Outcomes of Congenital Diaphragmatic Hernia: A Population-Based Study in Western Australia

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ABSTRACT. Objectives. There have been many recent reports of improved survival rates for congenital diaphragmatic hernia (CDH), largely derived from institution-based data. These are often flawed by case selection bias. The objectives of this study were to document the true incidence, management, and outcomes of CDH in a geographically defined population over a 12-year period and to determine the changing trends in these over time. We also sought to ascertain the prenatal and postnatal factors associated with morbidity and death among these infants.

Methods. A retrospective study of all cases of CDH in Western Australia from 1991 to 2002 was conducted. Cases were identified from 5 independent databases within the Western Australian health network, including the Western Australian Birth Defects Registry. All fetuses and neonates diagnosed with CDH in Western Australia during this period were identified, including miscarriages, stillbirths, and terminations of pregnancies in which a diagnosis of fetal CDH had been made, as well as those diagnosed postnatally. Cases not known to involve CDH until diagnosis at autopsy were also included. Infants with diaphragmatic eventration were excluded from the study. Detailed information was obtained from review of maternal and infant medical records.

Results. One hundred sixteen cases of CDH were identified. Of these, 71 (61%) infants were born alive and 37 survived beyond 1 year of age (52% of live-born infants, 32% of all cases of CDH). Pregnancies involving 38 (33%) fetuses were terminated electively, 4 (3%) fetuses were aborted spontaneously, and 3 (3%) fetuses were stillborn. Another major congenital anomaly was present in 54 (47%) cases. Twenty-one (18%) cases had other anomalies that were likely to be fatal. Of all cases with an additional major anomaly, 42 (78%) died. Twenty-seven (71%) of 38 fetuses for whom the pregnancy was terminated had another major anomaly. Forty-three (52%) live-born infants had another major anomaly (4 of which were considered fatal conditions); however, this did not affect their survival rates. Fifty-three percent of cases were diagnosed prenatally, and 49% of these pregnancies were then terminated. Of live-born infants with prenatally diagnosed CDH, 10 (33%) survived beyond 1 year of age. The gestational age at diagnosis did not affect the survival rate for live-born infants. Postnatal diagnosis occurred in 55 (47%) cases. Of these, 41 (74%) case subjects were born alive and diagnosed on clinical grounds after birth. In the remaining 14 cases, the diagnosis was made in postmortem examinations of fetuses from pregnancies that were terminated for other reasons (8 cases) or after spontaneous abortion or stillbirth (5 cases). Significant differences were found between prenatally and postnatally diagnosed live-born infants. Among live-born infants, prenatal diagnosis was associated with a significantly reduced survival rate (33%, compared with 66% for postnatally diagnosed infants). Prenatally diagnosed live-born infants were of lower birth weight and were born at an earlier gestational age. There was no statistically significant difference between the 2 groups in the onset of labor (spontaneous or induced) or in the rate of elective cesarean sections. Prenatally diagnosed live-born infants were more likely to be delivered in a tertiary perinatal center and were intubated more commonly at delivery. No difference was found in the Apgar scores at either 1 or 5 minutes between the groups. Of 71 live-born infants, 37 (52%) survived to 1 year of age. The majority of deaths occurred within the first 7 days of life (44%). Preoperative air leaks occurred for 16 (22%) infants, of whom 14 (88%) died. Factors found to predict death of live-born infants included prenatal diagnosis, right-sided hernia, major air leak, earlier gestational age at birth, lower birth weight, and lower Apgar scores at 1 and 5 minutes. Over the course of the decade, there were significant increases in the proportion of cases in which the diagnosis of CDH was made with prenatal ultrasonography and in the number of live-born infants born at the tertiary perinatal center. The mortality rate for all cases, the mortality rate for live-born infants, and the proportion of pregnancies involving prenatally diagnosed cases that were terminated electively were all greater in the later epoch but not significantly so.

