Diaphragmatic Hernia in Children Admitted to Pediatric Hospital during 10 Years from 2009-19

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Abstract

Introduction: Diaphragmatic hernia is a congenital anomaly with significant mortality even in the best centers of the world. Numerous risk factors have been identified in studies as predictors of patient outcome. The aim of this study was to determine the status of diaphragmatic hernia and related outcomes in children admitted to pediatric hospital.

Materials and Methods: Data of diaphragmatic hernia was extracted from patients' records in Dr. Sheikh Hospital in Northeast of Iran who were admitted since 2009 till 2019. Demographic and birth information, disease diagnostic findings along with developmental defects or syndromes were recorded. In addition, more information about the patient and surgery was collected, including the length of

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the patient's stay in the intensive care unit (ICU), and the patient's condition before and after surgery. Also, data about recurrence of the disease, postoperative growth and development status of the child were gathered.

Results: Study included 153 patients, of whom 61.4% were male. Term gestational age, vaginal delivery, respiratory distress, and organ defects were seen in 81.7%, 54.9%, 91.5 %, and 24.2 % respectively. The overall hospital mortality of patients was 24.8%.The Apgar score of the live group was significantly higher than that of the deceased group. The length of ICU stay before surgery was significantly higher in the deceased group.Pco2 levels were significantly higher before and after surgery in the deceased group.HCo3 levels in the dead group were significantly higher than that of the living group.

Conclusion: The results of our study suggested that Apgar score and VBG (venous blood gas) status were probably related to patients' outcome.

Keywords

- Children
- Diaphragmatic hernia
- Mortality

Introduction

A congenital diaphragmatic hernia is an evolutionary defect in the diaphragm that allows the abdominal organs to enter the thorax; this prevents the appropriate growth of the lungs. The greater the pressure exerted on the chest by the abdominal organs, the greater the rate of pulmonary hypoplasia and vascular wall muscular hyperplasia, which in turn will increase pulmonary blood pressure.[1] In general, congenital diaphragmatic hernias can be divided into two categories: lateral posterior hernias (Bochdalek) and anterior hernias.[2] Various studies have stated different values as the prevalence rate of this disease, which varies between 1 to 4 cases per 10,000 live births.[3-5] An analysis of data from 31 population-based registries in Europe over a 29-year period involving more than 12 million live births reported an incidence of 2.3 per 10,000 live births.[5] One study reported that about 30% of congenital diaphragmatic hernias end in miscarriage or stillbirth.[4]

Patients with congenital diaphragmatic hernias usually develop respiratory distress in the early hours or days of life. The clinical manifestations of these patients range from severe and acute respiratory distress to asymptomatic neonates. Of course, the number of patients presenting with acute distress is much higher than asymptomatic patients.[1] Adrenal insufficiency is a common

finding in infants with diaphragmatic hernias. In a retrospective study of 58 patients, adrenal insufficiency was present in two-thirds of the 34 patients in whom adrenal function was assessed.[6] Abnormalities associated with congenital diaphragmatic hernias occur in about 50% of cases, including chromosomal problems, congenital heart disease, and neural tube defects.[1]

On physical examination, symptoms such as barrel-chest, scaphoid abdomen, and absence of respiratory sounds on the ipsilateral side can be detected. This lesion can be diagnosed using routine prenatal ultrasounds.[1] In 60% of cases of congenital diaphragmatic hernia, the complication is suspected in routine ultrasounds performed at 22-28 weeks of gestation.[4] However, in cases where the lesion is so small that the abdominal organs cannot reach the fetus' chest, the diagnosis may be delayed.[7] In infants whose diaphragmatic hernia is unknown during pregnancy, the lesion can be detected using a chest radiograph.[1]

The survival rate of these patients in level 3 centers has increased in recent years and is now about 70-92%.[1] This increase in survival is probably due to a shift in methods from early surgical interventions to increased preoperative support measures to avoid lung injury. Of course, this survival rate does not include infants who were stillborn or died in the womb or before reaching the level three centers.[4, 8-10] In general, problems that reduce survival include premature status of the infant,[8] cardiac abnormalities,[11] persistent and severe pulmonary hypertension,[12] need for mesh repair,[13] low preductal oxygen and high content of blood carbon dioxide,[14-17] and the size of the damage.[18, 19] Overall, studies have shown that early neonatal medical management and neonatal surgery immediately after birth increase the survival rate in infants with congenital diaphragmatic hernias.[20-23]

Despite all the advances, mortality in patients with congenital diaphragmatic hernia remains high. Patients who survive early-onset birth problems will also experience many complications in the future.[24] Research on patients with congenital diaphragmatic hernias is very limited and the studies performed are usually of the case series and no valid clinical trial has been performed on these patients. The lack of extensive and reliable studies has resulted in a lack of sufficient clinical information to deal with patients with congenital diaphragmatic hernia. The aim of this study was to evaluate the condition of children with congenital diaphragmatic hernia before and after surgery. To our knowledge, this was performed for the first time in Iran.

