# West Midlands Congenital Anomaly Register

## Congenital Diaphragmatic Hernia 1995-2000

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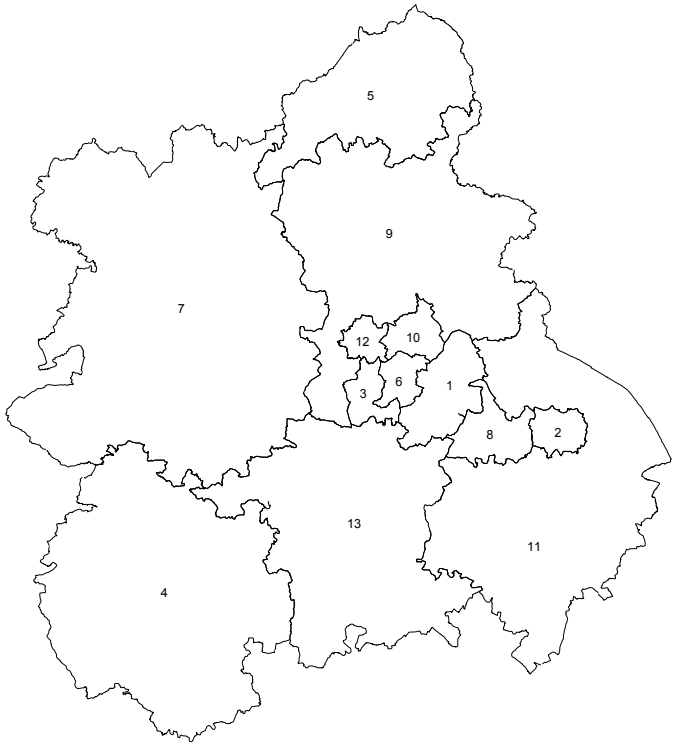
**District Health Authorities in the West Midlands Region (before April 2002)**




**KEY**

1 BIRMINGHAM
2 COVENTRY
3 DUDLEY
4 HEREFORDSHIRE
5 NORTH STAFFS
6 SANDWELL
7 SHROPSHIRE
8 SOLIHULL
9 SOUTH STAFFS
10 WALSALL
11 WARWICKSHIRE
12 WOLVERHAMPTON
13 WORCESTERSHIRE

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## EXECUTIVE SUMMARY

This report details cases of congenital anomalies of the diaphragm notified to the West Midlands Congenital Anomaly Register occurring in deliveries between 1995 and 2000 with a minimum follow up period of 12 months. We have included data on suspected as well as confirmed cases, giving an estimate of the sensitivity of prenatal diagnosis, and detailing the conditions that have been mistaken for congenital diaphragmatic hernia.

The optimal management of the neonate is assisted when the problem is suspected antenatally although it is not clear whether the outcomes are actually improved. These anomalies are a group that have a high mortality rate due to the presence of other anomalies or sequelae. However, isolated cases have the potential for a normal outcome following successful surgical correction.

### Incidence

The overall incidence of congenital diaphragmatic hernia between 1995-2000 in the West Midlands was 4.1/10,000 births (1:2,463). After natural losses and terminations, the incidence of congenital diaphragmatic hernia was 2.9/10,000 registerable births (1:3,391).

### Associated anomalies

46% of congenital diaphragmatic hernia cases had additional structural or chromosomal anomalies.

### Outcomes

For cases of congenital diaphragmatic hernia that are live born, the infant mortality rate was 317/1,000.

For isolated malformations, the infant mortality rate was 225/1,000 live births.

For complex cases (with additional structural anomalies or aneuploidy), the infant mortality rate was 533/1,000 live births. The relative risk of mortality for those with a complex lesion compared to an isolated lesion was 2.37.

### Prenatal diagnosis

Prenatal diagnoses were made in 66% of congenital diaphragmatic hernia cases.

For isolated malformations, prenatal diagnoses were made in 51% of cases.

For complex cases, prenatal diagnoses were made in 84% of cases.

In addition, there were a number of false positive diagnoses made by prenatal ultrasound. 14/121 cases (12%) of a prenatal diagnosis were incorrect, but of these 11 had other significant anomalies requiring attention.

### Key recommendations

- Serious consideration should be given to the possibility of other anomalies. Cardiac anomalies were present in 16% of cases and therefore it is best practice to arrange a fetal echocardiogram. 12% of cases diagnosed antenatally will prove to have other pathology or possibly be normal.
- An experienced paediatrician should attend the delivery. Neonatal intensive care including facilities for respiratory support should be available at the place of birth.
- Parents should be given access to high quality information, given in a sensitive manner by professionals experienced in the management of this condition. Professionals should co-operate to improve the information available to parents relating to the long term outcomes for this condition.

Mike Wyldes
March 2003

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## CLINICAL BACKGROUND OF CONGENITAL DIAPHRAGMATIC HERNIA

### Description

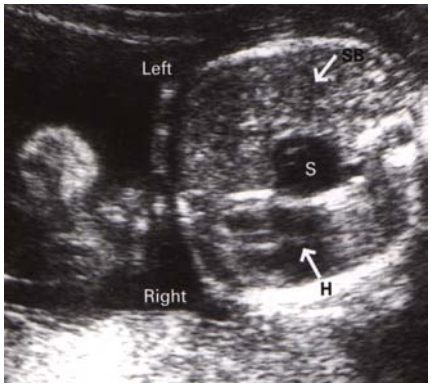
The diaphragm is a muscular membrane with a central tendon that separates the chest cavity from the abdominal cavity through which the oesophagus and major blood vessels pass. The diaphragm develops in early fetal life, and is usually fully formed by 9 weeks gestation. In cases of diaphragmatic hernia (CDH), a hole allows structures that are usually within the abdomen to protrude into the thorax.

The most common site for diaphragmatic hernia is the left side, through which the stomach, bowel, spleen, and liver can pass. The cause of congenital diaphragmatic hernia is essentially unknown, but it often occurs in combination with other structural malformations, particularly hypoplastic lungs and heart defects. The defect is often associated with an underlying anomaly of the fetal chromosomes, particularly trisomies.