Conclusions. This was a comprehensive, population-based study of CDH, with full case ascertainment, large sample size, and complete outcome data for all cases. The majority of published studies of CDH examined specific patient populations, such as neonates referred to tertiary pediatric surgical centers. Invariably, those studies failed to detect the demise of cases with CDH before arrival at the referral center, whether through termination of pregnancy, in utero fetal demise, or postnatal death occurring before transfer. Exclusion of these cases from calculations of mortality rates results in significant case selection bias. In our study, 35% of live-born infants died before referral or transport. The population of infants reaching the tertiary surgical center represented only 40% of the total cases of CDH. Wide variations in reported survival rates occur throughout the literature. These differences reflect the influence of this case selection bias, as well as variable referral policies and management practices. For our study population, survival rates differ...
fered vastly depending on the subgroup analyzed. Ninety-two percent of postoperative infants survived beyond 1 year of age, as did 80% of infants who reached the surgical referral center. However, only 52% of live-born infants, 32% of all cases, and 16% of all prenatally diagnosed cases survived. Therefore, the overall mortality rate for this condition remains high, despite increased prenatal detection, transfer to tertiary institutions for delivery, and advances in neonatal care, and is influenced significantly by the rate of prenatal termination. In our study, 33% of all cases of CDH and 49% of prenatally diagnosed fetuses underwent elective termination of pregnancy. This large number of fetal terminations confounds the accurate assessment of the true outcomes of this condition. Pediatrics 2005;116:356–363. URL: www.pediatrics.org/cgi/doi/10.1542/peds.2004-2845; congenital diaphragmatic hernia, outcome, population-based study.

ABBREVIATIONS. CDH, congenital diaphragmatic hernia; HFOV, high-frequency oscillation ventilation; INO, inhaled nitric oxide; ECMO, extracorporeal membrane oxygenation; CI, confidence interval; OR, odds ratio.

Congenital diaphragmatic hernia (CDH) occurs with an incidence of ~1 case per 2500 live births1–3 and is associated with significant morbidity and mortality rates. Over the course of the past decade, new therapies have emerged for the management of CDH, including delayed operative repair,4,5–7 inhaled nitric oxide (INO),8 high-frequency oscillation ventilation (HFOV),9,10 gentle ventilation with permissive hypercapnia,5,7,11 and extracorporeal membrane oxygenation (ECMO).4,7,12 Many centers have reported improved survival rates with the introduction of these modalities. However, the majority of these reports are derived from the experience of tertiary referral institutions. This leads to case selection bias and the existence of a “hidden mortality,” which is difficult to quantify.13 Investigating the true outcome of CDH is difficult and requires a population-based fetal and birth monitoring program.14,15 Few studies fulfill these criteria.

Western Australia has a geographically defined population of 1.9 million, with ~25 000 live births annually. All infants with significant congenital anomalies are registered with the Western Australian Birth Defects Registry, including those delivered from pregnancies that abort spontaneously or are terminated electively.16 Postmortem data are also included in this registry. Every infant born in the state requiring tertiary neonatal care is referred to a single Women’s and Children’s Health Service, comprising 2 NICUs.

The aims of this study were to describe the incidence, treatment, and outcomes of a population-based cohort of all infants diagnosed with CDH in Western Australia over a 12-year period and to determine the changing trends in these during this period. We also sought to ascertain the prenatal and postnatal factors associated with morbidity and death among these infants.

METHODS

Cases of CDH were identified from 5 independent databases, ie, the Western Australian Birth Defects Registry, the Western Australian Department of Health database, the Women’s and Children’s Health Service Fetal Medicine Unit database, and the databases of the 2 tertiary NICUs in the state. Cases were identified for the period from January 1991 to December 2002 inclusive. All fetuses and neonates diagnosed with CDH in Western Australia during this period were identified, including miscarriages, stillbirths, and terminations of pregnancies in which a diagnosis of fetal CDH had been made, as well as cases diagnosed postnatally. Cases not known to have CDH until diagnosis at autopsy were also included. Infants with diaphragmatic eventration were excluded from the study. Permission to conduct the study was obtained prospectively from the institutional ethics committee.

