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State-of-the-Art Paper

Birth Prevalence of Congenital Heart Disease Worldwide

A Systematic Review and Meta-Analysis

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Congenital heart disease (CHD) accounts for nearly one-third of all major congenital anomalies. CHD birth prevalence worldwide and over time is suggested to vary; however, a complete overview is missing. This systematic review included 114 papers, comprising a total study population of 24,091,867 live births with CHD identified in 164,396 individuals. Birth prevalence of total CHD and the 8 most common subtypes were pooled in 5-year time periods since 1930 and in continent and income groups since 1970 using the inverse variance method. Reported total CHD birth prevalence increased substantially over time, from 0.6 per 1,000 live births (95% confidence interval [CI]: 0.4 to 0.8) in 1930 to 1934 to 9.1 per 1,000 live births (95% CI: 9.0 to 9.2) after 1995. Over the last 15 years, stabilization occurred, corresponding to 1.35 million newborns with CHD every year. Significant geographical differences were found. Asia reported the highest CHD birth prevalence, with 9.3 per 1,000 live births (95% CI: 8.9 to 9.7), with relatively more pulmonary outflow obstructions and fewer left ventricular outflow tract obstructions. Reported total CHD birth prevalence in Europe was significantly higher than in North America (8.2 per 1,000 live births [95% CI: 8.1 to 8.3] vs. 6.9 per 1,000 live births [95% CI: 6.7 to 7.1]; $p < 0.001$). Access to health care is still limited in many parts of the world, as are diagnostic facilities, probably accounting for differences in reported birth prevalence between high- and low-income countries. Observed differences may also be of genetic, environmental, socioeconomical, or ethnic origin, and there needs to be further investigation to tailor the management of this global health problem. (J Am Coll Cardiol 2011;58:2241–7) © 2011 by the American College of Cardiology Foundation

Congenital heart disease (CHD) is the most common cause of major congenital anomalies, representing a major global health problem. Twenty-eight percent of all major congenital anomalies consist of heart defects (1). Reported birth prevalence of CHD varies widely among studies worldwide. The estimate of 8 per 1,000 live births is generally accepted as the best approximation (2). CHD, by definition, is present from birth. The most practical measurement of CHD occurrence is birth prevalence per 1,000 live births (3).

Massive breakthroughs have been achieved in cardiovascular diagnostics and cardiothoracic surgery over the past century, leading to an increased survival of newborns with CHD. Consequently, more patients with CHD reach adulthood, creating a completely new and steadily growing patient population: patients with grown-up congenital heart disease (GUCH). The prevalence of CHD is estimated to be 4 per 1,000 adults (4). Patients with GUCH often need long-term expert medical care and healthcare-related costs are high (5). Therefore, the global health burden as a result of CHD increases quickly.

It is important to have reliable information about worldwide CHD birth prevalence because this may lead to better insight into its etiology. In addition, dedicated care could be better planned and provided. Variation in CHD occurrences over time and worldwide has been suggested, but a complete overview is missing. In this systematic review and meta-analysis, we provide a complete worldwide overview of the reported birth prevalence of total CHD and the 8 most common subtypes of CHD from 1930 until 2010.

Methods

Search strategy. We conducted a PubMed literature search on September 23, 2010, using the following search terms: "heart defects, congenital/epidemiology," and "incidence" or "preva-

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Abbreviations and Acronyms

AoS = aortic stenosis
ASD = atrial septal defect
CHD = congenital heart disease
CI = confidence interval
Coarc = coarctation of the aorta
GUCH = grown-up congenital heart disease
PDA = patent ductus arteriosus
PS = pulmonary stenosis
TGA = transposition of the great arteries
TOF = tetralogy of Fallot
VSD = ventricular septal defect

lence." The search was limited to original research papers with English abstracts. No time restriction for publication dates was used. Reports of large governmental birth registries were searched online.

