A total of 27 cases was found. The diagnosis was proved by chest X-ray in all of them and confirmed operatively in 25 patients.

The patients were divided into four groups according to survival and age at which they started to be symptomatic.

- Group A (10 patients) Those who were symptomatic after 24 hours of age. This was taken as a control group.
- Group B (6 patients) Those who presented within 6 hours of age and succumbed.
- Group C (9 patients) Those who presented within 6 hours after birth and survived.
- Group D (2 patients) Those started to be symptomatic between 6 and 24 hours after birth.

Three types of risk factors were applied on each patient:

**a. Clinical risk factors** - History of maternal polyhydramnios, antenatal diagnosis, maturity, Apgar score, birth weight, associated congenital anomalies, age at presentation, age at admission, and age at operation.

**b. Ventilatory** - pH, PaO<sub>2</sub>, PaCO<sub>2</sub>, FiO<sub>2</sub>, Oxygenation Index (O.I.), Ventilation Index (V.I.), Alveolar-arterial oxygenation difference (A-a) DO<sub>2</sub>, and mechanical ventilation.

**c. Radiological risk factors** - Stomach position, dextrocardia, and pneumothorax (ipsi or contralateral).

The statistical significance was drawn out when Groups B, C, and D were separately compared to Group A (the control). All the results were tested using student T-test, linear regression analysis was applied on all the 27 patients on each parameter.

## Results

Out of the 27 cases, 14 were born at KFH. There were 20 males and 7 females, making male : female ratio of about 2.8 : 1, respectively. All but one patient were Saudi nationality and origin. As only 6 patients died, the mortality rate was 22 % all of them presented within 6 hours of birth and born in the hospital.

Out of the 27 patients, two died before surgical intervention, 22 patients had primary repair, and in 3 patients (11%), synthetic graft was used.

In 6 patients of the primary operative repair, absorbable suture was used. Surgical complications registered were wound dehiscence (1 patient), wound infection (1 patient) and septicemia (1 patient) all occurred in the latter group of patients only.

Synthetic graft was used in 3 patients (11%), two had almost absent left hemidiaphragm and one died 5 hours post-operatively. The third patient had a case of Cantrell's pentalogy. He is alive and well.

Full lung expansion was noted in 13 patients within the first 10 days post-surgery; 5 patients between 10-20 days; and 3 patients after the 20th postoperative day.

Six patients were surgically discharged within the first postoperative week; 9 patients during the second week; 5 patients during the third week; and 1 patient during the fifth postoperative week.

Tables 1 and 2 represent only the results of the statistically significant relation drawn from the study.

TABLE 1. Important factors affected mortality in patients presented within 6-hours of life compared with the control group.

Preoperative Parameter	Group B = Died (N = 6)		Group C = Survived (N = 9)	
	mean $\pm$ S.D	P	mean $\pm$ S.D	P
Birth weight (kg)	1.7 $\pm$ 0.5	< 0.01	2.9 $\pm$ 0.3	> 0.1
O.I.	96.7 $\pm$ 60.3	< 0.01	12.8 $\pm$ 5.3	> 0.1
PaO <sub>2</sub>	44.0 $\pm$ 28.7	< 0.05	84.0 $\pm$ 61.7	> 0.1
(A-a) DO <sub>2</sub>	583.6 $\pm$ 60.1	< 0.01	352.5 $\pm$ 203.7	< 0.05
PaCO <sub>2</sub>	62.3 $\pm$ 28.7	< 0.01	44.0 $\pm$ 13.5	< 0.05
pH	6.98 $\pm$ 0.22	< 0.01	7.21 $\pm$ 0.11	< 0.01
FiO <sub>2</sub>	0.86 $\pm$ 0.23	< 0.01	0.67 $\pm$ 0.26	< 0.01
VI	879.0 $\pm$ 258.2	< 0.01	810.0 $\pm$ 145.7	< 0.01
Thoracic Stomach	6 / 6	< 0.05	3 / 9	> 0.1

OI = Oxygenation Index

VI = Ventilation Index

(A-a) DO<sub>2</sub> = Alveolar-Arterial Oxygenation Difference

TABLE 2. Linear regression analysis of different preoperative respiratory parameters.

Parameters Correlated	r value	P value
OI & pH	0.798	< 0.001
OI & PaCO <sub>2</sub>	-0.643	< 0.01
(A-a) DO <sub>2</sub> & PaCO <sub>2</sub>	0.605	< 0.01
(A-a) DO <sub>2</sub> & VI	0.591	< 0.01
(A-a) DO <sub>2</sub> & OI	0.579	< 0.01
(A-a) DO <sub>2</sub> & pH	-0.55	< 0.01
FiO <sub>2</sub> & VI	0.54	< 0.05
VI & Birth Weight	0.512	< 0.05

OI = Oxygenation Index

(A-a) DO<sub>2</sub> = Alveolar Arterial Oxygenation Difference

VI = Ventilation Index

## Discussion

CDH is one of the neonatal surgical emergencies which must be diagnosed early and the patient has to be resuscitated promptly, and once stabilized should be operated upon urgently.

