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ORIGINAL PAPER

Frequency and spectrum of congenital heart defects among live births in Germany

A study of the competence network for congenital heart defects

Gerda Schwedler · Angelika Lindinger · Peter E. Lange · Ulrich Sax · Julianna Olchvary · Brigitte Peters · Ulrike Bauer · Hans-Werner Hense

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Abstract
Background Congenital heart defects (CHD) are the most common single organ malformations in humans. A comprehensive study was initiated within the Competence Network for Congenital Heart Defects to assess population-based nationwide prevalence data for Germany.
Methods Study register of demographic and medical data of live births with CHD born between July 2006 and June 2007.
Results Seven thousand two hundred forty-five live births and infants with CHD were registered in Germany by 260 participating institutions (prevalence 107.6 per 10,000 live births). The most common lesions were ventricular septal defect, atrial septal defect and valvular pulmonary stenosis with 52.7, 18.3 and 6.6 per 10,000 live births, respectively. A single ventricle, tetralogy of Fallot and the complete transposition of the great arteries were the most common severe cardiac lesions (3.0, 2.7 and 2.3 per 10,000 live births). Parents reported that prenatal echocardiography had been performed in 53.8% of severe CHD cases with a cardiac defect detected in 77.5% of them.
Conclusion The reported prevalences of severe CHD are within the range of regional and European comparative data. The prenatal detection rate of severe cardiovascular malformations is comparable to contemporary European registries. Postnatal diagnosis of the CHD has been made early in life.

Keywords Congenital heart defects · Prevalence · Live births · Competence network for congenital heart defects

G. Schwedler · P. E. Lange · U. Bauer
Deutsches Herzzentrum Berlin—Kompetenznetz Angeborene Herzfehler, Augustenburger Platz 1, 13353 Berlin, Germany

A. Lindinger · J. Olchvary
Klinik fürPädiatrische Kardiologie, Universitätsklinikum des Saarlandes, 66421 Homburg/Saar, Germany

U. Sax
Medical Informatics and Information Technology, University Medical Center Goettingen, Robert-Koch-Str. 40, 37075 Göttingen, Germany

B. Peters
Institut für Biometrie und Medizinische Informatik, Otto-von-Guericke-Universität Magdeburg, Leipziger Str. 44, 39120 Magdeburg, Germany

H.-W. Hense (✉)
Bereich Klinische Epidemiologie, Institut für Epidemiologie und Sozialmedizin, Universität Münster, Albert-Schweitzer-Campus 1, 48129 Münster, Germany
e-mail: hense@uni-muenster.de

Introduction

Congenital cardiovascular defects (CHD) are defined as structural anomalies of the heart or of the thoracic vessels which currently or potentially may be of functional significance [1]. They represent the most frequent congenital anomaly of a single organ [2, 3] and are characterised by a large variety of symptoms and a wide pathomorphological range. The spectrum ranges from mild defects, such as persistent arterial duct or atrial septal defect, through moderate defects (e.g. ventricular septal defect, valvular aortic stenosis or coarctation) to severe and complex lesions such as pulmonary valve atresia or hypoplastic left heart syndrome. Depending on the type of the cardiac defect, the clinical course may range from spontaneous relief up to a lifelong need for medical care with multiple interventional and surgical procedures, often starting in the newborn age. Surgical and interventional progress has improved the

treatment regimens for these children in recent decades with a significant impact on life expectancy and quality of life. Nowadays, survival rates of paediatric patients with CHD are reported to be about 90% up to adulthood.

To date, only regionally restricted registries have been available in Germany for assessment of CHD prevalences. Thus, congenital cardiovascular defects were registered retrospectively in Bavaria from 1984 to 1991 [4]. In the Rheinhessen region, congenital malformations of all organs have been recorded by the Mainz Birth Registry since 1990 [5]. Likewise, congenital anomalies have been registered in the administrative area of Magdeburg and in the federal state of Saxony-Anhalt by the Congenital Malformations Monitoring since 1980 [6]. Therefore, the aim of the PAN study was to collate population-based data on the current prevalence of congenital cardiac defects among live births from all over Germany.

The nationwide collaboration was facilitated by the foundation of the Competence Network for Congenital Heart Defects, which was funded by the Federal Ministry for Education and Research to investigate congenital cardiac defects in Germany [7, 8].

