

The Incidence of Congenital Heart Defects in Very Low Birth Weight and Extremely Low Birth Weight Infants

Max Godfrey BSc (Hons) MB BS¹, Michael S. Schimmel MD^{2,4}, Cathy Hammerman MD^{2,4}, Benjamin Farber MD^{3,4}, Joram Glaser MD⁵ and Amiram Nir MD^{3,4}

Departments of ¹Pediatrics and ²Neonatology, and ³Pediatric Cardiology Unit, Shaare Zedek Medical Center, Jerusalem, Israel

⁴Hebrew University-Hadassah Medical School, Jerusalem, Israel

⁵Pediatric Cardiology Service, Meuhedet Health Fund, Israel

ABSTRACT: **Background:** The incidence of congenital heart defects, reported to be 5–8/1000 in term infants, is not well established in very low birth weight infants.

Objectives: To establish the incidence of congenital heart defects in VLBW infants in the neonatal intensive care unit of our institution.

Methods: A retrospective analysis of the population in the NICU at our institution was performed. VLBW (BW ≤ 1500 g) infants born between 2001 and 2006 who survived more than 48 hours were included in the study. Infants with clinical signs of heart disease underwent echocardiography.

Results: During the study period 437 VLBW live-born infants met the inclusion criteria. Of these, 281 (64.3 %) underwent echocardiography. CHD was detected in 19 infants (4.4%, 95% confidence interval 2.4–5.4%), significantly higher than the incidence of 5–8/1000 in the general population ($P < 0.0001$). In the subgroup of 154 infants with BW < 1000 g there were 10 (6.5%) with CHD. In the subgroup of 283 infants with BW 100–1500 g there were 9 (3.2 %, $P = 0.19$ vs. VLBW) with CHD.

Conclusions: Our observations show an increased incidence of CHD in VLBW neonates, as compared to the general population. Since not all infants underwent echocardiography, and minor cardiac defects may have been missed in our VLBW infants, the true incidence may be higher than reported here.

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tion [4]. There are, however, few studies of the incidence in very low birth weight neonates; most studies relate to gestational age rather than birth weight [3]. The purpose of this study was to determine the incidence of CHD in VLBW neonates in a single institution.

PATIENTS AND METHODS

A retrospective analysis of the population in the level III B, 30-bed, university-affiliated neonatal intensive care unit at the Shaare Zedek Medical Center, Jerusalem, Israel, was performed. VLBW (BW ≤ 1500 g) infants born between 2001 and 2006 inclusive who survived for more than 48 hours were included. All the infants were examined daily by a physician, and infants with heart murmurs or other clinical signs of heart disease or persistent respiratory problems were referred for echocardiography. All echocardiographic examinations were performed by a senior pediatric cardiologist, and all echocardiography reports were reviewed by a senior pediatric cardiologist for study suitability. Findings of patent ductus arteriosus, patent foramen ovale and bicuspid aortic valve were not included in the analysis. Atrial septal defects 5.5 mm or larger were regarded as CHD. Comparison of proportions was performed using the chi-square test (SSI, San Jose, CA, USA).

RESULTS

During the study period 505 VLBW neonates were born. A total of 437 infants met the inclusion criteria, of whom 225 (51.5%) were males. Of the included infants, 281 (64.3 %) underwent echocardiography. CHD was detected in 19 infants (4.4%, 95% confidence interval 2.4–5.4%), which was significantly higher than the published incidence of 5–8/1000 live births in the general population ($P < 0.0001$). In the subgroup of 154 infants with BW < 1000 g, 10 (6.5%) had CHD. In the subgroup of 283 infants with BW 1000–1500 g, 9 (3.2%, $P = 0.19$ vs. ELBW) had CHD. The characteristics of the groups are shown in Table 1. The most common defects were ventricular septal defect (n=8, 42.1%), atrioventricular