Detailed information was obtained from review of maternal and infant medical records, including demographic characteristics; timing of detection (prenatal, postnatal, or postmortem); gestational age at diagnosis; prenatal ultrasonographic findings; presence of polyhydramnios; obstetric management; place of birth; method of delivery; obstetric complications; gestational age, birth weight, and Apgar scores at delivery; resuscitation at delivery; presence of associated anomalies; side of defect; age at surgery; contents and location of hernia; type of surgical repair; acute postoperative complications; use of INO and HFOV; durations of mechanical ventilation, INO, HFOV, total parenteral nutrition, oxygen requirement, and hospital stay; long-term morbidity; and postmortem findings. Outcomes were classified as spontaneous abortion, stillbirth, elective termination of pregnancy, neonatal death before 7 days, neonatal death between 7 and 28 days, postneonatal death between 29 days and 1 year, or survival beyond 1 year of age.

Other congenital anomalies were coded according to the Australia and New Zealand Neonatal Network guidelines.17 These anomalies were identified with prenatal ultrasonography, clinical findings, or postmortem examination. Ultrasonographic assessment of the degree of pulmonary hypoplasia was not undertaken routinely during the study period. Long-term morbidity data were collected from neonatal, pediatric, gastroenterology, and surgical outpatient medical records. Neurodevelopmental follow-up assessments consisted of parent-completed Ages and Stages Questionnaires18 at 6, 16, and 24 months, with Griffiths testing19 at 12 and/or 24 months for those with neurodevelopmental issues identified from the questionnaire.

Treatment of infants with CDH included elective intubation, sedation with or without muscle relaxation, and ventilation according to clinical criteria. HFOV and INO were available from 1996. INO was used after echocardiography, at an oxygenation index (mean airway pressure × fraction of inspired oxygen × 100/partial pressure of oxygen) of >20. HFOV was used in conjunction with INO, with both being used largely as rescue modalities in the treatment of critically ill infants. To ascertain whether these new modalities had affected survival rates, data were divided into 2 epochs for analysis, ie, 1991 to 1995 and 1996 to 2002. Throughout the study period, a policy of delayed surgery after perioperative stabilization of the infant was practiced. All surgery was performed at the single tertiary pediatric surgical center in the state, after transfer of infants from their birth hospital to this center. Permissive hypercapnea was not practiced during the study period. ECMO was not used for any patient, because it was not available in this state.

Continuous data were summarized with median and interquartile range values (presented as 25th–75th percentile), to account for lack of normality. Categorical data were summarized with frequency distributions. Univariate analyses of continuous and categorical variables were conducted with the Mann-Whitney test and χ2 test or Fisher’s exact test, respectively. Binary outcomes were analyzed with univariate logistic regression analyses, and odds ratios (ORs) and 95% confidence intervals (CIs) were reported. Statistical analyses of data were performed with SPSS for Windows (version 10.0) statistical software (SPSS, Chicago, IL). P values of <.05 were considered significant.

RESULTS

Patient Characteristics

One hundred sixteen cases of CDH were identified in Western Australia during the study period, yielding an incidence of 3.8 cases per 10 000 total births. Perinatal characteristics and outcomes of the study
population are demonstrated in Tables 1–3. Of these 116 case subjects, 71 (61.2%) were born alive and 37 survived beyond 1 year of age (52.1% of live-born infants, 31.9% of all cases of CDH).

**Associated Congenital Anomalies**

Another major congenital anomaly was present in 54 (46.6%) cases, with minor congenital anomalies being present in 45 (38.8%) cases. These anomalies included significant dysmorphic features (n = 33), genitourinary anomalies (n = 24), musculoskeletal anomalies (n = 21), cardiovascular anomalies (n = 18), neurologic anomalies (n = 18), other gastrointestinal anomalies (n = 15), chromosomal anomalies (n = 12), and craniofacial anomalies (n = 6). Five case subjects had a recognized syndrome. Twenty-one (18.1%) case subjects had other anomalies that were likely to be fatal. Of all case subjects with an additional major anomaly, 42 (77.7%) died.

