

## ORIGINAL ARTICLE

# Poor outcome of very low birthweight babies with serious congenital heart disease

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*Arch Dis Child Fetal Neonatal Ed* 2002;**87**:F31–F33

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Accepted  
8 January 2002

**Objective:** To evaluate incidence and mortality of congenital heart disease in very low birthweight babies.

**Method:** Retrospective analysis of a 12 year period.

**Results:** Forty seven babies were diagnosed with severe congenital heart disease. The most common lesions were ventricular septal defect and coarctation of the aorta. Mortality attributed to congenital heart disease was 32%. Coarctation of the aorta, the second most common lesion, was fatal in 62% of cases. Closure of a patent ductus arteriosus with indomethacin proved to be detrimental in babies with undiagnosed coarctation, causing rapid deterioration in some.

**Conclusion:** Very low birthweight neonates with severe congenital heart disease have a higher mortality than babies with higher birth weight. A contributing factor is closure of a patent ductus arteriosus if an underlying lesion has not been recognised. This could be of significance if the use of prophylactic treatment with indomethacin becomes more common.

Congenital heart disease (CHD) in the newborn has a reported prevalence of 3–12/1000 live births.<sup>1–6</sup> Depending on the severity of the lesion, wide ranges of mortality have been reported.<sup>7–11</sup> Although there are a few reports that focus on management of low birthweight babies with CHD,<sup>7–10</sup> there are no reports specifically on the incidence in and impact of CHD on very low birthweight (VLBW) babies. The outcome of preterm infants has improved because of better obstetric and neonatal care compared with just a few decades ago. There has also possibly been an increase in antenatal diagnosis, better surgical outcome, and thus a change in antenatal counselling. It may be possible that these factors impact on incidence and mortality of CHD in small babies. We report a retrospective study of severe CHD in all VLBW babies treated at our hospital over the last 12 years.

## METHODS

We reviewed the data pertaining to all babies with birth weight  $\leq$  1500 g treated between 1 January 1988 and 31

December 1999. Patients were identified from a prospectively maintained computer database used in the neonatal unit.

We defined severe CHD as all cases excluding atrial septal defect, minor pulmonary stenosis, and patent ductus arteriosus, as babies with atrial septal defect and minor pulmonary stenosis all survived, and none showed any physiological instability requiring treatment. Information from the charts of all babies with severe CHD was collected, and gestational age, birth weight, day and method of diagnosis, treatment, and outcome at discharge were recorded.

Mortality in VLBW babies with CHD was compared with mortality in VLBW babies without.

Differences in proportion were tested for statistical significance with the  $\chi^2$  test or Fisher's exact test where appropriate. Significance was defined as  $p < 0.05$ .

## RESULTS

### Overview

Over 12 years, 2020 babies of birth weight  $\leq$  1500 g were treated at our hospital, of which 266 (13.2%) died. There were 760 (37.6%) babies of  $\leq$  1000 g, of which 200 (26.3%) died. We identified 47 babies with severe CHD, giving an incidence of 2.3%. Mean gestational age was 29.3 weeks (range 24–36), and mean birth weight was 1014 g (range 450–1499). The most common cardiac defect was ventricular septal defect (VSD), and the second most common was coarctation of the aorta (CoA) (table 1). Of the 47 patients with CHD, seven (15%) had dysmorphic features. One of these was diagnosed with trisomy 21; no syndromal diagnosis could be made in the other six babies.

### Mortality

Mortality in the babies with significant CHD was 40% (19/47), significantly higher than the 13.2% mortality of all VLBW babies (table 2). Mortality deemed to be due to the underlying lesion was 32% (15/47), also higher than overall mortality in

**Table 1** Outcome of congenital heart disease (CHD) in babies  $\leq$  1500 g

CHD	No	No who died	Death due to CHD
VSD	25	4	0
CoA	8	5	5
PA	3	2	2
TOF	3	2	2
DORV	2	1	1
TAPVD	2	2	2
TA	1	1	1
TGA	1	1	1
HLHS	1	1	1
AV-canal	1	0	0
Total	47	19 (40%)	15 (32%)

VSD, Ventricular septal defect; CoA, coarctation of aorta; PA, pulmonary atresia; TOF, tetralogy of Fallot; DORV, double outlet right ventricle; TAPVD, total anomalous pulmonary venous drainage; TA, tricuspid atresia; TGA, transposition of great arteries; HLHS, hypoplastic left heart syndrome; AV, atrioventricular canal defect.