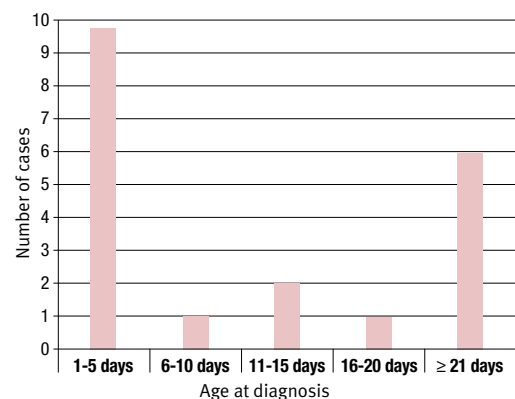
The incidence of congenital heart defects in neonates has been studied thoroughly and is usually reported to be 5–8/1000 [1–3]. This incidence rate is thought to be constant worldwide, although it is obviously dependent on case defi-

VLBW = very low birth weight
NICU = neonatal intensive care unit
CHD = congenital heart disease

Table 1. Gender, birth weight and gestational age of infants with CHD and without ('cohort') congenital heart defects

	Cohort (n=418)	CHD (n=19)
Gender (M:F)	214:204 51.2:48.8%	11:8 57.9:42.1%
Birth weight (g)		
Range	413–1500	663–1475
Mean ± SD	1113 ± 265	1027 ± 274
Median	1130	990
Gestational age (completed weeks)		
Range	23–37	24–35
Mean ± SD	29.1 ± 2.9	29.2 ± 3.2
Median	29	29

Figure 1. Age at diagnosis (days) vs. number of cases



septal defect (n=4, 21.1%) and pulmonic valve stenosis (n=2, 10.5%). There was one case each of tetralogy of Fallot, coarctation of the aorta, mitral valve prolapse, aorto-pulmonary collaterals, and atrio-ventricular canal defect. The age of the neonates at the time of diagnosis is shown in Figure 1.

Of the 19 infants with CHD, 2 were syndromic. One of them had trisomy 21, and the other was suspected to have Cornelia de Lange syndrome.

DISCUSSION

Our observation shows a sevenfold higher incidence of CHD in the VLBW neonates and an elevenfold higher incidence in the extremely low birth weight population, as compared to the reported incidence of 0.5–0.8% in the general population [1-3].

A population-based study has shown low birth weight, small for gestational age and preterm birth to be associated with many forms of CHD [5]. Interestingly, transposition of the great arteries and aortic stenosis were not associated with these variables in that study. A more recent study of non-syndromic CHD showed a twofold increase in likelihood

of being small for gestational age, a threefold increased risk of prematurity, and a reduced mean birth weight in the CHD population [6]. The latter study found the associations to be valid for all types of CHD tested. Our results did not show a statistically significant relationship between birth weight and incidence of CHD within the VLBW population, although this may have been due to the small numbers involved.

Our findings could represent a true increase in CHD in the VLBW population. The reasons for the higher incidence of CHD observed in premature infants remain unclear. We speculate that it may be due to the fact that small septal defects close spontaneously *in utero*, and thus fewer may be apparent in mature infants. This would not, however, explain the reported increased incidence of non-septal defects in our LBW population. It is also possible that CHD may be independently associated with premature birth and/or low birth weight. It is generally accepted that the causes of CHD are multifactorial, involving a wide range of genetic (including non-syndromic) and environmental risk factors [7,8]. Thus, prematurity and/or intrauterine growth retardation or small-for-gestational age weight may be causally related to the same factor(s) that precipitated the CHD.