### Prenatal diagnosis and pregnancy management

The routine use of ultrasound scanning has lead to many cases being diagnosed during pregnancy. The diagnosis rests upon obtaining clear images of the upper abdomen and chest. The most common finding is displacement of the fetal stomach into the chest. This sequence leads to displacement of the fetal heart to the right side of the chest. It is important to examine the orientation of the apex of the fetal heart. Large defects with significant displacement of the fetal heart are most easily recognised, and therefore prenatal diagnosis will select a group with a relatively poor prognosis. The diagnosis of congenital diaphragmatic hernia is most commonly made at around 20 weeks during the fetal anomaly screening scan. Following a diagnosis, the fetus should be examined for other defects, particularly cardiac anomalies, which are present in up to 30% of cases. Even when the anomaly is apparently isolated, fetal karyotyping is strongly recommended, as trisomy 21 and 18 are often associated with this defect.

**Figure 1 - Ultrasound image of congenital diaphragmatic hernia**




The following features can be seen in Figure 1:

- Heart deviated to the right (H),
- Intrathoracic stomach ‘bubble’ (S),
- Asymmetry of LV/RV dimensions,
- Small bowel in fetal chest (SB),
- Polyhydramnios,
- Hydrops fetalis (usually in right-sided lesions).

The prognosis for congenital diaphragmatic hernia diagnosed at this stage of pregnancy is generally poor. The main cause of death is pulmonary hypoplasia, caused by associated abnormal development of the fetal lungs in utero. This is difficult to predict with any degree of certainty. Fetal surgery has been attempted for this condition in the USA, with mixed results. The operation involves significant risk to both the fetus and mother and at this time there is no clear evidence that this intervention carries any benefits. The procedure involves opening the uterus, opening the fetal chest or abdomen to allow a surgical repair to take place. Theoretically, this could allow development of the fetal lungs, but the practicalities of when and how to perform this type of major intervention remain to be clarified. This type of surgery is not currently available in UK centres.

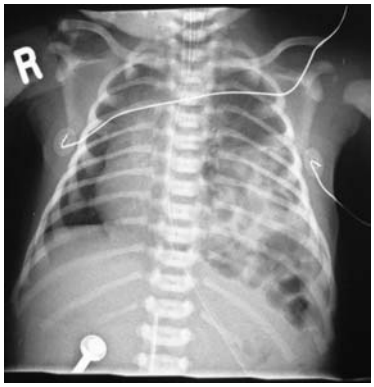
In utero surgery can also include the PLUG procedure in which the trachea is occluded so allowing fluid production to expand the lung (Plug the trachea Until the Lung Grows). The occlusion is released at birth with the hope that the lung is larger and less hypoplastic. Fetoscopic procedures are being developed which aim to avoid the problems associated with hysterotomy, again the benefits are unclear.

## Paediatric management and surgery

### Making the diagnosis

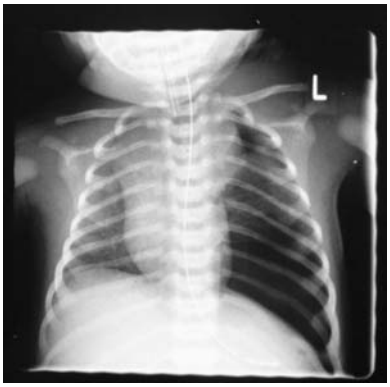
This may have been made antenatally and is confirmed or refuted on a chest/abdominal X-ray, the differential diagnosis includes: cystic adenomatoid malformation, cystic teratoma, pulmonary sequestration, bronchogenic cysts, and neurogenic tumours. The child usually has a measure of respiratory distress and a scaphoid abdomen.

**Figure 2 - X-ray of congenital diaphragmatic hernia case before surgery**




In Figure 2 note the heart pushed to the right and gas-filled loops of intestine in the left chest.

**Figure 3 - X-ray of congenital diaphragmatic hernia case after surgery**




In Figure 3 note the repair of the left diaphragm and the hypoplastic left lung.

### Treatment

The key is stabilisation before surgical repair. Neonates with CDH and in severe respiratory distress need aggressive intervention with added oxygen, endotracheal intubation, paralysis, and ventilation. The options available include conventional mechanical ventilation CMV, high-frequency ventilation (HFV), high-frequency oscillatory ventilation (HFOV), inhaled nitric oxide, and extracorporeal membrane oxygenation (ECMO). Prolonged mask ventilation can distend the stomach and small bowel making ventilation difficult and is best avoided. A large bore nasogastric tube is passed. Normovolaemia is aimed for and hypoxia, hypercarbia, and acidosis managed promptly. An echocardiograph is needed to confirm any heart defect and look at signs of pulmonary hypertension, left ventricular hypoplasia and shunting. Inotropes can augment left ventricular function to oppose shunting. Shunting can be assessed by pre and post ductal monitoring. Barotrauma is a major concern and some centres permit a degree of hypercarbia after studies have shown increased survival when compared with historical controls.

### Surgery

The repair is usually through the abdomen with reduction of herniated contents and excision of any sac preceding repair. The defect may be closed primarily or a muscle patch or inert graft may be needed. Some surgeons leave a chest drain to drain fluid from the thoracic cavity. Sometimes there is malrotation of the small intestine with an unstable mesentery requiring a Ladd's procedure to place the intestine in the non-rotated position.

If the baby is able to survive the initial resuscitation but remains too unwell to undergo immediate surgery there may be a role for extra corporeal membrane oxygenation (ECMO), which is available in a limited number of centres in the UK. ECMO allows additional oxygen into the circulation to stabilise the baby before surgery.

## METHODS

### West Midlands Congenital Anomaly Register

The West Midlands Congenital Anomaly Register (CAR) was set up in June 1994 and is administered by the West Midlands Perinatal Institute. The register aims to collect information on the occurrence of suspected and confirmed congenital anomalies of West Midlands residents, detected before and after birth. A number of minor anomalies are excluded from the register.

### Reporting

Notifications are received at the register by three methods. The first method is a notification card, which is used to notify the register of suspected anomalies. The card includes details of the type of anomaly and the estimated date of delivery and is most often completed by ultrasound departments. The second method is through an obstetric notification form, which contains much of the data set used for the Confidential Enquiry into Stillbirths and Deaths in Infancy (CESDI) but has additional details relating to the date that the anomaly was first suspected. The obstetric notification forms are usually completed by midwives or obstetricians. There is also a paediatric notification form completed by paediatric or neonatal staff, used to record postnatal data and the final diagnosis.