**Abbreviations:** CHD, congenital heart disease; VLBW, very low birth weight ( $<$  1500 g); VSD, ventricular septal defect; CoA, coarctation of aorta

**Table 2** Mortality of very low birthweight (VLBW) babies and subgroups

Group	CHD	No CHD	RR	95% CI	p Value*
VLBW	19 (40.4)	247 (12.5)	3.2	2.2 to 4.7	<0.0001
ELBW	11 (47.8)	189 (25.6)	1.9	1.2 to 2.9	0.02
1001–1500 g	8 (33.3)	58 (4.7)	7.1	3.8 to 13.2	<0.0001
Multiple gestation	5 (29.4)	65 (11.5)	2.6	1.2 to 5.5	0.03
IUGR	8 (44.4)	37 (11.1)	4	2.2 to 7.3	<0.0001

Values in parentheses are percentages.

\* $\chi^2$  test.

CHD, Congenital heart disease; RR, relative risk; CI, confidence interval; ELBW, extremely low birth weight; IUGR, intrauterine growth retardation.

**Table 3** Characteristics of very low birthweight neonates and subgroups

	Group I	Group II
Number	760	1260
Gestational age (weeks)	27 (24–32)	31 (26–37)
Birth weight (g)	734 (450–1000)	1251 (1005–1500)
Congenital heart disease	23 (3%)	24 (1.9%)

Unless otherwise indicated, values are mean (range). Group I, birth weight  $\leq$  1000 g; group II, birth weight 1001–1500 g.

VLBW babies. When the cohort was divided into two groups according to birth weight (group I: birth weight  $\leq$  1000 g; group II: birth weight 1001–1500 g), we found that CHD was associated with a higher mortality in both groups (tables 2 and 3).

None of the babies with VSD succumbed to the cardiac lesion alone. The causes of death were intraventricular haemorrhage, hepatic failure, and bronchopulmonary dysplasia ( $n = 5$ ). The last of these could have been worsened by cardiac failure from the VSD.

If we exclude all babies with VSD from our cohort, mortality increased appreciably. In group I, mortality increased from 39% (9/23) in babies with CHD to 82% (9/11) in babies with CHD other than VSD ( $p = 0.06$ ). In group II, mortality increased from 25% (8/24) in babies with CHD to 54% (6/11) in babies with CHD other than VSD ( $p = 0.23$ ). Although the rise in mortality is not significant, these numbers indicate a strong trend towards a worse outcome in babies affected by a heart disease that is not a VSD, especially in the extremely low birthweight babies.

### Coarctation of the aorta

CoA was the second most common lesion found. Six of the eight babies with CoA weighed  $\leq$  1000 g at birth. In total, five babies (62%) died, and four of these were of  $\leq$  1000 g birth weight. Six were treated with indomethacin before the diagnosis of CoA was made. In three babies, this considerably worsened their condition—that is, worsening of cardiac failure with hypotension, renal failure, and metabolic acidosis. In total, six babies were treated surgically, and two died before surgery. Three of the six surgically treated babies died in spite of the surgical correction; all weighed  $\leq$  1000 g at birth.

### Surgery

Sixteen of the 47 babies (34%) had either palliative or corrective surgery: six babies with CoA, five babies with VSD, two babies with pulmonary atresia, as well as one baby each with atrioventricular canal defect, double outlet right ventricle, and total anomalous pulmonary venous drainage. Seven of these babies, that is 44%, died after surgery (1–62 days), with the highest mortality being in the babies with CoA (50%).

## DISCUSSION

Our study shows that CHD in VLBW neonates is associated with high mortality. As far as we know, this retrospective study is the first to evaluate incidence and outcome of only VLBW babies with CHD. Previous reports focused on either low birthweight infants having surgery<sup>12,13</sup> or premature infants per se.<sup>14</sup> None reported outcome of VLBW infants only.