Alternatively, because such a high percentage of the neonates were studied echocardiographically, our results might merely reflect a more accurate picture of the incidence of CHD in the neonatal population as a whole, which previously may have been underestimated. Rougin et al. [9] reported an incidence of VSD in the healthy neonatal population of 53.2/1000, based on echocardiographic studies of 1053 consecutive term neonates. They found a similar incidence (56.6/1000) in a study of 159 consecutive preterm neonates [10]. They suggest that their findings represent the 'true' incidence due to the lack of selection bias inherent in their methodology. In fact, one of the findings of the Baltimore-Washington Infant Study was that the rate of diagnosis of CHD on echocardiography more than doubled between the years 1981 and 1984, in contrast to diagnoses made on catheterization, autopsy or surgery. The clear implication is that increasing technological advances are allowing diagnoses to be made that would previously have been missed [11].

Our study has some important limitations. Only two-thirds of the infants underwent echocardiography, and minor cardiac defects may have been missed on clinical examination, although this implies that, if anything, we underestimated the incidence of CHD in our study population. Also, it represents the experience of a single center, and the overall number of CHD cases is small as a result. However, the incidence of CHD is thought to be relatively stable across populations [4]; therefore, no significant bias is expected as a result of the data being collected from a single center.

VSD = ventricular septal defect

Recent statistics from Israel show an incidence of CHD of 11.5/1000 live births in the year 2000, although the inclusion criteria seem to have been more liberal (Israel Ministry of Health statistics, personal communication). Similarly, a report published by the Israel Neonatal Network on the national statistics for VLBW infants for the years 1995–2002 showed an incidence of 28/1000 live births [12], although, again, the case definition seems to have been broader. Previously unpublished data from our own institution show an incidence of 9/1000 admissions to the newborn nursery in 2006. These data used the definition of CHD described above (i.e., atrioventricular septal defect > 5.5 mm, all VSDs, coarctations, valve stenosis, major structural abnormalities, but not PDA, bicuspid aortic valve or patent foramen ovale). This is broadly in line with currently accepted statistics for the incidence of CHD in term neonates, as mentioned above. Thus, it is unlikely that the population served by our institution is at increased risk of CHD, which would have been a source of selection bias.

The majority (52.6%) of cases of CHD in this study were diagnosed in the first 5 days of life. However, a sizeable minority (31.6%) were diagnosed at age 3 weeks or more. This raises questions regarding the clinical significance of some of the lesions, such as small VSDs, which are widely considered to be congenital heart defects.

Finally, there is no consensus as to what constitutes CHD for the purposes of defining incidence. We included even small VSDs, despite the fact that these may close with time and are unlikely to be associated with significant sequelae. As has become accepted in the literature, we did not include bicuspid aortic valve, although this lesion may progress with time to be a source of morbidity. We excluded PDA as this may be physiological or iatrogenic in the setting of VLBW infants in a neonatal intensive care unit, and therefore not a reflection of a true 'congenital heart defect'. However, some of the PDAs may have been truly congenital and not related to treatment of prematurity-associated conditions in the neonatal ICU. This again would suggest an underestimation of the incidence.

PDA = patent ductus arteriosus
ICU = intensive care unit

In summary, our results suggest a CHD incidence of at least 44/1000 in the VLBW neonatal population. Although not statistically significant, there was a trend towards a higher incidence in the ELBW population. Larger, prospective studies are called for to further elucidate the true incidence of heart defects in preterm, and indeed term infants.

Correspondence:

Dr. M. Godfrey

Dept. of Pediatrics, Shaare Zedek Medical Center, Jerusalem 91031, Israel

Phone: (972-2) 566-0216

Fax: (972-2) 563-7519

email: maxegodfrey@hotmail.com

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“You write to communicate to the hearts and minds of others what's burning inside you. And we edit to let the fire show through the smoke”

Arthur Plotnik (born 1937), American editor and author

“And if there were a God, I think it very unlikely that He would have such an uneasy vanity as to be offended by those who doubt His existence”

Bertrand Russell (1872-1970), British philosopher, logician, mathematician, historian, socialist, pacifist and social critic. He is considered one of the founders of analytic philosophy along with his protégé Wittgenstein, and is widely held to be one of the 20th century's premier logicians