Twenty-seven (71.1%) of 38 fetuses for whom the pregnancy was terminated had another major anomaly. The other anomaly was a potentially fatal condition for 14 of these fetuses. The presence of an additional major anomaly was associated with a poor survival rate overall (OR: 2.6; 95% CI: 1.1–5.9; \( P < .024 \)). Twenty-three (32.4%) live-born infants had an additional major anomaly (4 of which were considered fatal conditions); however, this did not affect their survival rate.

**Prenatal Diagnosis**

The diagnosis of CDH was made on the basis of prenatal ultrasound findings in 61 (52.6%) cases. The median gestational age at diagnosis was 19 weeks 1 day (range: 11 weeks 3 days to 39 weeks). Polyhydramnios was identified in 9 (14.8%) pregnancies. In cases with documented prenatal ultrasound findings, mediastinal shift was most commonly reported (95.5%), followed by an intrathoracic stomach bubble (76.7%), intrathoracic bowel (34.8%), and the presence of liver in the chest (13.9%). None of these findings was found to predict outcomes for live-born infants. Additional major congenital anomalies were detected on ultrasonography in 24 (39.3%) cases and, when clinical and postmortem findings were included, were present in 31 (50.8%) prenatally diagnosed pregnancies.

Of cases diagnosed prenatally, 30 (49.2%) pregnancies were terminated electively, 1 (1.6%) subject was stillborn, and 30 (49.2%) subjects were live born. Termination was performed more commonly for infants with another major congenital anomaly detected on ultrasonography (OR: 3.3; 95% CI: 1.1–9.8; \( P = .03 \)). Elective termination was performed at a median of 19 weeks of gestation (range: 15 weeks 4 days to 26 weeks).

Of live-born infants with prenatally diagnosed CDH, 10 (33.3%) survived beyond 1 year of age. The gestational age at diagnosis did not affect the survival rate for live-born infants (\( P = .61 \)). However, because elective termination was more likely to be performed for infants with earlier gestational age at diagnosis (\( P < .01 \)), the gestational age at diagnosis did affect the overall survival rate (\( P = .01 \)).

**Postnatal Diagnosis**

Postnatal diagnosis occurred in 55 cases (47.4%). Of these, 41 (74.5%) case subjects were live born, with the diagnosis made on clinical grounds after birth. In the remaining 14 cases, the diagnosis was made in postmortem examinations of fetuses from pregnancies terminated for other reasons (8 cases) or after spontaneous abortion or stillbirth (5 cases). Postmortem diagnosis was also made for 1 live-born infant who then died. Among infants diagnosed postnatally, 50% were diagnosed by day 1 of life (range: day 1–87).

**Comparison of Prenatal Diagnosis and Postnatal Diagnosis**

Differences between prenatally and postnatally diagnosed live-born infants are shown in Table 4. Among live-born infants, prenatal diagnosis was associated with a significantly reduced survival rate. Prenatally diagnosed live-born infants were of lower birth weight and were born at an earlier gestational age. There was no statistically significant difference between the 2 groups in the onset of labor (sponta-
neous or induced) or in the rate of elective cesarean sections \( (P = .20) \). Prenatally diagnosed live-born infants were more likely to be delivered in a tertiary perinatal center \( (P < .001) \) and were more commonly intubated at delivery \( (P < .001) \). No difference was found between the groups in the Apgar scores at either 1 or 5 minutes.

**Live-Born Infants**

Seventy-one infants were born alive, with 37 (52.1%) surviving to 1 year of age. The majority of deaths occurred within the first 7 days of life \( (n = 31, 43.7\%) \) and were largely attributable to a major air leak, which was a strong predictor of death. Preoperative air leaks occurred for 16 (22.5%) infants, of whom 14 (87.5%) died. Factors associated with death among live-born infants are presented in Table 5.