The Congenital Anomaly Register is maintained on the same database as the register of CESDI notifications of fetal and infant deaths. In this way, the number of infants with lethal fetal anomalies can be validated. All anomalies are coded using the International Classification of Disease version 10 (ICD 10).

Additional information is also received from cytogenetics laboratories and Departments of Public Health. Inpatient episode data of infants with anomalies are also received from hospital information departments. These extra data are matched to the existing notifications and additional clinical information is added in some cases.

### Definition of congenital diaphragmatic hernia

Within the ICD10 classification system there is a code for congenital diaphragmatic hernia, sub divided into sites. In addition to this code, there are other diaphragmatic malformations such as eventration, hemidiaphragm and absent diaphragm. These are included in this report as it is often difficult to distinguish between these diagnoses until surgery and all share the same potential problems and outcomes.

### Numerators & denominators

The numerator comprises confirmed cases of congenital malformation of the diaphragm, including all affected fetal losses and terminations of pregnancy. We have also included an analysis of the false positive cases, i.e. those reported, but later found to be incorrect.

The denominator includes the numerator plus all babies who had any possibility of having a congenital diaphragmatic hernia. Therefore the appropriate denominator for calculating incidence rates is the total number of deliveries regardless of gestation, but this information is unavailable. This report uses the sum of the number of births (live and stillborn), the number of terminations of pregnancy for fetal anomaly at any gestation and late fetal losses notified to the West Midlands Perinatal Institute.

Comprehensive clinical information is usually available for cases of fetal anomaly, but similar detail is not available for all births in the denominator. Therefore the analysis of outcomes is severely limited by the available denominator data.

## Outcomes

This report divides outcomes of pregnancy into the following groups:

Late fetal loss less than 24 weeks (LFL),
Stillbirth 24 weeks or more (SB),
Neonatal death under 28 days (NND),
Postneonatal death 28 days up to 1 year of age (PNND),
Alive.

Termination of pregnancy (TOP) is defined as a therapeutic termination undertaken under the 1967 Abortion Act, and excludes situations of induction following spontaneous fetal death in utero. Some terminations of pregnancy may result in a registerable stillbirth, or indeed a live birth regardless of gestation.

## Data Sources

| | |
|---|---|
| **Numerator data** | West Midlands Congenital Anomaly Register |
| **Denominator data** | Office for National Statistics (ONS), registerable births<br>West Midlands Perinatal Institute, fetal losses above 20 weeks gestation<br>West Midlands Congenital Anomaly Register, fetal losses (all gestations) and terminations of pregnancy of fetal anomaly cases |

## Definitions

**Denominators**
The population at risk in the calculation of rate or ratio.

**Late fetal losses**
For CESDI a late fetal loss is defined as a spontaneous abortion (miscarriage) occurring from 20 weeks 0 days (140 days) up to the end of 23 weeks 6 days (167 days). If gestation is unknown or uncertain, birthweights of 300 grams or above are reported.

**Neonatal death**
Death during the first 28 days of life, 0-28 completed days (on or before the 28th day of life, 0-27 days 23 hours 59 minutes).

**Post neonatal death**
Death between 1 month and 1 year of age (28 days and over, up to just before 1st birthday).

**Registerable births/deaths**
Births or deaths that must be legally notified to the Registrar for Births and Deaths include all those delivered after 24 completed weeks of pregnancy, and all live births.

**Stillbirth**
Legal definition England & Wales.
"A child which has issued forth from its mother after the 24th week of pregnancy and which did not at any time after being completely expelled from its mother breathe or show any other signs of life".

## INCIDENCE RATES

There were 161 cases of malformations of the diaphragm born to West Midlands residents between 1995 and 2000. Of these, there were 155 singleton pregnancies and 6 twin pregnancies. In all the twin pregnancies, there was only one affected twin. Two of the singleton cases were born to the same mother during this time.

**Table 1 - Congenital malformations of the diaphragm, West Midlands 1995-2000**

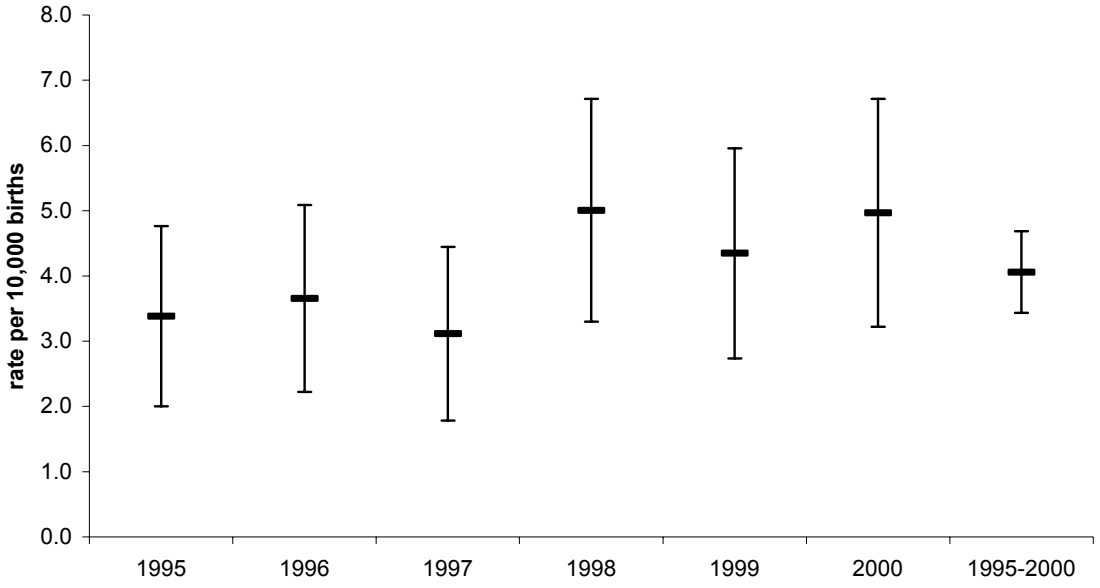
| Type of malformation | n |
|---|---|
| Congenital diaphragmatic hernia | 145 |
| Congenital eventration of diaphragm | 8 |
| Congenital hemidiaphragm | 2 |
| Congenital absent diaphragm | 2 |
| Other congenital malformations of diaphragm | 4 |
| **Total** | **161** |

Table 1 shows the type of diaphragm malformations that are included in this report. The majority (90%) have been described as congenital diaphragmatic hernia. The congenital anomaly register is notified of cases antenatally and postnatally and we feel it is unlikely that significant numbers of cases have been missed. We recognise the often subtle distinction between these groups, and within the remainder of this report have included all these cases under the umbrella heading of CDH.