In this report data are presented from neonates and infants, born alive between July 2006 and June 2007 in Germany. The involvement and contribution of different categories of collaborating institutions to this register are described. The prevalences of all CHD and of single lesions determined in this study are compared with concurrent regional and European data and the relation of different cardiac defects with prenatal diagnosis is considered.

Materials and methods

This report includes live births in Germany in the period July 1, 2006–June 30, 2007 and whose CHD was diagnosed within the first year of life. The study was approved by the Ethical Committee of the Charité, Berlin, and the data protection offices of all federal states had approved the data processing and storage procedures.

Data collection

All paediatric cardiologists in Germany were contacted and asked for participation [9]. Electronic data transfer into a central database was implemented by means of a web-based remote data entry system. Double recording or false record linkage was prevented by the creation of a unique identification code for each patient [10, 11] which was merged with the individual demographic and medical data. Only a restricted anonymous data set was available in cases of missing consent from the parents or legal guardians. All data entries were continuously checked for completeness and plausibility by internal (e.g. plausibility, consistency and correctness) as well external (e.g. monitor visits) quality controls.

Management of cardiac diagnoses

All congenital structural anomalies of the heart and the thoracic vessels were included with the following exceptions:

- persistent arterial duct in full-terms of up to 4 weeks after birth and in premature births of up to 4 weeks after calculated delivery date
- physiological stenosis of the pulmonary arterial branches
- isolated persistent foramen ovale
- isolated persistent left superior vena cava
- isolated bicuspid aortic valve
- isolated dextrocardia
- heart tumours
- cardiomyopathies
- cardiac arrhythmias

The cardiac diagnoses were arranged in accordance with the nomenclature and classification of the European Paediatric Cardiac Code of the "Association for European Paediatric Cardiology" (EPC code) [12]. In combined cardiac defects, either the haemodynamically leading structural anomaly or the defect requiring the earliest intervention was assessed as the major diagnosis. Thus, for example, in case of coarctation and ventricular septal defect, the coarctation was classified as the leading lesion. Finally, the cardiac defects were categorised as "mild", "moderate" and "severe", according to their degree of severity (Table 1).

Prenatal diagnosis

All parents or guardians were asked whether a prenatal echocardiography has been performed and whether a cardiac defect has been detected prenatally. This information was not available in patients with an anonymous data set (see above).

Statistical analyses

Numbers and prevalences are presented for the total of all CHD, for the CHD groups 'mild', 'moderate' and 'severe' and for single lesions. As the denominator for prevalence estimators we used the official numbers of live births as given by the German Statistical Bureau (http://www.destatis.de). These results were compared with recently published figures from local German registers (Rheinhessen region and Saxony-Anhalt) [13] as well as from EUROCAT, based on contributions of 20 European countries [13], and from nationwide studies in Croatia [14] and in Belgium

Table 1 Classification of congenital heart defects by severity

Mild CHD
Ventricular septal defect (small or muscular)
Atrial septal defect
Persistent arterial duct
Pulmonary valve stenosis
Others
Moderate CHD
Ventricular septal defect (all others)
Atrioventricular septal defect
Aortic valve stenosis
Coarctation of aorta
Partial anomalous pulmonary venous connection
Others
Severe CHD
Single ventricle (all types)
Tetralogy of Fallot
Pulmonary atresia with ventricular septal defect
Pulmonary atresia with intact ventricular septum
Double outlet right ventricle
Complete transposition of the great arteries
Congenitally corrected transposition of the great arteries
Truncus arteriosus communis
Interrupted aortic arch
Total anomalous pulmonary venous connection
Ebstein's malformation
Others

[15]. All analyses were performed using the programming package, SPSS 17.0.

Results

Coverage of data acquisition

A total of 260 institutions providing paediatric cardiologic care participated in collection of patients with CHD. According to their level of specialised care three groups of cooperating institutions were distinguished (Table 2) which contributed differently to the entirety of cardiac lesions (Fig. 1). Thus, while mild CHD were reported in similar proportions by each institutional category, about 80% of the severe cardiac defects were contributed by departments of paediatric cardiology/congenital heart defects.

Timing of postnatal diagnosis

In 82.1% of the patients the postnatal diagnosis of the heart defect was made within the first 3 months of life; severe cardiac lesions were diagnosed in 96.3% within this period.