**Table 3.** Outcomes of Live-Born Cases of CDH in Western Australia, 1991–2002

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Live-Born Patients ( (N = 71) )</th>
<th>Prenatal Diagnosis ( (N = 30) )</th>
<th>Postnatal Diagnosis ( (N = 41) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survived to surgical center</td>
<td>46 (65)</td>
<td>13 (43)</td>
<td>33 (80)</td>
</tr>
<tr>
<td>Survived to surgery</td>
<td>40 (56)</td>
<td>12 (40)</td>
<td>28 (68)</td>
</tr>
<tr>
<td>Survived &gt;1 y</td>
<td>37 (52)</td>
<td>10 (33)</td>
<td>27 (66)</td>
</tr>
<tr>
<td>Died at &lt;7 d</td>
<td>31 (44)</td>
<td>18 (60)</td>
<td>13 (32)</td>
</tr>
<tr>
<td>Died at 7–28 d</td>
<td>2 (3)</td>
<td>1 (3)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Died at 29 d to 1 y</td>
<td>1 (1)</td>
<td>1 (3)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

**Table 4.** Comparison of Prenatal Diagnosis and Postnatal Diagnosis for Live-Born Infants With CDH in Western Australia, 1991–2002

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n (%)</th>
<th>P</th>
<th>OR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall survival</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Survival to surgical center</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Survival to surgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of HFOV†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of INO†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative air leak‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other major anomaly</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestational age at birth, wk‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth weight, g‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-min Apgar score‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-min Apgar score‡</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Odds of each characteristic for prenatal diagnosis relative to postnatal diagnosis.
† Live-born, \( N = 40; 1996–2002 \) only.
‡ Data are presented as median (interquartile range).
§ Mann-Whitney \( U \) test.

**Table 5.** Predictors of Death Among Live-Born Infants With CDH in Western Australia, 1991–2002

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Survivors ( (N = 37) )</th>
<th>Nonsurvivors ( (N = 34) )</th>
<th>P</th>
<th>OR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other major anomaly</td>
<td>12 (32)</td>
<td>11 (32)</td>
<td>.936</td>
<td>1.0 (0.4–2.8)</td>
</tr>
<tr>
<td>Prenatal diagnosis†</td>
<td>10 (27)</td>
<td>20 (59)</td>
<td>.008</td>
<td>3.9 (1.4–10.4)</td>
</tr>
<tr>
<td>Right-sided hernia†</td>
<td>2 (5)</td>
<td>7 (29)</td>
<td>.012</td>
<td>7.7 (1.4–41.0)</td>
</tr>
<tr>
<td>Inborn</td>
<td>13 (35)</td>
<td>23 (68)</td>
<td>.007</td>
<td>3.9 (1.4–10.3)</td>
</tr>
<tr>
<td>Preoperative air leak‡</td>
<td>2 (5)</td>
<td>14 (52)</td>
<td>&lt;.001</td>
<td>18.8 (3.8–94.3)</td>
</tr>
<tr>
<td>Use of HFOV§</td>
<td>4 (11)</td>
<td>13 (38)</td>
<td>.011</td>
<td>6.5 (1.5–27.5)</td>
</tr>
<tr>
<td>Use of INO§</td>
<td>6 (16)</td>
<td>11 (32)</td>
<td>.184</td>
<td>2.4 (0.7–9.1)</td>
</tr>
<tr>
<td>Gestational age at birth, wk†</td>
<td>38 wk 3 d (30 wk 1 d to</td>
<td>37 wk 4 d (27 wk to</td>
<td>.026</td>
<td></td>
</tr>
<tr>
<td></td>
<td>41 wk 2 d; 37.0–40.0)</td>
<td>41 wk 6 d; 32.9–39.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth weight, g†</td>
<td>3095 (1415–4775; 2632–3410)</td>
<td>2802 (833–3865; 1691–3279)</td>
<td>.009</td>
<td></td>
</tr>
<tr>
<td>1-min Apgar score‡</td>
<td>6 (1–9–4–7)</td>
<td>4 (1–8–2–6)</td>
<td>.009</td>
<td></td>
</tr>
<tr>
<td>5-min Apgar score‡</td>
<td>8 (3–10;6–9)</td>
<td>5 (0–9–4–8)</td>
<td>.001</td>
<td></td>
</tr>
</tbody>
</table>

* Odds of each characteristic for nonsurvivors (died within the first year of life) relative to survivors (lived beyond 1 year of age).
† Live-born, \( N = 61; \) side of hernia not known in 10 cases.
‡ Live-born, \( N = 64; \) missing data in 7 cases.
§ Live-born, \( N = 40; 1996–2002 \) only.
∥ Data are presented as median (minimum to maximum; interquartile range).
¶ Mann-Whitney \( U \) test.
Western Australia. The survival rate of live-born inborn infants was lower than the survival rate of live-born outborn infants.