**Table 2 - Congenital diaphragmatic hernia: annual rates, West Midlands 1995-2000**

| All cases | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | 1995-2000 |
|---|---|---|---|---|---|---|---|
| cases | 23 | 25 | 21 | 33 | 28 | 31 | **161** |
| rate per 10,000 births | 3.4 | 3.7 | 3.1 | 5.0 | 4.3 | 5.0 | **4.1** |
| 95% confidence interval | 2.0 - 4.8 | 2.2 - 5.1 | 1.8 - 4.4 | 3.3 - 6.7 | 2.7 - 6.0 | 3.2 - 6.7 | **3.4 - 4.7** |
| Births | 68,005 | 68,413 | 67,427 | 65,925 | 64,405 | 62,402 | **396,577** |

**Chart 1 - Congenital diaphragmatic hernia: annual rates, West Midlands 1995-2000**




Vertical bars indicate 95% confidence intervals

Table 2 and Chart 1 show that there is no significant trend over the six year period (Chi square for trend) , with an overall rate of 4.1/10,000 births. The inclusion of all cases, not just registerable births, means that the incidence rates are not subject to variation in prenatal detection and termination of pregnancy rates. There were no changes in data collection methods during this time.

**Table 3 - Congenital diaphragmatic hernia, all cases: other regional registers 1995-2000**

| All cases | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | Total |
|---|---|---|---|---|---|---|---|
| **WMCAR** | | | | | | | |
| cases | 23 | 25 | 21 | 33 | 28 | 31 | **161** |
| rate per 10,000 births | 3.4 | 3.7 | 3.1 | 5.0 | 4.3 | 5.0 | **4.1** |
| 95% confidence interval | 2.0 - 4.8 | 2.2 - 5.1 | 1.8 - 4.4 | 3.3 - 6.7 | 2.7 - 6.0 | 3.2 - 6.7 | **3.4 - 4.7** |
| Births | 68,005 | 68,413 | 67,427 | 65,925 | 64,405 | 62,402 | **396,577** |
| **NorCAS** | | | | | | | |
| cases | 16 | 7 | 11 | 6 | 14 | 17 | **71** |
| rate per 10,000 births | 4.7 | 2.1 | 3.3 | 1.9 | 4.6 | 5.7 | **3.7** |
| 95% confidence interval | 2.4 - 6.9 | 0.5 - 3.6 | 1.4 - 5.3 | 0.4 - 3.4 | 2.2 - 7.0 | 3.0 - 8.4 | **2.8 - 4.5** |
| Births | 34,333 | 33,868 | 33,056 | 32,203 | 30,339 | 29,785 | **193,584** |
| **CARIS - Wales** | | | | | | | |
| cases | NA | NA | NA | 10 | 14 | 11 | **35** |
| rate per 10,000 births | | | | 3.0 | 4.3 | 3.5 | **3.6** |
| 95% confidence interval | | | | 1.1 - 4.8 | 2.1 - 6.6 | 1.4 - 5.6 | **2.4 - 4.8** |
| Births | | | | 33,610 | 32,266 | 31,449 | **97,325** |

Similar methodology has been used to collect all cases occurring in the Northern Region by NorCAS (Northern Congenital Abnormality Survey) and in Wales by CARIS (Congenital Anomaly Register and Information Service) since 1998 , the incidence rates are broadly similar for these two geographical areas[1]. This geographical comparison demonstrates that there is no significant difference in the incidence of this anomaly between the West Midlands, Welsh and Northern populations. We believe there is unlikely to be a major problem with ascertainment of cases.

**Table 4 - Congenital diaphragmatic hernia, registerable births: national register 1995-2000**

| Registerable only | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | Total |
|---|---|---|---|---|---|---|---|
| **WMCAR** | | | | | | | |
| Registerable cases | 19 | 15 | 16 | 24 | 19 | 23 | **116** |
| rate per 10,000 reg births | 2.8 | 2.2 | 2.4 | 3.7 | 3.0 | 3.7 | **2.9** |
| 95% confidence interval | 1.5 - 4.1 | 1.1 - 3.3 | 1.2 - 3.6 | 2.2 - 5.1 | 1.6 - 4.3 | 2.2 - 5.2 | **2.4 - 3.5** |
| Registerable births | 67,500 | 67,920 | 66,888 | 65,400 | 63,857 | 61,845 | **393,410** |
| **ONS - National** | | | | | | | |
| Registerable cases | 45 | 52 | 72 | 49 | 63 | NA | **281** |
| rate per 10,000 reg births | 0.7 | 0.8 | 1.1 | 0.8 | 1.0 | | **0.9** |
| 95% confidence interval | 0.5 - 0.9 | 0.6 - 1.0 | 0.9 - 1.4 | 0.5 - 1.0 | 0.7 - 1.2 | | **0.8 - 1.0** |
| Registerable births | 651,315 | 651,315 | 651,315 | 651,315 | 651,315 | | **3,256,575** |

National data are available but are restricted to registerable births (live births and stillbirths). A comparison between the WMCAR and ONS demonstrates a threefold difference in incidence. This demonstrates the major effect of different methods of collection of data, with the ONS system concentrating on postnatal registration, therefore under-representing cases of termination of pregnancy