Prevalence and spectrum of cardiac defects

A total of 7,245 cardiac defects were included in the study register within the observation period of 1 year: this amounts to an overall prevalence of 107.3 per 10,000 live births in Germany. Of them, 60.6% were classified as mild, 27.4% as moderate and 12.0% as severe lesions (Table 2).

The proportions of the different cardiac defects in relation to all CHD cases are shown in Fig. 2; the numbers and prevalences of the different single lesions are shown in Table 3. The most frequent lesion was the ventricular septal defect (prevalence 52.7 per 10,000 live births), of which 11.0% were classified as small and 52.8% as muscular. The most frequent severe cardiac defects were the univentricular hearts (3.0 per 10,000 live births) followed by the tetralogy of Fallot, a complete transposition of the great arteries and a double outlet right ventricle (Table 3).

Notably, the prevalence of CHD varies substantially between register studies. We compared the prevalences determined by the PAN study with those from two regional registries in Germany (Mainz Birth Registry and Saxony-Anhalt Malformation Monitoring). The lower prevalence for all CHD found in PAN was mostly related to the lower rates of mild CHD, in particular ventricular and atrial

Table 2 Numbers of institutions, numbers of CHD cases, and proportions of mild, moderate and severe CHD reported by the different groups of participating institutions

	University hospitals/departments of paediatric cardiology		General paediatric clinics with cardiologic care		Practitioners in paediatric cardiology		Total	
Numbers of institutions	34		154		72		260	
Numbers of CHD	2,761 (38.1%)		2,600 (35.9%)		1,884 (26.0%)		7,245	
Thereof:	*n*	%	*n*	%	*n*	%	*n*	%
Mild CHD	1,239	44.9	1,677	64.5	1,475	78.3	4,391	60.6
Moderate CHD	826	29.9	792	30.5	370	19.6	1,988	27.4
Severe CHD	696	25.2	131	5.0	39	2.1	866	12.0

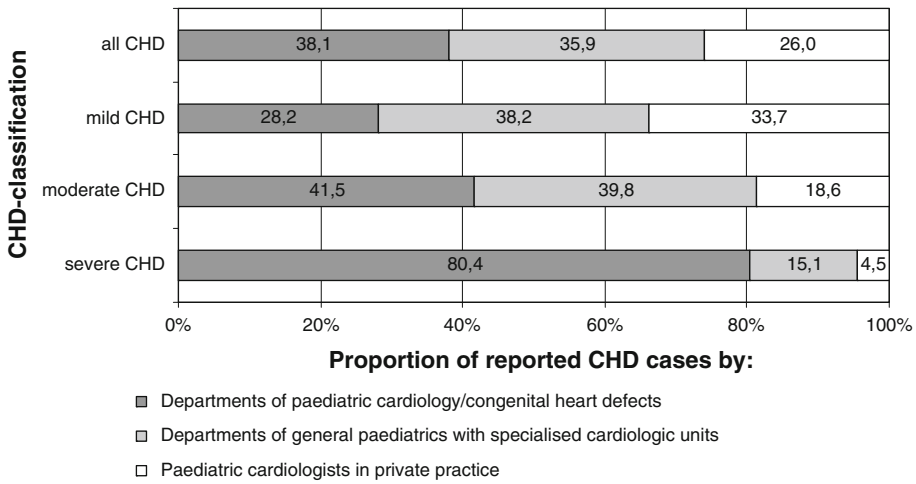

Fig. 1 Proportion of mild, moderate and severe congenital heart defects reported by the different institution groups

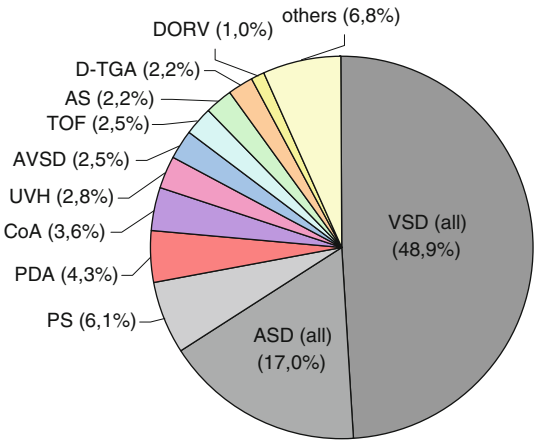

Fig. 2 Proportions of the leading congenital heart defects among all reported CHD cases. For abbreviations, see legend to Table 3

defects. The prevalences of moderate and severe cardiac defects were widely comparable in the three German registries (Table 3). By contrast, PAN produced much higher prevalences than the studies in Belgium and Croatia and the international database from EUROCAT, which displayed particularly low rates for the ventricular and atrial defects.