Right-sided CDH was present for 9 (15%) live-born infants and was associated with an increased mortality rate. The presence of polyhydramnios during pregnancy seemed to be associated with a poorer prognosis, although this did not reach statistical significance (OR: 4.2; 95% CI: 0.8–20.4; P = .08).

Forty (56.3%) live-born infants survived to undergo surgical repair. Characteristics of this group are documented in Table 6. Thirty-seven (92.5%) infants who underwent surgery survived beyond 1 year of age. Three (7.5%) infants died postoperatively; 1 death was attributable to complications of surgery. The treatment and long-term morbidities of survivors are documented in Table 7.

Epochs

A comparison of outcomes between the 2 epochs is outlined in Table 8. Over the course of the decade, there were significant increases in the proportion of cases in which the diagnosis of CDH was made on the basis of prenatal ultrasound findings and in the number of live-born infants born at the tertiary perinatal center. The mortality rate for all cases, the mortality rate for live-born infants, and the proportion of pregnancies involving prenatally diagnosed cases that were terminated electively were all greater in the later epoch but not significantly so.

**DISCUSSION**

This is one of the most complete population-based studies of CDH conducted to date. The majority of published studies of CDH examined specific patient populations, such as fetuses diagnosed with prenatal ultrasound findings, neonates referred to tertiary pediatric surgical centers, or cases with postmortem findings of CDH. Population-based studies with full case ascertainment are few, and those with large study populations incorporate the practices of multiple institutions, which affects variably both morbidity and mortality rates. No study published to date has reviewed a large number of cases attained through population-based review, while reflecting the management practices of a single institution.

**Mortality Rates**

The overall mortality rate of 68% in this study is similar to that reported in other population-based studies. Elective termination accounted for 48% of all deaths; therefore, the overall mortality rate for CDH in our population was influenced significantly by the rate of elective termination. This finding was described recently by other workers.

It is important to note that the deaths attributable to elective termination and in utero fetal demise would not have been ascertained had we examined solely cases of CDH managed at the tertiary surgical center. In addition, 35% of live-born infants died before referral or transport. Therefore, the population of infants reaching the tertiary surgical center represented only 40% of the total cases of CDH. This disparity reflects the “hidden mortality” of CDH, as first described by Harrison et al. This refers to the death of infants with CDH before their arrival at a referral center, whether through termination of pregnancy, in utero fetal demise, or postnatal death occurring before transfer. Exclusion of these cases from calculations of mortality rates results in significant case selection bias.

Among our study population, survival rates differed vastly depending on the subgroup analyzed.

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**TABLE 6. Characteristics of Surgical Patients With CDH in Western Australia, 1991–2002 (N = 40)**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival to surgery among live-born infants</td>
<td>40/71 (56)</td>
</tr>
<tr>
<td>Survival of surgical patients</td>
<td>37/92 (92)</td>
</tr>
<tr>
<td>Type of repair</td>
<td>Patch 6 (15)</td>
</tr>
<tr>
<td>Age at surgery, d*</td>
<td>4 (1–87; 2.2–5.0)</td>
</tr>
<tr>
<td>Acute postoperative complications</td>
<td>Any acute postoperative complication 18 (45)</td>
</tr>
<tr>
<td>Postoperative pneumothorax requiring drainage</td>
<td>5 (12)</td>
</tr>
<tr>
<td>Pleural effusion requiring drainage</td>
<td>4 (10)</td>
</tr>
<tr>
<td>Prolonged (≥30-d) requirement for alimentation</td>
<td>6 (15)</td>
</tr>
<tr>
<td>Neurodevelopmental delay‡</td>
<td>6 (15)</td>
</tr>
<tr>
<td>Gastrointestinal tract complications</td>
<td>Aspiration 10 (27)</td>
</tr>
<tr>
<td>Adhesions</td>
<td>7 (18)</td>
</tr>
<tr>
<td>Ischemia</td>
<td>3 (8)</td>
</tr>
<tr>
<td>Obstruction</td>
<td>4 (10)</td>
</tr>
<tr>
<td>Perforation</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (8)</td>
</tr>
<tr>
<td>None</td>
<td>30 (75)</td>
</tr>
</tbody>
</table>