**Table 5 - Congenital diaphragmatic hernia: district of residence, West Midlands 1995-2000**

| District | n | rate | 95% CI | Births |
|---|---|---|---|---|
| Birmingham | 42 | 4.6 | 3.2 - 6.0 | 90,579 |
| Coventry | 10 | 4.3 | 1.6 - 6.9 | 23,305 |
| Dudley | 6 | 2.7 | 0.5 - 4.8 | 22,269 |
| Herefordshire | 3 | 2.8 | 0.0 - 5.9 | 10,811 |
| Sandwell | 6 | 2.5 | 0.5 - 4.5 | 24,019 |
| Shropshire | 15 | 5.0 | 2.5 - 7.6 | 29,892 |
| Solihull | 7 | 5.3 | 0.0 - 9.2 | 13,291 |
| North Staffordshire | 8 | 2.6 | 0.0 - 4.3 | 31,358 |
| South Staffordshire | 21 | 5.2 | 3.0 - 7.5 | 40,130 |
| Walsall | 10 | 4.8 | 1.8 - 7.8 | 20,822 |
| Warwickshire | 14 | 4.1 | 2.0 - 6.3 | 34,105 |
| Wolverhampton | 4 | 2.1 | 0.0 - 4.2 | 19,011 |
| Worcestershire | 15 | 4.1 | 0.0 - 6.1 | 36,985 |
| **WEST MIDLANDS** | **161** | **4.1** | **3.4 - 4.7** | **396,577** |

Rate: rate per 10,000 births

The data are presented by district health authority, in most districts the number of cases is small with wide confidence intervals.

None of the districts have incidence rates that differ significantly from the West Midlands rate.

[1] Morgan M, Greenacre J. Annual Report 2000. Swansea: Congenital Anomaly Register and Information Service, 2001.

## OUTCOMES AND SURVIVAL

**Table 6 - Congenital diaphragmatic hernia: outcomes, West Midlands 1995-2000**

| Outcome | Isolated | Complex | Total |
|---|---|---|---|
| Late fetal loss | 1 | 1 | **2** |
| Late fetal loss - TOP | 8 | 35 | **43** |
| Stillbirth | 5 | 6 | **11** |
| Stillbirth - TOP | 0 | 4 | **4** |
| Neonatal death | 15 | 13 | **28** |
| Post neonatal death | 1 | 3 | **4** |
| Alive | 55 | 14 | **69** |
| **Total** | **85** | **76** | **161** |

Isolated congenital diaphragmatic hernia led to termination of pregnancy in eight cases (9%). Six cases died spontaneously in utero. There were 71 live births, of which 16 died in the first year of life, an infant mortality rate of 225/1,000 live births. Fourteen of the infant deaths occurred prior to surgery, the majority (n=12) within the first day of life.

In contrast, the complex cases (with additional structural anomalies or aneuploidy) had a higher rate of termination of pregnancy (51%) and seven cases of spontaneous fetal loss. There were 14 complex congenital diaphragmatic hernia cases that survived to one year of age, giving an infant mortality rate of 533/1,000 live births. Of the 16 infant deaths, three died following surgery.

**Table 7 - Congenital diaphragmatic hernia: relative mortality risk (RR), complex versus isolated, West Midlands 1995-2000**

| Cohort | n | RR | 95%CI | Mortality outcome |
|---|---|---|---|---|
| All cases | 161 | 2.31 | 1.70 - 3.14 | All TOPs, fetal losses and infant deaths |
| All cases excluding TOPs | 114 | 2.18 | 1.41 - 3.36 | Fetal losses and infant deaths |
| All live births | 101 | 2.37 | 1.37 - 4.09 | Infant deaths |

Table 7 shows that the presence of additional anomalies significantly increases all measures of mortality in cases of congenital diaphragmatic hernia.

**Chart 2 - Congenital diaphragmatic hernia: gestation at delivery, West Midlands 1995-2000**

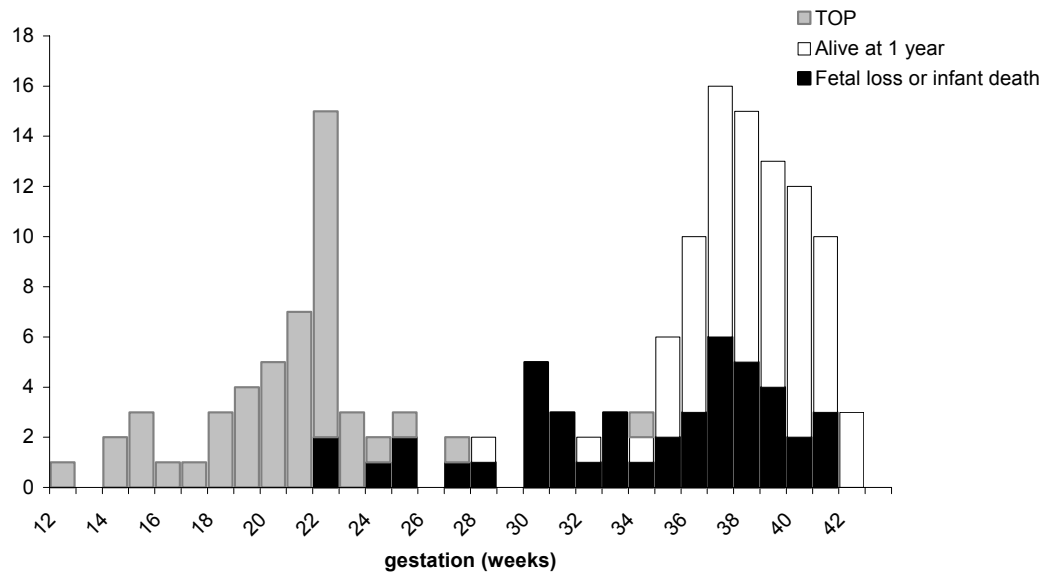



Chart 2 demonstrates that survival in cases of CDH is extremely unlikely before 34 weeks gestation. In view of the potential problems with respiratory function in these cases it is predictable that the mortality rates are extremely high in cases born prematurely. If obstetric complications occur in association with a CDH the survival rates quoted to parents must take account of the gestation. Delivery for fetal reasons before 34 weeks gestation is not justified.