Prenatal CHD diagnosis

Parents' reports on prenatal diagnosis of cardiac defects were available in 4,796 live births with CHD. According to this source of information, prenatal echocardiography has been performed in 30.7% of all CHD pregnancies; cardiac defect was detected in 39.3% of them, giving an overall prenatal detection rate of CHD of 12.1%. In children with severe cardiac defects, however, a prenatal echocardiography has been performed in 53.8% with a detection rate of 77.5% (Table 4).

Discussion

It was the aim of this registry to determine the prevalence of congenital heart defects in Germany. The PAN study was based on a targeted cooperation of specialists in paediatric cardiology and supported by the infrastructure of the Competence Network for Congenital Heart Defects [7, 8]. The contribution of the different participating institutions to the spectrum of the registered cardiac lesions is reflecting the structure of paediatric cardiologic care in Germany: approximately 40% of all newborns and infants with CHD, in particular 80% of patients with severe cardiac defects, were diagnosed and included into the study by departments of paediatric cardiology/congenital heart defects. On the other hand, mild cardiac defects were enrolled in approximately 70% by departments of general paediatrics with specialised cardiologic units or by paediatric cardiologists in private practice.

The total prevalence of congenital cardiac defects determined by the PAN study was 107.6 per 10,000 live births [9]. This prevalence is lower than that presented by the Malformation Monitoring of Saxony-Anhalt and the Mainz Birth Registry, both with a longstanding experience and functioning [5, 16]. The high total prevalence in the Mainz Birth Registry may be due to the restriction to a small region with a high coverage of newborns as well as on an active diagnostic pursuit shortly after delivery with sonographic and clinical examination within the context of a newborn screening programme. Rather expectedly, this resulted in a high detection rate of ventricular septal defects in the Mainz Birth Registry and in small numbers for the more severe and rare cardiac lesions which then may result in imprecise and unstable prevalence estimates. In the Congenital Malformation Monitoring of Saxony-Anhalt the persistent foramen ovale was included as a congenital heart defect [17], which is responsible for the

Table 3 Prevalences of all and single congenital heart defects

	PAN-study		Mainz birth registry [13]	Congenital malformation monitoring Saxony-Anhalt [13]	EUROCAT total [13]	Croatia [14]	Belgium [15]
Registration period	7/2006 – 6/2007		2002 – 2006	2005 – 2007	2005 – 2007	2002 – 2007	2002
Total number of live births of the registration period	673,282		15,781	ca. 51,500	3,589,286	205,051	111,225
	Number		Prevalence per 10,000 live births				
All CHD	**7,245**	**107.6**	**161.0**	**124.9**	**71.1**	**72.2**	**82.8**
VSD (all)	3,545	52.7	101.50	42.4	33.1	25.0	27.2
VSD muscular	*1,871*	*27.8*	–	–	–	–	–
VSD small	*389*	*5.8*	–	–	–	–	–
VSD (all others)	*1,285*	*19.1*	–	–	–	–	–
ASD (all)	1,235	18.3	23.0	50.1	18.1	11.5	15.0
ASD II	*1,219*	*18.1*	–	–	–	–	*14.6*
ASD (all others)	*16*	*0.2*	–	–	–	–	*0.4*
PS	443	6.6	6.3	6.8	3.2	3.6	7.9
PDA	310	4.6	–	–	–	7.1	2.5
CoA	264	3.9	6.3	3.7	2.9	2.3	4.1
UVH (all types)	202	3.0	4.0	1.8	2.0	–	1.7
HLHS	*101*	*1.5*	*1.6*	*1.2*	*1.3*	*1.7*	*0.9*
AVSD	183	2.7	5.6	2.5	2.7	3.1	3.3
TOF	179	2.7	4.0	3.1	2.4	2.4	4.7
AS	161	2.4	–	–	–	2.4	3.2
D-TGA	156	2.3	8.7	2.9	2.7	2.4	2.6
DORV	76	1.1	–	–	–	–	1.2
PA/VSD	44	0.7	–	–	–	–	0.5
TAPVC	43	0.6	0.0	0.8	0.4	–	–
TAC	33	0.5	0.8	0.8	0.5	–	0.6
Ebstein's anomaly	27	0.4	1.6	0.0	0.3	–	0.3
PAPVC	26	0.4	–	–	–	–	–
L-TGA	25	0.4	–	–	–	–	0.3
IAA	22	0.3	–	–	–	–	–
PA/IVS	21	0.3	–	–	–	–	–
AVSD partial	18	0.3	–	–	–	–	–
Miscellaneous	223	3.3	–	–	–	–	–