Materials and Methods

This cross-sectional and analytical study was performed on diaphragmatic hernia patients admitted to Dr. Sheikh Pediatric Hospital over a period of 10 years from 2009 to 2019.Inclusion criteria included all children who underwent surgery with a diagnosis of diaphragmatic hernia and whose information was fully available. If there was a defect in the information (patient outcome as well as age and sex), the patient was excluded from the study. A checklist was used to collect information from health Information System and patient records. The checklist included: demographic data (age, sex), birth data

(gestational age, type of delivery, parental age, family relationship between parents, physical disability, primary respiratory symptoms, non-respiratory problem, medicine consumption by the mother during pregnancy, Apgar score, birth weight and discharge weight),diagnostic findings related to hernia (hernia findings in CXR and how to diagnose hernia, presence or absence of hernia diagnosis based on prenatal ultrasound),accompanying developmental defects or the presence of syndromes, duration of hospitalization in the ICU before and after the surgery, medical treatment of the patient in the ICU, type of surgery, patient status after surgery, relapse status, and the growth and development of the child at 6 months and one year after surgery. The main measurable outcome was the patient's postoperative condition and secondary outcomes included discharge status and recurrence rate.

Patients' data was recorded in encrypted form and kept confidential. All stages of this study followed the ethical principles of Helsinki and were approved by the ethics committee of Mashhad University of Medical Sciences (MUMS).This research was approved by the Organizational Ethics Committee of the Faculty / Regional of MUMS with the code IR.MUMS.fm.REC.1396.714.

Data were analyzed by SPSS version 24. The characteristics of the subjects were presented by descriptive statistical methods including central indices, dispersion and frequency distribution. To compare quantitative variables, in case of normal distribution of data, independent t-test and otherwise Mann-Whitney test were used. Chi-square test and Fisher's exact test were used to compare qualitative variables. In all calculations, values less than 0.05 were considered significant levels. Due to the nature of the census study, there was no need to calculate the sample size and all eligible items in the study period were included.

Results

There were a total of 176 patients. With respect to the inclusion and exclusion criteria, 153 patients were finally included in the study. 94 patients (61.4%) were males. In terms of gestational age and type of delivery, 125 patients (81.7%) were term neonates and 84 patients (54.9%) were resulted from vaginal delivery. The mean birth weight was 2.95 ± 1.34 kg.The mean age of neonates (≤28 days) was 2.59 ± 3.20 days and the mean age of late cases (> 28 days) was 278.91 ± 170 days. The mean age of mother was 28.45 ± 6.22 years and that of father was 33.09 ±6.06 years.

53% of patients' parents had a family relationship. About 52% of patients were referred from counties and about 40% from maternity wards. Ninety five and half percent of patients had no physical abnormalities. Eleven patients (7.2%) were syndromic. Ninety one and half percent of patients had respiratory distress. Ninety two percent of mothers had a history of medicine consumption during pregnancy. Among the patients who had undergone echocardiography(about 30% of the total patients), 69% had abnormal echocardiography and most of the echo problems included atrial septal defect (ASD), patent ductus arteriosus (PDA),

and pulmonary hypertension (PH). None of the patients had a family history of diaphragmatic hernia.

