

ORIGINAL ARTICLE

Factors Affecting Survival in Congenital Diaphragmatic Hernia: A Prospective Study at a Tertiary Center

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ABSTRACT

Background: The outcome of congenital diaphragmatic hernia depends on associated anomalies, degree of pulmonary hypoplasia, and hypertension. We evaluated the postnatal prognostic factors which can be used to predict the outcome.

Methods: This study was conducted at a tertiary center (Vali-e-Asr Hospital, Imam Khomeini Complex, Tehran, Iran) during 2013-2019. The predictors of survival were evaluated.

Results: A total of 49 infants with congenital diaphragmatic hernia were born during 2013-2019. The patients' mean gestational age and weight at birth were 37.51±1.75 weeks and 2871±562 g, respectively. The mortality rate in patients with surgery (n = 41) was 31.3% and eight patients died before surgery. Mortality had significant relationships with five-minute Apgar score, peak inspiratory pressure before and after surgery, partial pressure of arterial oxygen (PaO₂), and pH during first 24 hours after birth (p= 0.01, 0.001, and 0.01, respectively). The predicted and true survival rates in the patients were 66% and 52%, respectively (p= 0.001).

Conclusion: Predicting survival rate after birth is remarkable but controversial. This estimate should not affect patient care and should only help parents in the process of decision-making.

Key words: Congenital heart disease; Diaphragmatic hernia; Predictive outcome; Survival

INTRODUCTION

The prevalence of congenital diaphragmatic hernia (CDH) is approximately one in 2500-4000 live births.[1-3] The severity of the disease and thus final outcome are variable and depend upon comorbidities and the degree of associated pulmonary hypoplasia and pulmonary hypertension.[4,5] Other determinants of disease severity are the side of hernia, the position of the liver, the amniotic fluid volume, lung parameters (e.g. lung to head circumference ratio), central nervous system defects, complex syndromes, and chromosomal defects.[6,7]

The survival of children with CDH has steadily improved to 70%-90% over the past decades because

of increased application of standardized protocols and gentle ventilation strategies, including permissive hypercarbia, high-frequency ventilation, inhaled nitric oxide, and extracorporeal membrane oxygenation (ECMO).[4,8] Moreover, surgical interventions are no longer considered emergent perinatal surgery and can be delayed and performed as elective surgery in health centers equipped with modern facilities.[4,8,9]

The Congenital Diaphragmatic Hernia Study Group (CDHSG) has developed models to predict postnatal outcomes based on one- and five-minute Apgar scores. The Wilford Hall/Santa Rosa clinical prediction formula (WHSRpf) is also used to predict post-

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Submitted: 28-10-2019

Conflict of interest: None

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Accepted: 08-03-2020

Source of Support: Nil

natal survival.[7,10,11] The present study was conducted to compare the survival rates predicted by the above-mentioned methods with true survival rates.

MATERIALS AND METHODS

This prospective study was performed on all patients with CDH born during 2013-2019 in a tertiary center at Vali-e-Asr Hospital, Imam Khomeini Complex, Tehran, Iran. The study approved by Ethics Committee of Imam Khomeini Hospital, Tehran University Sciences (Approval Code: IR.Tums.IKHC.REC.1396.4255)

Demographic and clinical data, including birth weight, five-minute Apgar score, presence of a cardiac defect, arterial blood gas levels, and survival (until hospital discharge), were evaluated. All patients were electively intubated owing to respiratory distress with minimal barotrauma (peak inspiratory pressure-PIP was set at 18-27 cmH2O and synchronized intermittent-mandatory ventilation-SIMV was used in all cases). Inotropic agents (e.g. dobutamine and/or dopamine 5-10 µg/kg/min) and intravenous pulmonary vasodilators were administered if deemed necessary. Total Parenteral Nutrition (TPN) was also given instead of oral feeding before surgery. Intravenous pulmonary vasodilators prescribed when necessary according to echocardiography and response of the patient to inotropes. All infants underwent delayed surgery by a single surgeon. Predicted survival rates were calculated according to the equation published by the CDHSG in 2001.[11]

$$\text{Probability of survival} = 1 - 1/(1 + e^{-X})$$

$$-X = -5.0240 + 0.9165(\text{BW} + 0.4512 (\text{Apgar } 5))$$

Where BW is birth weight in kg and Apgar 5 is the five-minute Apgar score.