The prevalence of CHD in babies of  $\leq$  1500 g birth weight born at this hospital is greater than that seen elsewhere. It may be that the transfer of babies with a postnatal diagnosis of CHD has an impact in this small group of babies. Many of the less severe lesions in babies born elsewhere would not come to our attention, so the true population incidence of CHD cannot be determined from analysis of our own hospital's data alone. We therefore compared VLBW babies with and without CHD in order to estimate the effect of CHD on mortality.

Mortality in this cohort of babies is comparable to that in a recent study,<sup>14</sup> in which mortality of preterm infants weighing less than 2500 g with CHD was twice as high as in infants without CHD. In that study, the mean age of the babies was 33 weeks and the mean birth weight 1852 g, so these babies were older and larger than the babies in our population. Nevertheless both studies indicate a trend to higher mortality in preterm infants with CHD. The reasons for the high mortality in this selected group of babies are multiple. In the premature infant stressful circumstances cause rapid changes in pH, lactate, glucose, and temperature. The myocardium is less compliant, less tolerant of increases in afterload, and less responsive to increases in preload. Immaturity of liver and kidneys leads to decreased hepatic synthetic function and altered drug metabolism. Premature infants have decreased nutritional reserve, but, on the other hand, have a higher metabolic rate and oxygen consumption.<sup>15</sup> These differences from term babies place the VLBW infant with CHD at a high risk of adverse outcome.

CoA was the second most common lesion and was associated with a high mortality. This is in contrast with the reported mortality of  $< 5\%$  in term neonates with CoA. It seems that VLBW babies with this heart defect have an unexpectedly poor outcome. The reason is not known. In our unit, echocardiographic examinations by a paediatric cardiologist are performed twice a week and on an on-call basis. Despite this, treatment of a suspected patent ductus arteriosus is sometimes started on clinical grounds without an echocardiogram. We found that treatment with indomethacin may not only unmask the previously undetected coarctation but may also worsen the condition of some babies. It remains unknown whether early diagnosis and early surgical repair would have made a difference to the outcome. Mortality soon after surgery in neonates with CoA has been reported to be up to 17%.<sup>11</sup> Correction of the defect in such small babies has not been reported. The reasons for the unexpectedly high mortality in VLBW babies with CoA seem to be directly related to the baby's size: it is difficult to diagnose by echocardiogram; possible poor condition of the baby before the operation; high rate of complications after the operation.

As reported by others, treatment of a patent ductus arteriosus with indomethacin reduces morbidity.<sup>16-19</sup> A recent multicentre trial<sup>20</sup> compared the short and long term effects of indomethacin prophylaxis in extremely low birthweight babies with placebo. There were no differences in mortality, cerebral palsy, cognitive delay, deafness, or blindness at a corrected age of 18 months. The babies treated prophylactically with indomethacin had a reduced incidence of patent ductus arteriosus and severe periventricular and intraventricular haemorrhage. This study may have prompted a trend to prophylactic treatment with indomethacin of babies of birth weight  $\leq 1000$  g. In the light of our findings, we may have to consider echocardiographic investigation of all these babies before such treatment.

Mortality of babies who had cardiac surgery was high, highest in infants with birth weight  $< 1000$  g who had surgery for CoA. Previously reported mortality for infants  $< 2.5$  kg having surgery was 16.5%,<sup>12</sup> and 17% for infants  $< 2$  kg.<sup>13</sup> The babies in these reports were more mature than those in our study, and this may explain the better outcome.

Overall it can be said that CHD in VLBW babies is associated with considerable mortality. This reflects the serious effect that cardiac lesions have on these small babies and should be kept in mind when counselling parents. Reasons for the poor outcome are multiple and include severe growth restriction, difficulties in diagnosing the lesion, problems during surgical treatment, postoperative complications, and, possibly, prophylactic treatment with indomethacin worsening the baby's condition if the underlying lesion has not been previously recognised.

We conclude the following.

- There is a high mortality of VLBW babies with CHD
- Closure of patent ductus arteriosus, if an underlying lesion is not recognised, contributes to morbidity
- Cardiac evaluation of extremely low birthweight babies may be needed before prophylactic treatment with indomethacin

#### ACKNOWLEDGEMENTS

We thank Dr B Lingwood for reviewing the manuscript.

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