**Chart 3 - Congenital diaphragmatic hernia: Kaplan-Meier survival curve by intervention, West Midlands 1995-2000**

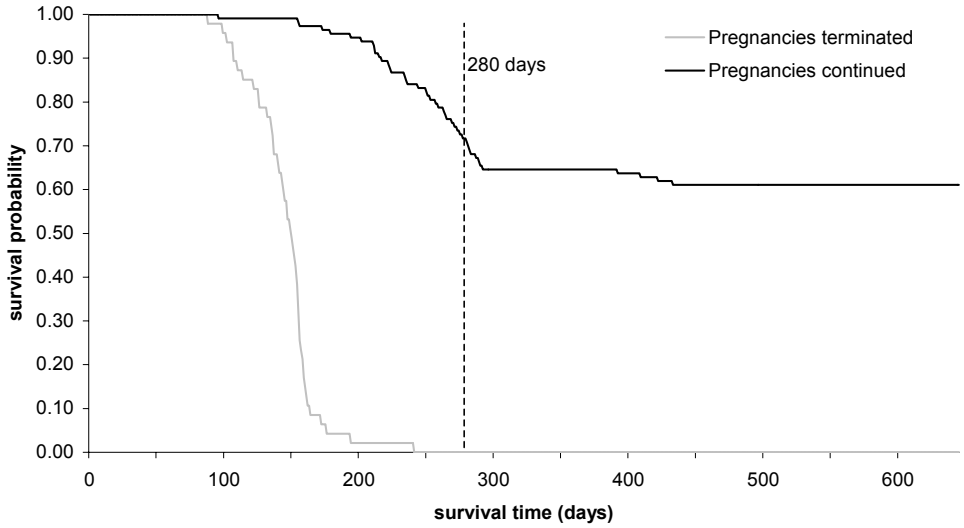



Chart 3 shows two survival curves with the termination of pregnancy curve falling steeply during the period of pregnancy where routine ultrasound assessment is undertaken between 17 and 23 weeks. The pregnancies not terminated show a drop to a survival probability of 0.65 in the immediate neonatal period with only a small subsequent drop of 0.04 to the end of the first year of life.

**Chart 4 - Congenital diaphragmatic hernia: Kaplan-Meier survival curve for isolated and complex cases, West Midlands 1995-2000**

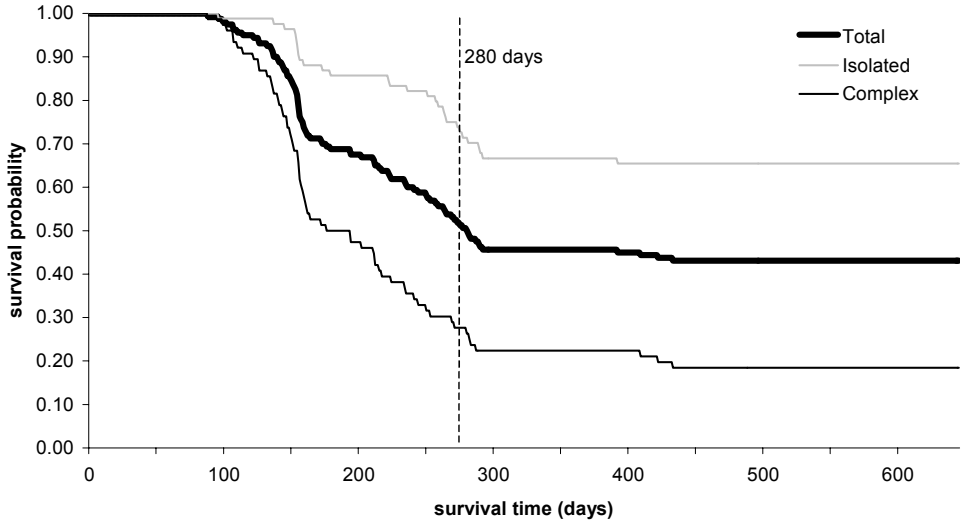



Chart 4 demonstrates the importance of the additional anomalies in predicting the outcome for the case. The survival rate for cases with additional anomalies is considerably lower than for isolated cases, with the majority of mortality occurring within the neonatal period (first 28 days of life). The early divergence of the isolated and complex curves represents the impact of prenatal diagnosis and termination of pregnancy. The curves continue to diverge demonstrating the high attrition rate of complex cases, regardless of detection and intervention.

## DETECTION

### Prenatal diagnosis

In Table 8 and Table 9 the "no prenatal diagnosis" group included cases where no prenatal diagnosis notifications were received by the CAR. Sensitivity rates calculated here may be lower than the true sensitivity if notifications were not sent for cases where a prenatal diagnosis was made.

**Table 8 - Isolated congenital diaphragmatic hernia: outcome by prenatal diagnosis, West Midlands 1995-2000**

| Outcome | Diagnosed < 24 weeks | Diagnosed >=24 weeks | No prenatal diagnosis | Total |
|---|---|---|---|---|
| Late fetal loss | 1 | | | **1** |
| Late fetal loss - TOP | 8 | | | **8** |
| Stillbirth | 4 | | 1 | **5** |
| Stillbirth - TOP | | | | **0** |
| Neonatal death | 6 | 3 | 6 | **15** |
| Post neonatal death | | 1 | | **1** |
| Alive | 12 | 8 | 35 | **55** |
| **Total** | **31** | **12** | **42** | **85** |

Table 8 demonstrates that prenatal diagnosis was made in 43 of 85 cases of isolated congenital diaphragmatic hernia, giving an overall sensitivity of 51%. Prenatal diagnosis before 24 weeks gestation was made in 31 cases, giving a sensitivity below 24 weeks of 36%.

Of those diagnosed prenatally, 8 (19%) of these isolated cases were terminated, none of the cases diagnosed after 24 weeks were terminated. The infant death rate following prenatal diagnosis was 333/1,000 live births, compared to 146/1,000 live births when the diagnosis was not made (not statistically significant).