KFH is the only referral centre to such cases in the Southwest region of Saudi Arabia. The approximate population of which is about 300,000 inhabitants and since 96.3% of our patients were Saudis in origin so this study represents the actual fre-

quency of the diagnosed disease in the region.

The male : female ratio in the present study was 2.8 : 1 which is much higher than other studies<sup>[7, 8]</sup>.

Age at presentation was considered as the age at which the patient began to be symptomatic as some of them do not reach our centre until a few hours passed due either to transportation problems or delayed referral.

The incidence of congenital diaphragmatic hernia differs from study to another, e.g., in Liverpool, it occurs in one in 4,500 live births; (1990) which looks lower than what was published in other studies as the reports of Butler and Claireau, David *et al.*, and Harrison and De Lorimies which document the incidence to be about one per 2,240 live births<sup>[7]</sup>. Although most cases are sporadic, scattered reports indicate the occurrence in siblings, twins; in two generations of the same family<sup>[9]</sup>; and even autosomal recessive factors has been reported<sup>[7]</sup>. When we reviewed the family history of the patients in this study, we did not succeed to find any other same family member with the disease.

As only 14 patients were born in our hospital during the study period in which the total number of live birth deliveries was 32,580; therefore, the calculated incidence of this disease at the Southwestern region is about 1 ; 2,320 live births or 0.429 / 1,000 live births.

When comparing the incidence in Southwest region in our study with that of Holy Makkah (1 : 2,397 live births)<sup>[10]</sup> and that of the Eastern province (1 : 3,000 live births)<sup>[12]</sup>. We noticed that it is slightly higher in the Southwest region of Saudi Arabia which could be due to higher incidence of consanguinity in this region.

The reported incidence of anomalies involving other system, e.g., cardiopulmonary, genito-urinary, and central nervous system, varies from 17-50% in different reports. A number of secondary thoracic anomalies accompany the condition and presumably represent the effect of herniated abdominal viscera. These include: pulmonary hypoplasia, enlarged chest cavity, left ventricular hypoplasia, and non-fixation of the mesentery with malrotation of the intestinal tract<sup>[11]</sup>.

The associated other congenital anomalies were seen in 48% of our patients as follows:

Three patients had intestinal malrotation, Meckel's diverticulum was seen in two patients, cardiac anomaly in 2 patients, cleft-lip and palate in 2 patients, and cryptorchidism in 2 patients. One patient had Cantrell's Pentalogy and the only patient diagnosed to have Down's syndrome had a history of repeated chest infection presented at 20 months of age and a Morgagni defect that was discovered incidentally on his chest X-ray.

The anatomical distribution of the defects on the diaphragm showed that the left hemidiaphragm was involved in 81.4% of cases seen, and this is the usual pattern seen [8, 9]. It is of note that all deaths were in this subgroup of patients. All non left-sided hernia patients survived and were either later presenters (3 days 6 days, 8 months, and 20 months) or non-serious cases from the start. None of our cases had bilateral defect.

The type of repair of diaphragmatic defect usually goes with the following order:

Primary suturing of the defect and if not practical then use of muscle flap based postero-laterally to bridge the defect. Finally, if this was inapplicable due to the huge defect then the use of an artificial graft like teflon, Prolene, marlex, or others, will bridge the gap in the diaphragm<sup>[5]</sup>.

The same rule was followed in our series, it was possible to close the defect using primary suturing in 22 patients, in 6 of them, the suture material used was absorbable type (polyglycolic acid).

Although the only three surgical complications noted in our patients: wound infection, septicemia, and wound dehiscence (one patient each) occurred in the patients who had absorbable suture defect repair. We do not think that any of the mentioned complications can be attributed to the suture material used especially when we say that none of the 27 patients presented had hernial recurrence.

In three patients only, synthetic graft was used. Two patients had almost absent left hemidiaphragm, one of them died 5 hours after surgery. The third one was a case of Cantrell's Pentalogy with a central diaphragmatic defect, the patient is alive and well. This means that the rate of synthetic graft used was 3/27 (11.1%).

The vast majority of Morgagni hernias present after the neonatal period, its mode of presentation varies from symptoms involving respiration or gastrointestinal system to no symptoms and signs<sup>[13, 14]</sup>.

The patient who had Morgagni defect presented when he was 20 months old to our hospital with a chest infection and Down's syndrome and the defect was discovered incidentally on the chest X-ray for infection. He had an Apgar score of 7 at one and 9 in 5 minutes. He was a product of breech vaginal delivery with abdominal stomach. During the operation his colon was found passing through the defect which was closed primarily using silk sutures. The patient was fed 4 days after the operation and sent home on 8th postoperative day.