Comparison of the prevalence found in the PAN study with those concurrently reported by the Mainz birth registry, the Monitoring of Congenital Malformations of Saxony-Anhalt, the EUROCAT register and national studies in Croatia and Belgium

VSD ventricular septal defect, *ASD II* atrial septal defect, secundum type, *PS* valvular pulmonary stenosis, *PDA* persistent arterial duct, *CoA* coarctation of aorta, *UVH* univentricular heart, *HLHS* hypoplastic left heart syndrome, *AVSD* atrioventricular septal defect, *ToF* tetralogy of Fallot, *AS* valvular aortic stenosis, *D-TGA* complete transposition of the great arteries, *DORV* double outlet right ventricle, *PA/VSD* pulmonary atresia with ventricular septal defect, *TAPVC* total anomalous pulmonary venous connection, *TAC* truncus arteriosus communis, *PAPVC* partial anomalous pulmonary venous connection, *L-TGA* congenitally corrected transposition of the great arteries, *IAA* interrupted aortic arch, *PA/IVS* pulmonary atresia with intact ventricular septum

obviously uncommonly high proportion of atrial septal defects in this registry. On the other side, the prevalences determined throughout Europe in the EUROCAT group as well as in the recently published national studies from Croatia and Belgium [13–15] were substantially lower than the prevalences determined in the PAN study. The rates for ventricular septal defects thereby turned out to be the decisive factor in determining the total prevalence of congenital heart defects [18, 19]. Thus, despite a passive diagnostic pursuit, the relatively high proportion of

Table 4 Prenatal echocardiography and diagnosis of CHD (according to parents' reports) within the different CHD severity groups

	All CHD	Mild CHD	Moderate CHD	Severe CHD
Numbers	4,796	2,892	1,307	586
Thereof: percentage with prenatal echocardiography (numbers)	30.7% (1,472)	25.8% (746)	31.1% (406)	53.8% (315)
Thereof: percentage with prenatal CHD diagnosis (numbers)	39.3% (579)	23.2% (173)	39.2% (159)	77.5% (244)
Percentage of overall detection	12.1%	6.0%	12.2%	41.6%

Only live births with complete data set (see text) are included

ventricular septal defects detected in the PAN study seems to reflect a broadly available, well-established and qualified diagnostic system of postnatal cardiology care in Germany.

The prenatal diagnosis of a congenital heart defect may affect both the prenatal management of the foetus as well as the peri- and postnatal treatment and prognosis of the child. The proportion of congenital heart defects diagnosed prenatally has increased in recent decades [20] depending on the level of medical care as well as on the type of the cardiac lesion [21]. Investigations of the Eurofetus study, performed from 1990 to 1993 in 61 European birth centres, estimated a prenatally diagnosed proportion of haemodynamically relevant cardiac defects of 38.8% [22]. In the Euroscan study from 20 European registries, carried out from 1996 to 1998, the rate of CHD diagnosed in foetal life amounted to 25% [21]. These data, however, included stillbirths and abortions, the proportion of which may be high in particular cardiac defects [23]. In the PAN study which included live births only, the proportion of prenatally detected severe cardiac defects after echocardiography was 77.5%, giving an overall detection rate of 41.7% within this severity group.

In summary, the PAN study data confirm that the CHD prevalence among live births in Germany is comparable to that of other European countries. In particular, the frequencies of various severe cardiac defects are very similar. Self reports of parents of newborns with CHD seem to indicate that the prenatal detection, in particular of severe cardiac defects leaves diagnostic room for improvement. The PAN study created a large and valid database that may be used to perform prospective studies on various cardiac defects.

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Conflict of interest The authors declare that they have no conflict of interest.

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