**Table 9 - Complex congenital diaphragmatic hernia cases: outcome by prenatal diagnosis, West Midlands 1995-2000**

| Outcome | Diagnosed < 24 weeks | Diagnosed >=24 weeks | No prenatal diagnosis | Total |
|---|---|---|---|---|
| Late fetal loss | 1 | | | **1** |
| Late fetal loss - TOP | 35 | | | **35** |
| Stillbirth | 4 | 2 | | **6** |
| Stillbirth - TOP | 2 | 2 | | **4** |
| Neonatal death | 9 | 3 | 1 | **13** |
| Post neonatal death | 1 | 1 | 1 | **3** |
| Alive | 2 | 2 | 10 | **14** |
| **Total** | **54** | **10** | **12** | **76** |

Table 9 presents the prenatal diagnosis rates and outcomes for the complex cases (with additional structural anomalies or aneuploidy). As expected the presence of other anomalies increases the proportion of cases in which a prenatal diagnosis is made with 64 cases being diagnosed (sensitivity 84%), and 54 diagnoses made before 24 weeks (sensitivity 71%). In complex cases of congenital diaphragmatic hernia, the first malformation detected by ultrasound may not be the hernia.

Termination of pregnancy was the outcome for 37 of the 54 cases where prenatal diagnosis was made before 24 weeks (69%) and 2 of the 10 cases made after 24 weeks (20%).

## Additional anomalies

Table 10 presents the additional malformations present in congenital diaphragmatic hernia cases. The rows are mutually exclusive groups. The column headings are not mutually exclusive and count all additional anomalies. Cases with a single additional anomaly appear in the "CDH + one other system" row, and appear in the column which describes the additional malformation. Those case with more than one additional anomaly will appear within the "multiple systems", "chromosomal", or "syndrome" groups but will also be counted once in any of the columns detailing the additional anomalies.

**Table 10 - Congenital diaphragmatic hernia: additional anomalies, West Midlands 1995-2000**

| | Central nervous system | Limb/skeletal | Cardiac/ cardiovascular | Urogenital | Digestive/ abdominal wall | Other | **Total cases** | **%Total** |
|---|---|---|---|---|---|---|---|---|
| Multiple systems | 14 | 16 | 10 | 10 | 9 | 11 | **26** | **16%** |
| Chromosome | 14 | 8 | 7 | 6 | 2 | 7 | **22** | **14%** |
| Syndrome | 0 | 2 | 1 | 4 | 1 | 1 | **4** | **2%** |
| CDH + one other system | 6 | 4 | 7 | 2 | 3 | 2 | **24** | **15%** |
| Isolated CDH | | | | | | | **85** | **53%** |
| **Total** | **34** | **30** | **25** | **22** | **15** | **21** | **161** | **100%** |
| **%Total** | **21%** | **19%** | **16%** | **14%** | **9%** | **13%** | **100%** | |

47% of congenital diaphragmatic hernia cases had additional structural or chromosomal malformations. The most common additional anomalies were malformations of the central nervous system, present in 21% of cases.

Cardiac malformations occur in 16% of cases and it is therefore best practice to arrange a fetal echocardiogram. Features that are sequelae of the congenital diaphragmatic hernia such as malposition of the heart are excluded.

**Table 11 - Congenital diaphragmatic hernia: karyotype of cases with chromosomal anomalies, West Midlands 1995-2000**

| karyotype | n |
|---|---|
| 47XX+18 or 47XY+18 | 9 |
| 47XX+13 or 47XY+13 | 3 |
| 47XY, inv(4)(?p14?q21.1),+13 | 1 |
| 47XY, +der(22) t(11;22)(?;q11) | 1 |
| 47XY, +der(22) t(11;22)(q23.3;q11.2)mat | 1 |
| 46XX,+13, der (13;) (q10;q10) de novo | 1 |
| 46XY, der(2) t(2; 8) (q37; p11.2)pat | 1 |
| 46XX, der(13) t(4; 13)(p11; p11)[9]/46XX[76] | 1 |
| 46XX, add(6)(q23 or 25) | 1 |
| 46XY, del(2)(q33q35 or q3537)de novo | 1 |
| 46XX/46XX 12p+ | 1 |
| 47XY+mar/46XY | 1 |

Table 11 lists the karyotypes of the 22 cases of congenital diaphragmatic hernia that had chromosomal anomalies. Twelve cases were meiotic non-disjunction trisomies of 18 or 13, the remaining were other complex rearrangements.

Although rapid karyotyping is recommended in cases of diaphragmatic hernia because of the high prevalence of associated aneuploidy, a full karyotype is required to identify complex rearrangements which also occur.

## ULTRASOUND DIAGNOSIS

**Chart 5 - Congenital diaphragmatic hernia: gestation at ultrasound diagnosis, West Midlands 1995-2000**

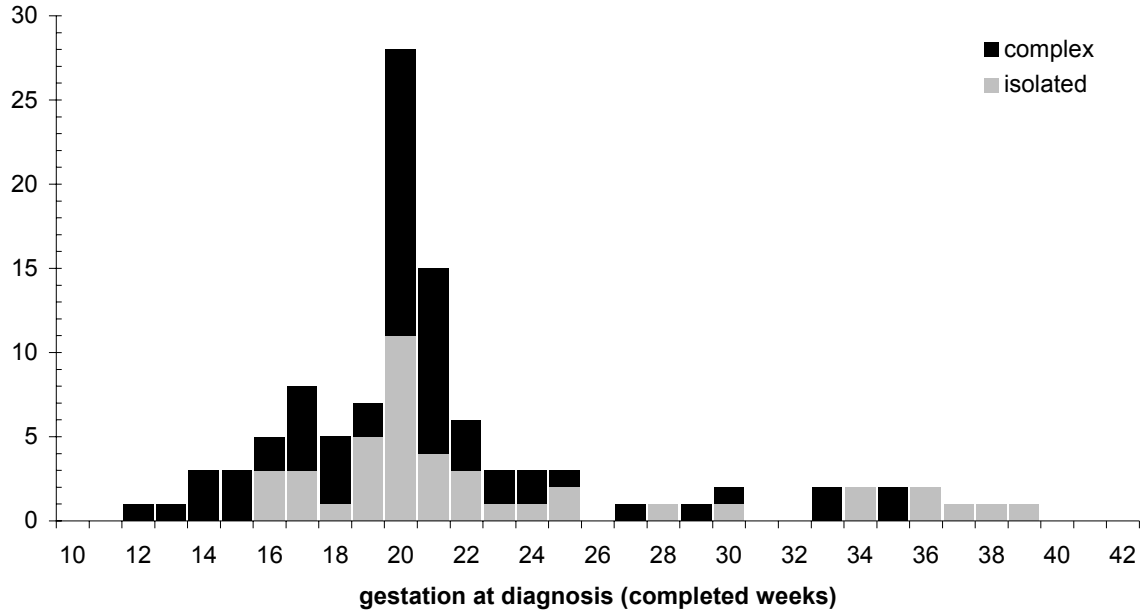



Chart 5 illustrates that the peak gestation of prenatal diagnoses for both isolated and complex cases is at the time of the routine fetal anomaly screening scan (18 to 22 weeks). Polyhydramnios, growth restriction and other pregnancy complications can lead to the diagnosis being made in later pregnancy, this may occur at any time up until term.