All titles and abstracts were screened for study population (live births, children), type of CHD, and birth prevalence. Studies were eligible if they reported the birth prevalence of total CHD or 1 of the 8 most common CHD subtypes: ventricular septal defect (VSD), atrial septal defect (ASD), pulmonary stenosis (PS), patent ductus arteriosus (PDA), tetralogy of Fallot (TOF), coarctation (Coarc), transposition of the great arteries (TGA), and aortic stenosis (AoS). CHD was defined according to the definition of Mitchell et al. (6); namely, "a gross structural abnormality of the heart or intrathoracic great vessels that is actually or potentially of functional significance." This definition excludes PDA in premature infants, Marfan syndrome, bicuspid aortic valve, mitral valve prolapse, cardiomyopathies, and congenital arrhythmias. Papers studying only specific groups (e.g., only Down syndrome), rheumatic heart disease, or case studies of rare defects were excluded. Papers focusing on etiology, (pre-natal) diagnosis, treatment, prognosis, or animal research were also excluded.

After exclusion on the basis of the title and abstract, full papers were carefully read and reconsidered according to all abovementioned inclusion and exclusion criteria. Studies focusing on CHD prevalence in schoolchildren age >5 years or including only severe forms of CHD were excluded. When a study was eligible for inclusion, we verified the denominator and numerator and recalculated the estimated birth prevalence to check accuracy. Studies with incorrect or missing denominators or numerator were excluded. Three authors performed the search independently using these inclusion and exclusion criteria. In case of disagreement, an agreement was negotiated. References of selected papers were crosschecked with the same inclusion and exclusion criteria.

Data extraction. Selected papers were reviewed and study characteristics were tabulated in a MS Excel for Windows (Microsoft Corporation, Redmond, Washington) and Review Manager version 5.0 (Review Manager, The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). The following study characteristics were registered: time period during which the study was performed, country, study design (retrospective or prospective), age of patients, diagnostic method, number of live births, number of patients with CHD, and birth prevalence of total CHD and 8 CHD subtypes. Studies were grouped according to 5-year time periods since 1930 to demonstrate time trends. Time period is taken as the period in which the study was performed. Before 1970, many differences in availability of diagnostic and registration facilities between the continents existed, so we used only those studies performed after 1970 to compare continents and income groups. World Bank Income groups based on gross national income per capita in 2008 were defined as: low income (≤$975), lower-middle-income ($976 to $3,855), upper-middle-income ($3,856 to 11,905), and high income (≥$11,906) (7).

Statistical analysis. Statistical analyses were done in Review manager 5.0, MS Excel, and SPPS version 15.0 (SPSS, Chicago, Illinois). Birth prevalence of total CHD and the 8 most common subtypes were pooled using the inverse variance method. Pooled group estimates were compared with a chi-square test. Time trends were plotted by using the Savitzky-Golay smoothing technique. Heterogeneity on basis of study design (retrospective vs. prospective), study size, continents, income groups and time periods was explored by using the Q and the I^2 statistics and by means of funnel plots.

Results

Search results. The systematic literature search yielded 1,136 potential eligible studies. After exclusion, cross-referencing, and reaching agreement on 3 studies, 114 studies were included in this systematic literature review and meta-analysis (Fig. 1, Online Table 1). This resulted in a total study population of 24,091,867 live births with CHD identified in 164,396 individuals. There were 12 reports of prospective birth defect registries. Seventy-six studies used echocardiography as the main diagnostic tool; the rest used combinations of diagnostic tools, such as death certificates, autopsy and surgical reports, physical examination, x-rays, and catheterization.

Total CHD birth prevalence. Over time, the reported total CHD birth prevalence increased substantially (Fig. 2), from 0.6 per 1,000 live births (95% confidence interval [CI]: 0.4 to 0.8) in 1930 to 1934 to 9.1 per 1,000 live births (95% CI: 9.0 to 9.2) after 1995. The increase over time was S-shaped, with a first steep increase from 1930 to 1960, followed by stabilization around 5.3 per 1,000 live births from 1961 to 1975, a second steep increase from the late 1970s until 1995, and eventually stabilization around 9.1 per 1,000 live births in the last 15 years.

Significant geographical differences were found (Fig. 3A). The highest reported total CHD birth prevalence was found in Asia (9.3 per 1,000 live births [95% CI: 8.9 to 9.7]) and the lowest in Africa (1.9 per 1,000 live births [95% CI: 1.1 to 3.5]). Reported total CHD birth prevalence in Asia was significantly higher compared with all other continents (all, $p < 0.001$). Europe had the second highest reported total CHD birth prevalence (8.2 per 1,000 live births [95% CI: 8.1 to 8.3]).