Postoperative lung expansion is always subjected to different factors like the accuracy in reading the radiograph, the time at which the X-ray was repeated, the frequency at which the chest X-ray were taken and the severity of lung hypoplasia, *etc.* In the present study, we noticed that 13 patients had full lung expansion within 10 days of sur-

gery. another 5 patients had it between the 10th and 20th postoperative days. Two patients had full lung expansion relatively late one at 25 days and the last at 46 days.

In CDH as most neonatal illnesses, the patient might be surgically discharged but is kept hospitalized for a variable period of time for many different reasons, *e.g.*, very low weight, food intolerance, and different abnormal biochemical test results. In reviewing the period of time needed before the patients were cleared surgically, the results were as follows:

Six patients were surgically discharged within the first week postoperatively, 9 patients within the second week, 5 patients within the third week, and the last patient was surgically discharged on the fifth week. As the prognosis and outcome differ according to age at presentation, in such a way that the earlier the presentation, the worse the prognosis<sup>[9]</sup> which is especially seen in the neonates presenting at less than 6 hours of age<sup>[4-6]</sup>, we focused our interest into this age group.

We divided the patients into the mentioned 4 groups according to the time at which they became symptomatic and to mortality. About 30 different pre- and post-operative factors covering respiratory, radiological, and clinical data mentioned by different authors<sup>[1-19]</sup> were statistically studied using different methods like student T-test, liner regression analysis, and simple correlation. These include: pre- and post-operative (A-a) DO<sub>2</sub>, FIO<sub>2</sub>, PaCO<sub>2</sub>, VI, OI, pH, mechanical ventilation, age at operation, birth weight, hospitalization period, age at examination, lung expansion, surgical discharge, TPN, GIT feeding, maturity, inotropic drugs, associated anomalies, stomach position, pneumothorax, Apgar score, antenatal diagnosis, and polyhydramnios.

The above factors were applied on each of the four groups with an aim to define what are the factors to blame for increasing the mortality in Group B in comparison with the other groups mainly Group C which match Group B in age at presentation. Only 9 factors were found to be adversely affecting the mortality in Group B (the died patients) with a statistically significant difference.

It was clear from this present study, that all deaths occurred in patients presented within 6 hours of life, *i.e.*, it is the high risk group.

Since most of the patients who presented after 24 hours of age did not need pre- or post-operative ventilation and none of them died, this group was taken as a control to which all the other 3 groups correlated.

Because Group D (6-24 hours) was small in number, we did not present its results value at comparison.

As shown in Material and Methods and in Table 1, 15 patients presented with 6 hours of birth, 14 of them were born in our hospital.

The death rate was high in this group as expected 6/15 (40%) which matches other studies<sup>[12, 20]</sup>. But, when taking the gross mortality rate, it was 22% which is relatively low, as none of the 12 patients presented after the first 6 hours of life died in this study.

The presence of polyhydramnios in association with a fetus with congenital diaphragmatic hernia has been shown to be a predictor of poor outcome with a mortality in this group about 90%<sup>[18, 21]</sup>. On the other hand, some papers appeared to question this factor<sup>[22, 23]</sup>. But because of poor antenatal visit in this study's patients, only 3 of them were found to have polyhydramnios associated with pregnancy so we cannot draw an effective conclusion.

None of the patients presented within the first 6 hours of life and survived (Group C) had a PaO<sub>2</sub> less than 40 torr or PaCO<sub>2</sub> more than 60 torr. A simple bedside risk factor predictor is Alveolar-arterial oxygenation difference (A-a) DO<sub>2</sub> which is calculated as [(FiO<sub>2</sub> x 713) - PaCO<sub>2</sub> - PaO<sub>2</sub>] showed that all Group B (the died patients) has an (A-a) DO<sub>2</sub> value of more than 560.

Normal stomach site on antenatal ultrasound examination of CDH fetus is associated with 100% survival and only 20% of significant persistent fetal circulation; whereas, babies with a thoracic stomach antenatal had a high mortality rate (75%) and a more frequently developed significant persistent fetal circulation (85%)<sup>[3]</sup>. This high risk predictor can be extended to postnatal period when doing chest and abdominal X-rays. All the patients who died in this present study had thoracic stomach; whereas, only three out of the nine of the survivors of the matching group had thoracic stomach and the difference between both groups was statistically significant.

As noted from Table 1, Groups B and C when compared to control Group A, showed that (A-a) DO<sub>2</sub>, FIO<sub>2</sub>, VI, pH, and PaCO<sub>2</sub> had an equally, significant statistical difference; so, it is clear that none of them, although they are very important, are adversely affected the mortality in this study's patients. On the other hand, OI, PaCO<sub>2</sub>, birth weight and thoracic stomach showed significant difference in the died Group B but not the survivors, which indicate that these factors did adversely affected the mortality n patients presented within 6 hours after birth.