Complex cases were more likely to be diagnosed before 18 weeks gestation. The mean gestational age of diagnosis was 20 weeks for complex cases and 23 weeks for isolated cases. Although the timing of diagnosis in these groups is broadly similar, Table 8 and Table 9 show that the proportion of cases diagnosed prenatally was 51% for isolated and 84% for complex.

## False positive ultrasound cases

**Table 12 - Congenital diaphragmatic hernia: false positive cases on ultrasound, West Midlands 1995-2000**

| Final diagnosis | n |
|---|---|
| **Respiratory malformations** | |
| Cystic adenomatoid malformation | 3 |
| Bronchogenic cyst | 1 |
| Hydrothorax | 1 |
| Hypoplasia/effusions | 1 |
| Pleural effusions | 1 |
| Lung sequestration | 1 |
| | |
| **Gastrointestinal malformation** | |
| Duodenal atresia | 1 |
| Malrotation gut | 1 |
| | |
| **Malformation of other systems** | |
| Meckel Gruber syndrome | 1 |
| | |
| **No malformation** | 3 |
| | |
| **Total** | **14** |

Table 12 shows the cases where congenital diaphragmatic hernia was diagnosed by ultrasound at some stage during pregnancy. It shows the final diagnosis of all false positive ultrasound cases.

There were 14 false positive cases in total, their final diagnoses are reported above. Of the 14 cases, 6 were initially diagnosed with other problems and were referred to the regional fetal medicine centre, where a diagnosis of congenital diaphragmatic hernia was made. The diagnoses were modified after delivery. Of the remaining 8 cases where the first suspicion was of CDH, 6 were referred and the diagnosis was then changed prenatally. Of the 2 cases that were not referred, one was resolved antenatally with subsequent ultrasound locally and one remained a false positive until delivery.

False positive diagnosis is extremely important to consider in this group of conditions, particularly when counselling parents prenatally. A total of 107 true positive diagnoses were made, giving 121 prenatal diagnoses in total. Those undertaking ultrasound screening and diagnosis should be aware that a relatively high proportion, 14/121 cases (12%) of a prenatal diagnosis were incorrect, although other pathology requiring investigation and treatment was present in 11 of the 14 false positive cases.

## POSTNATAL DATA

### Surgery

**Table 13 - Congenital diaphragmatic hernia: surgical interventions and outcomes, West Midlands 1995-2000**

| Outcome | Surgery | No surgery | Not known | Total |
|---|---|---|---|---|
| Fetal loss, all gestations inc TOPs | | 60 | | 60 |
| Neonatal death | 2 | 26 | | 28 |
| Post neonatal death | 3 | 1 | | 4 |
| Alive | 67 | 0 | 2 | 69 |
| **Total** | **72** | **87** | **2** | **161** |

Of the 101 live born cases, 72 (71%) underwent surgery, of which 67 (93%) were alive at 1 year of age.

**Table 14 - Congenital diaphragmatic hernia: hospital of surgery for live births, West Midlands 1995-2000**

| Surgery | Died | Alive | Total |
|---|---|---|---|
| Birmingham Children's Hospital | 3 | 55 | **58** |
| Leicester Royal Infirmary | 0 | 4 | **4** |
| Glenfield | 2 | 1 | **3** |
| Alder Hey | 0 | 5 | **5** |
| Nottingham | 0 | 2 | **2** |
| none | 27 | 0 | **27** |
| unknown | 0 | 2 | **2** |
| **Total** | **32** | **69** | **101** |

Table 14 illustrates the hospitals that undertook surgery for West Midlands cases. This reflects the normal referral patterns for paediatric surgery from the West Midlands, with the majority of the cases (58/72) 81% being operated on at the Birmingham Children's Hospital.

## RECOMMENDATIONS

### 1. ANTENATAL CARE

1.1. Following diagnosis the case should be reviewed by a specialist in fetal medicine within 7 days of the initial suspicion:

1.1.1. Serious consideration should be given to the possibility of other anomalies. Cardiac anomalies were present in 16% of cases and therefore it is best practice to arrange a fetal echocardiogram.

1.1.2. Polymerase chain reaction (PCR) analysis and full karyotyping should be offered in all cases.

1.1.3. 12% of cases diagnosed antenatally will prove to have other pathology or possibly be normal.

1.2. Termination of pregnancy should be offered in cases where significant handicap is considered likely.

1.3. The paediatric team who will care for the baby should be informed of the diagnosis, and appropriate arrangements made for both immediate neonatal intensive care and surgery. Antenatal counselling by the paediatric surgical team should be offered.

1.4. Delivery for fetal reasons before 34 weeks should not be offered, because the consequence will almost always be neonatal death.

### 2. INTRAPARTUM CARE

2.1. The paediatricians should be informed as soon as it is clear that delivery is imminent.

2.2. Normal labour care is appropriate.

2.3. There is no proven benefit to caesarean section delivery.

### 3. POSTPARTUM CARE

3.1. An experienced paediatrician should attend the delivery.

3.2. Active resuscitation should be immediately available if required.

3.3. Neonatal intensive care including facilities for respiratory support should be available at the place of birth.

3.4. Consideration should be given to the use of ECMO if traditional ventilatory methods are failing.

3.5. Referral for consideration of surgical repair should be planned immediately after stabilisation of the neonate.

3.6. Surgery should take place in units, and within teams, experienced in the management of this condition.

3.7. Paediatric intensive care cots must be available for the management of this condition as required.

### 4. GENERAL

4.1. Parents should be given access to high quality information, given in a sensitive manner by professionals experienced in the management of this condition.

4.2. Professionals should co-operate to improve the information available to parents relating to the long term outcomes for this condition.