* Data are presented as median (minimum to maximum; interquartile range).
Ninety-two percent of postoperative infants survived, as did 80% of infants who reached the surgical referral center. However, only 52% of live-born infants and 33% of prenatally diagnosed infants survived. These wide variations in survival rates for different subsets of infants with CDH occur throughout the literature. Studies of cases with a prenatal diagnosis frequently report mortality rates of \( \geq 75\% \).\(^{20,21,30,31} \) In contrast, the mortality rates for infants referred to tertiary centers are often reported as \(< 30\% \).\(^{4,5,7,32} \) These differences reflect the influence of case selection bias, variable referral policies, and management practices.

There exists also a “hidden incidence” of CDH. To ascertain the true incidence of this condition, it is vital that autopsies of stillbirths, terminations, and neonatal deaths be performed.\(^{15} \) In our study, 13% of cases were diagnosed in postmortem examinations.

### Additional Major Anomalies

The proportion of infants with coexisting major anomalies in our study population was 47%. This is consistent with other population-based studies, which reported rates of 37% to 47%.\(^{1,2,6,11,14,15,24,25,28,30–32,34} \) The proportion of infants with other major anomalies varied according to the group studied. Other anomalies were found in 51% of prenatally diagnosed cases, compared with 32% of live-born infants. Fetuses for whom the pregnancy was terminated and case subjects who underwent postmortem examinations had high rates of coexistent anomalies (72% and 69%, respectively). Higher rates of associated anomalies tend to be reported in population-based studies, compared with results derived from single-center or multicenter, institution-based studies.\(^{15} \) This is likely attributable to an increased hidden mortality rate among patients with additional malformations, including an increased rate of termination.\(^{15} \)

The presence of another major anomaly did not affect the survival rate for live-born infants. However, because pregnancies involving infants with another anomaly were significantly more likely to be terminated than were those involving infants with an isolated CDH, the presence of an additional major anomaly was associated with poor overall survival rates. Most other studies,\(^{1,2,6,11,14,15,24,25,28,30–32,34} \) but not all,\(^{22} \) found associated major anomalies to be important predictors of mortality rates.

### Prenatal Diagnosis

In our population, 53% of cases were diagnosed on the basis of prenatal ultrasound findings. The prenatal detection rate for CDH varies enormously in published studies, from 10%\(^{12} \) to 79%\(^{35} \), reflecting differences in local protocols of prenatal care and variable sonographic expertise. In our study, we do not know how many of the postnatally diagnosed infants had prenatal scans; therefore, the false-negative rate cannot be determined. This rate was reported as \( \sim 47\% \) in other studies.\(^{27,36} \) We observed a significant increase in the prenatal detection of CDH during the decade studied. An increased rate of prenatal ultrasound testing\(^{26} \) and increased detection over time have been reported elsewhere.\(^{26} \)

The median gestational age at diagnosis in our population correlates with the gestational age at which routine prenatal “anatomy” scans are performed in our state. The gestational age at diagnosis did not affect the survival rate for live-born infants. The literature on this matter is conflicting, with some studies reporting increased mortality rates for infants diagnosed earlier\(^{20,21} \) and others failing to find such an association.\(^{27,30–32} \) Many sonographic predictors of outcomes have been proposed, including polyhydramnios,\(^{20,21,30} \) intrathoracic stomach,\(^{30,31} \) abdominal circumference,\(^{37} \) and major mediastinal shift.\(^{30,31} \) None of these was found to predict mortality rates for live-born infants in our study. Recently described techniques for assessment of pulmonary hypoplasia, such as MRI lung volumetry,\(^{38} \) determination of fetal lung-head ratios,\(^{39,40} \) measurement of pulmonary artery diameters,\(^{41} \) and fetal pulmonary artery Doppler ultrasonography,\(^{42} \) were not used regularly in our cases and have not yet been validated for widespread use.