Based on the patient's condition before surgery, the patient's referral origin ($p = 0.024$), echocardiographic findings ($p < 0.0001$) and concomitant anomalies ($p = 0.045$) showed a significant difference between alive and dead patients. Accordingly, 100% of patients who were referred by a pediatrician were finally discharged. Patients with echocardiography tests were 51.5%, of which 15.5% had normal results. Mortality was seen in 34% of neonates without echocardiography and 5.4% of patients with abnormal echocardiography. Organ associated abnormality was recorded for 75.8% of patients, while15.5% of them died. Of the 12.4% of patients who died before surgery, all had abnormal echocardiography; also, the rate of associated organ abnormalities was higher in patients who survived. Based on the patient's condition at discharge, blood type ($p = 0.001$) and type of surgery ($p = 0.049$) showed a significant difference between the two conditions of discharge including the stable condition and personal consent of clearance under unstable condition. Accordingly, discharge of the patient in unstable conditions was observed in 43% of people with AB blood type, while discharge in these conditions was observed in less than 3% of patients with other blood groups. Thoracoscopy and open surgery were performed for 40 and 72 cases, respectively. Among open surgery cases 4.2 % were discharged in unstable conditions. In terms of postoperative status in the neonatal group (28 days), 93 patients (72.1%) survived (83.8%) and 18 patients (16.2%) died. In the late group (> 28 days), 21 patients (95.5%) survived and 1 patient (4.5%) died.

Underlying characteristics of the patients were compared based on the patient's final condition (live, dead) and recurrence (none, 6 months later, more than 6 months later). Accordingly, gestational age at birth ($p = 0.035$), location of liver ($p = 0.002$), medicine consumption in ICU ($p < 0.0001$) and type of surgery ($p = 0.012$) showed significant differences based on the final condition of the patient. There were 20 preterm patients, 30% of whom eventually died. Of the 111 term-born patients, 10.8% died after surgery. In 16 patients, the liver was located in the thorax, of which 43.8% died. Among 20 patients who had a history of taking inotropes during ICU stay, 30% died. Of the 20 patients with a history of sildenafil consumption at the time of ICU admission, only one death occurred. Of 13 patients with a history of sildenafil/milrinone consumption during admission to the ICU, 30.8% died. In 41 cases of thoracoscopic surgery, only 1 death was observed, while in 89 open surgeries, 17 deaths were observed. Gender ($p = 0.032$) was the variable that showed significant differences in terms of recurrence. In 84.6% of male patients, no recurrence of the disease was observed after surgery at different time intervals. In 47.1% of girls, recurrence of the disease was observed at different time intervals after surgery. Among the total number of patients with recurrence (43 patients), 14% (6 patients) had recurrence in the first

6 months after surgery and 14% (6 patients) showed recurrence more than 6 months later.

Table 1 shows a comparison of quantitative data based on the patient's final condition. As is clear; the Apgar score of the live group was significantly higher than that of the dead group (8.40 ± 1.39 vs. 6.78± 2.00 ; p = 0.003). Also, the duration of ICU stay before surgery was significantly higher in the dead group (4.00±2.18vs. 2.70± 2.12; p = 0.012).Pco2 levels were significantly higher in the dead group before and after surgery. The pH level before and after surgery was significantly higher in the live group. In addition, HCo3 levels in the dead group were significantly higher than the living group.

Table 1. Comparison of quantitative data based on patient status

Characteristic	Final status of the patient		P-value (T test)
	live	dead	
Age (days)	58.4± 184.6	20.4±8.05	0.436
Birth weight (kg)	2.95±0.49	2.95±0.58	0.803
discharge weight (kg)	3.87±2.16	3.39±0.69	0.945
Apgar	8.40±1.39	6.78±2.00	0.003
Duration of ICU hospitalization before surgery	2.70±2.12	4.00±2.18	0.012
Duration of ICU hospitalization after surgery	11.05±11.09	13.52±22.91	0.139
HCo3 levels before surgery	21.19±6.76	21.16±6.55	0.573
PCo2 levels before surgery	41.51±18.26	52.86±19.09	0.007
pH levels before surgery	7.33±0.16	7.21±0.14	0.001
HCo3 levels after surgery	21.76±5.02	25.77±5.38	0.002
PCo2 levels after surgery	37.62±8.50	53.86±17.89	<0.0001
pH levels after surgery	7.36±0.06	7.29±0.13	0.01
Z score of weight 6 months later	1.19±-1.46	1.20±-1.054	0.224
Z score of height 6 months later	0.57±-1.37	0.62±-1.24	0.942
Z score of weight 12 months later	1.04±-1.69	1.24±-1.36	0.543
Z score of height 12 months later	0.33±-1.09	0.41±-0.94	0.766

Of the 153 patients, 19 died and 134 survived to the operation; of the remaining patients, 19 died after surgery and only 115 remained, leaving a postoperative mortality rate of 14.3%.The mortality rate was 16.2% among infants and 4.5% among late cases. In total, according to the results of the study, only 12 cases had recurrences. The overall mortality rate was 24.8%.