The true survival rate was also calculated, and the collected data were analyzed using t-tests. The true and predicted survival rates were then compared using a one-sample binomial test and p-value less than 0.05 was considered significant.

The survival rate was also predicted by the WHSRpf based on blood gas values measured during the first 24 hours of life. The highest partial pressure of arterial oxygen (PaO2) and partial pressure of carbon dioxide (PaCO2) (with a cut-off value of ≥ 0) were also determined. Values ≥ 0, indicated higher chance of survival. [7] All statistical analyses were performed using SPSS 18.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

The mean gestational age and birth weight were 37.51 ± 1.78 weeks and 2871 ± 562 g, respectively. Twenty patients (42.9%) were born to primigravida.

Twenty-four patients were males and 25 were females (M: F 0.96). Forty three patients (87.8%) had prenatal diagnosis and thirty four (69.4%) of them born through cesarean section (all because of maternal indication). There were two familial cases. Seven (14.3%) mothers had history of previous medical problem such as diabetes mellitus or hypertension.

Echocardiography was performed in all patients and 26 patients had congenital heart disease, the most common was aortic coarctation (5 of 49, 10.2%). Others congenital heart disease were atrial septal defect (4 of 49, 8.1%),ventricular septal defect (4 of 49, 8.1%), PDA (4 of 49, 8.1%), hypoplastic left heart disease (2 of 49, 4.08%), tricuspid regurgitation (4 of 49, 8.1%), pulmonary stenosis (3 of 49, 6.1%).

Thirty-nine patients had pulmonary hypertension (79.6%) and it was with increased risk of mortality. (p=0.047). In seven cases (14.3%), there were other anomalies. Four patients had esophageal atresia, one was VACTERL syndrome and 2 patients had chromosomal anomaly. Right-sided defect was present in 2 of the patients (4%) and in 18 of the patients liver was in the thorax (36.7%). The stomach was in thorax in 25 of 49(51%).

Eight patients died before surgery. In the patients underwent surgery, Mesh was used in 14 of patients because of large defect and poor diaphragmatic remnants (34.1%). Fifteen patients (36.5%) died after surgery. PIP was 20.8 ± 8.20 and 24.35 ± 7.92 cm H2O respectively before and after surgery in those who were expired after surgery. The corresponding values were 18.76 ± 3.85 and 19.44 ± 4.46 cm of H2O in patients who survived (p= 0.03). The patients who died before surgery required higher PIP (more than 27 cm H2O) and the relationship between PIP and mortality was statistically significant in these patients (p= 0.001). There was no significant correlation between size of defect and either mortality (p= 0.74) or length of the hospitalization (p= 0.80).

Table1: Factors with positive effect on survival.

Mean PIP ≤ 21.7±6.03	p-value = 0.02
5 min APGAR ≥ 7.6	p-value = 0.04
Preoperative PaO₂ ≥ 77mmHg	p-value = 0.01
Preoperative PH ≥ 7.35 mmHg	p-value= 0.03

The mean five-minute Apgar score was 7.8 in patients who survived and about 5.8 in those who died (p= 0.01). Preoperative PaO2 was 73 mmHg in patients who survived versus 53 mmHg in those who died (p= 0.01). Factors with positive effect on survival are shown in Table1. The patients who died and those who survived also had a significant difference in the mean first preoperative pH (7.15 vs. 7.30; p= 0.01). Type of delivery and side of the diaphragmatic hernia had no effect on mortality rate.

Based on the WHSRpf, predicted survival rates were 61% and true survival rate was 52% ($p=0.049$) (Fig.1).

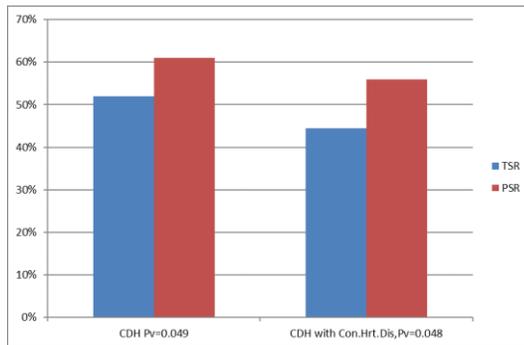


Figure 1: Comparison of true survival rate and predictive survival rate in congenital diaphragmatic hernia with and without congenital heart disease. TSR: true survival rate, PSR: predictive survival rate.