For 49% of prenatally diagnosed cases in our study, pregnancies were terminated electively. The termination rate is highly variable across different populations, ranging from 1% to 50%.\(^{37} \) Termination was performed more commonly for fetuses with associated anomalies and those diagnosed at earlier...
gestational ages, making both of these factors important predictors of mortality rates in this group.

Prenatal diagnosis itself was an important predictor of mortality rates for live-born infants, with a 33% survival rate, compared with a 67% survival rate for postnatally diagnosed infants. Prenatal diagnosis was found commonly to predict mortality rates, although this was not a universal finding. Prenatally diagnosed infants were delivered at earlier gestational ages and were of lower birth weights than those diagnosed postnatally, which was not explained by differences in the rates of induced labor or elective cesarean sections. There was no difference between the groups in the proportions with other anomalies or in Apgar scores that might have explained the altered survival rates. It is possible that prenatal diagnosis detects cases with a greater degree or longer duration of visceral herniation and thus an increased severity of pulmonary hypoplasia.

Live-Born Infants

Ours and other studies demonstrated gestational age at birth, birth weight, Apgar scores, right-sided hernia, and pneumothorax to be predictive of mortality rates in CDH. We also found use of HFOV to predict mortality rates, which is likely because HFOV was used solely for critically ill infants. Inborn infants had significantly lower survival rates than outborn infants, which might be accounted for by the fact that almost all prenatally diagnosed infants were inborn.

The 22% rate of pneumothorax in our population and its strong association with early death were important findings. A postmortem study of CDH showed that barotrauma-induced damage to hypoplastic lungs contributed significantly to mortality rates. During the study period, hyperventilation with high ventilatory pressures was a standard therapy for infants with CDH, which likely contributed to the 48% mortality rate for live-born infants.

Many institutions have reported significant improvements in the survival rates for neonates with CDH in the past decade. However, these reports refer invariably to select populations of patients and often impose dubious exclusion criteria. We found no change in the overall CDH mortality rate over the 12 years studied or in the survival rate for live-born infants. Other population-based studies also found consistent mortality rates over the past 30 years, ranging from 66% in the 1970s to 62% in the 1990s. Therefore, although specific subgroups of infants may show improved survival rates, compared with their predecessors, the overall mortality rate for this condition remains static.

Morbidity

This study was not intended to be a comprehensive study of morbidity among CDH survivors. The follow-up monitoring of our infants was not conducted according to a standardized prospective protocol, and we did not have access to follow-up monitoring conducted outside the tertiary pediatric hospital. It is thus likely to be incomplete in some respects. However, Western Australia has a geographically captive population, and any significant medical or surgical problems in childhood are treated at our single tertiary pediatric center. Follow-up case records were not found for only 1 of 37 survivors. Our rates of gastroesophageal reflux, failure to thrive, and neurodevelopmental abnormalities correlate very closely with those of a more comprehensive, recently published, morbidity study. Other studies reported higher incidences of nutritional, pulmonary, and neurologic morbidity, particularly among survivors treated with ECMO. The management protocols and survival rates at different institutions affect significantly the morbidity rates among survivors, and this must be taken into consideration when these comparisons are made.

CONCLUSIONS

This is a comprehensive, population-based study of CDH, with full case ascertainment, large sample size, and complete outcome data for all cases. The overall mortality rate for this condition remains high, despite increased prenatal detection, transfer to tertiary institutions for delivery, and advances in neonatal care, and is influenced to a large extent by the high rate of elective termination of pregnancies involving prenatally diagnosed fetuses.

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