Oxygenation index(O.I.) is another simple bedside predictor, can be calculated as

$$\frac{\text{FiO}_2 \times 100 \times \text{mean airway pressure}}{\text{PaO}_2}$$

Bartlett outlet, *et al* put the risk figures for oxygenation index as a value of 25 defines a 50% mortality and a value of 40 an 80% mortality<sup>[24]</sup>. It was found in this present study that all except one of the died group had an O.I. value more than 100; whereas, all but one of the survivors had O.I. value less than 20.

When looking back into the factors which we think that they adversely affected mortality, *i.e.*, birth weight, PaO<sub>2</sub>, OI, and thoracic stomach they have something in com-

mon which is the affection of lung gas exchange either directly (OI and PaO<sub>2</sub>) or indirectly like thoracic stomach and birth weight (by the lung immaturity).

There was a positive correlation between OI and both pH and (A-a) DO<sub>2</sub> with a *r* value of 0.798 and 0.579, respectively, and both corresponded to a high statistical significant values. ( $P < 0.001$ ) and  $< 0.01$ ), respectively).

Also, there was a positive correlation between (A-a) DO<sub>2</sub> and both VI and PaCO<sub>2</sub> with a *r* value of 0.591 and 0.605, respectively. These correlation match high statistical significance with  $P < 0.01$  on either relations.

When (A-a) DO<sub>2</sub> was correlated to pH values there was a negative correlation as expected with a *r* value of -0.55 and a *P* of  $< 0.01$ .

On the other hand, when OI and PaCO<sub>2</sub> were correlated, it showed a *r* value of -0.643 and a *P* of  $< 0.01$ .

VI was positively correlated with FIO<sub>2</sub> and negatively with the birth weight and having a *r* value of above 0.51 and a *P* value of  $< 0.05$  on either relation.

Surprisingly, PAO<sub>2</sub> did not have high significant relation to any other preoperative ventilation parameter when linear regression analysis was applied. But actually, it had low significant figures with a *r* value between 0.4 - 0.5 which we did not want to stress on because of the small number of patients. These include its relation to (A-a) DO<sub>2</sub>, OI, and PaCO<sub>2</sub>.

The conclusions from the present study are:

1. The incidence of CDH in Southwest region of Saudi Arabia is 1 : 2,320 live births.
2. An overall mortality of 22% which goes to 40% in patients presented within the first 6 hours of life.
3. The major high risk factors adversely affecting survival of patients presented within 6 hours of life include: low birth weight, preoperative PaO<sub>2</sub>, preoperative oxygenation index, and thoracic stomach.
4. Some less significant risk factors affecting the same group of patients included: preoperative PaCO<sub>2</sub> and preoperative (A-a) DO<sub>2</sub>.

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## فتق الحجاب الحاجز الخلقي : عوامل الخطورة ، خبرة العلاج في المنطقة الجنوبية ، المملكة العربية السعودية

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جدة - المملكة العربية السعودية

المستخلص . يعتبر فتق الحجاب الحاجز الخلقي من الطوارئ الشائعة في المواليد في مراكز الاحالة الطبية، وقد قمنا بدراسة عوامل و جوانب عديدة لما قبل وبعد العملية مرتباً بالعلامات السريرية و التنفسية و نتائج الفحص بالاشعة، و قمنا بربطها بتوقعات نتائج العلاج. ٢٧ حالة أدخلت لمستشفى الملك فهد بالباحة ( المنطقة الجنوبية الغربية بالمملكة العربية السعودية) خلال الفترة من أكتوبر ١٩٨١ حتى أكتوبر ١٩٩٢ م وقد بلغ معدل الوفيات ٢٢٪ ولكن عند اعتبار الحالات التي شخّصت أعراضها خلال الست ساعات الأولى فقط فقد ارتفع معدل الوفيات إلى ٤٠٪، و لقد قمنا بدراسة ٣٠ عامل خطورة مع إجراء التحليل الإحصائي لذلك وقد أظهرت نتائج الدراسة أن معدل حدوث فتق الحجاب الحاجز الخلقي في المنطقة الجنوبية من المملكة العربية السعودية ١: ٢٣٢٠. وقد اتضح أن العوامل التي تشكل خطورة بالغة على حياة المواليد الذين يعانون من فتق الحجاب الحاجز الخلقي تشمل الوزن المنخفض للمولود، ضغط الاكسجين بالدم ، معامل الأكسجة في الدم و موقع المعدة في الصدر، كما أن هناك عوامل أخرى أقل خطورة و تشمل معامل الأكسجة الهوائية و الدم الشرياني و نقدم في هذه الدراسة تفاصيل تلك العوامل المذكورة.