DISCUSSION

Predicting survival of CDH before and after birth is of interest to practitioners and has thus been the focus of many studies. This study predicted the survival after birth based on weight, five-minute Apgar score, and arterial blood gas levels. The values were then compared with the true survival rates.

According to the formula recommended by the CDHSG in 2001, [11] the predicted survival rate was 61% in patients who underwent surgery. The true survival rate in these patients was 52% ($p=0.004$). Downard et al, studied 39 patients during 2002-2006 and reported the predicted and true survival rates as 68% and 98%, respectively ($p=0.001$). [10] They used extracorporeal membrane oxygenation (ECMO) for all the patients in their study, but as we have not ECMO in our center we did not use it. This may explain the difference of the results. Pylvaste et al, assessed the mortality rate among 34 newborns during 2001-2008: although the mortality rate was high in patients with five-minute Apgar score < 7 and a low pH in the first 24 hours of birth, these factors had no significant effects on mortality rates. [12] The survival rate in our study was higher than that reported by Pylvaste et al, and this improvement had significant associations with five-minute Apgar score (mean = 7.8; $p=0.01$) and pH in the first 24 hours after birth (mean 7.30; $p=0.01$). According to our findings, the predicted survival rate based on the formula recommended by the CDHSG in 2001 had a significant relationship with true survival rate ($p=0.049$).

Grizelj evaluated 44 patients during 2000-2014, and found significantly lower cutaneous carbon dioxide tension ($PcCO_2$) in patients who survived than in those who died ($p=0.02$). [13] We found similar results regarding $PcCO_2$, but the difference in our study was not statistically significant. Like the findings of Grizelj, the first arterial blood gas tests

in our study showed significantly higher pH in infants who survived than in those who died ($p=0.01$). [13]

Bojanić et al, conducted a two-phase study on 83 patients during 1990-1999 and 2000-2014. The survival rates in the first and second phases were 42% and 67%, respectively ($p=0.039$). Lower $PcCO_2$ on the first day was responsible for the improved survival rate. [14] Similarly in our study, we found similar results regarding $PcCO_2$ but was not statistically significant. While they used nitric oxide to reduce pulmonary hypertension, we only applied drug therapy in our patients with pulmonary hypertension (as we do not have access to nitric oxide or ECMO).

We also evaluated impact of associated congenital heart anomalies on the survival rate of patients with CDH. Previous studies documented low survival rates in these patients. [11] Graziano et al, performed a study in 82 centers during 1995-2005 and reported the survival rate in patients with CDH and associated congenital heart disease as 41.1% ($p=0.001$). The most common congenital anomaly in their study was ventricular septal defect (VSD) [15] but it was coarctation of the aorta in our study. Menon et al, documented congenital heart disease in 18% of patients with CDH. The most common anomalies reported were hypoplastic left heart syndrome and coarctation of the aorta. [16] The true 250-day survival rate in their study was 40%. In our study, however, the true 60-day survival rate was 44.5% and the predicted survival rate was 56%. ($p=0.049$) In our study, a higher mortality rate might be attributed to the fact that no pregnancy was terminated due to the severity of the disease. Moreover, we did not have access to ECMO or nitric oxide which might also lead to higher mortality in our series. This is also a limitation in our study.

CONCLUSION

Lower PIP for ventilation accompanied with survival. In our study pulmonary hypertension didn't have significant effect on survival but prolonged hospital stay. Predicting survival rate after birth is interesting and controversial. This estimate should not affect patient care and should only help parents in the decision-making process. In addition, its comparison with true survival rates allows health centers to modify and improve their planned interventions.

Acknowledgements: This study was supported by Tehran University of Medical Sciences. We are thankful to all participants and their parents and to all nurses and other medical staffs who helped us in this project.

Consent: Authors declared that they have taken informed written consent, for publication clinical photographs/material (if any used), from the legal

guardian of the patient with an understanding that every effort will be made to conceal the identity of the patient however it cannot be guaranteed.

Author Contributions: All the authors contributed fully in concept, literature review, and drafting of the manuscript and approved the final version of this manuscript.

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