The results of quantitative data showed that Apgar score at birth was significantly higher in the live group. The mean duration of ICU stay was 2.81 days before surgery and 11.40 days after surgery. However, the duration of ICU stay in deceased patients was significantly longer than the surviving group. In addition, people with more severe metabolic acidosis had a worse prognosis.

Discussion

In a study, Carmichael et al.[25] examined data on 658 cases of congenital diaphragmatic hernia over 5 years. A total of 180 patients died in this study, of which 67% died before surgery and 33% died after reconstructive surgery. The results of the study of risk factors related to patient mortality showed that patients who were underweight or had cardiac and non-cardiac abnormalities, had an Apgar score of less than 5. Moreover, patients that their mother did not provide prenatal care or performed it late, were at greater risk for death. In the present study, the Apgar score was significantly lower in the group that died after surgery. However, the presence or absence of prenatal diagnosis was not significantly different between the two groups.

Shanmugam et al.[26] conducted a 13-year study of the condition of a diaphragmatic hernia in the United States. A total of 227 cases of congenital diaphragmatic hernia were found in their center during the study period, most of which were boys, as in the present study. Rate of syndromic patients in US study was 13.2% while it was 7.2% in the present study. They showed the higher chance of diagnosing syndromic patients during pregnancy. The mortality rate of diaphragmatic hernia patients was 32.5%, which was higher than our study (24.8%). In the study discussed, the factors that were most associated with mortality included the presence of liver in the chest and Apgar score less than 5. In our study, Apgar scores were significantly lower in deceased individuals.

Dehdashtian et al.[27] examined congenital diaphragmatic hernia in Ahvaz, Iran for 5 years. The results showed that 60 infants had this defect, which was higher in males. 91.7% of hernia cases in this study were on the left; 6.7% were on the right and 1.7% were bilateral. In our study, 84.3% were on the left, 15.0% on the right, and 0.7% on both sides. Preterm cases percentage was 21.7%, while that was 17.0% in our study. In this study, gestational age and delivery method showed a significant difference between the living and dead groups before surgery, while in our study, gestational age showed a significant difference between the dead and living groups after surgery, in contrast

to the method of delivery, which did not show a significant difference between the dead and alive groups before surgery. The survival rate of patients in this study was 41.6%, which was much higher in the present study and was about 75%.

Hinton et al.[28] reviewed data from 25 years of diaphragmatic hernia retrospectively. In this study, the mortality rate was 41%, which was higher than our study (24.8%).In this study, the duration of treatment and the presence of comorbid anomalies were risk factors for patient survival, while in our study there was no significant difference between surviving and deceased patients in terms of comorbid anomalies.

In a study conducted in Croatia by Grizelj et al.[29], 145 hernia cases were found in a duration of 12 years, most of which were male. The rate of prenatal diagnosis was 30.4%, compared with 45.3% in our study. Also, 21.4% of patients were preterm. The postoperative survival rate in this study was 66.9%, which was slightly lower than that of our study. Similar to our study, the presence or absence of prenatal diagnosis did not show a significant difference between living and dead cases. However, in contrast to our study, the hernia side showed a significant difference in the patient's condition after surgery (alive or dead).

Despite the many advances that have been made in recent years, congenital diaphragmatic hernia is still a challenging issue, of which the etiology and pathogenesis are not well understood.

However, the important role of genetic and environmental factors in the development of this problem has been largely proven. In addition, there are shortcomings in the treatment of these patients and no method has been accepted as a complete and perfect method in the management of these patients. In previous studies, extensive research has been recommended to access the appropriate sample size in order to achieve a reliable result in the future.[24]

Conclusion

This study showed that patients' gestational age, liver status, Apgar score, pH and blood gas parameters may be associated with the outcome of diaphragmatic hernia patients and therefore should be further investigated.

Strengths and weaknesses

This study examined more contextual variables than other few studies in Iran. Also, the type of surgery and VBG of patients were compared between living and dead cases, which was not present in other studies. In the data of early years in present research, patient echocardiography results were not included in the paper records. Our information resources were limited to the paper records and access to most families was not available to follow the patient's condition and completing the information.

Ethical Consideration

This study was approved by Ethical Committee of Mashhad University of Medical Sciences.

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Conflict of interests

There is no conflict of interest

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