Spectrum of congenital heart defects in Croatia

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Abstract:

The aim of our study was to investigate the incidence of congenital defects in children born in Croatia during a period of 5 years, its association with extracardiac malformations, its treatment and outcome. Medical information about the patients was obtained from 14 paediatric cardiology centres that cover the whole country. Diagnosis was made by clinical findings, electrocardiography, chest X-ray, echocardiography, catheterisation or autopsy. Between October 1, 2002 and October 1, 2007, there were 205 051 live births in Croatia, 1480 of which were patients diagnosed with congenital heart disease, accounting for 0.72% of the live-born children. The distribution was made up of 34.6% children with ventricular septal defect, 15.9% with atrial septal defect, 9.8% with patency of arterial duct, 4.9% pulmonary valvar stenosis, 3.3% tetralogy of Fallot, 3.3% transposed great arteries, 3.3% aortic stenosis, 3.2% aortic coarctation, 4.3% atrioventricular septal defect and common atrioventricular orifice, 2.3% hypoplastic left heart syndrome and 8.3% other severe defects. The average age in the time of diagnoses is 70.41 days (SD 188.13), with low average time of diagnoses of severe heart defects, 9.6 days, SD 32.52. Among patients, 14.5% had chromosomal defects, syndromes and/or other congenital major anomalies. During the study, 57 patients died because of cardiac anomalies or other related problems, 24 who died were operated.

Conclusion: The rates of specific cardiac defects and association with extracardiac malformations are generally comparable with those reported in similar studies. In spite of all problems, mortality rate of 3.85% is low but could be improved.

Keywords: congenital heart disease, prevalence, extracardiac anomalies, treatment

Introduction

Congenital heart disease are amongst the most frequent of all congenital anomalies [20]. They constitute a major cause of infant mortality and morbidity in childhood and in later adult life [25]. On the other hand, the number of adults with some form of congenital heart disease is growing rapidly as therapy becomes increasingly effective [23]. Quantification of birth prevalence and spectrum of malformations, along with analysis of past trends of management, allow for future planning of health services [7]. Congenital cardiac malformations are frequently associated with other non-cardiac congenital malformations and chromosomal anomalies. Conversely, syndromic infants constitute a substantial proportion of all children with congenital heart disease [6,11].

There is a wide variation between reports on prevalence of congenital heart disease and incidence of associated extracardiac malformations. Recent population-based epidemiological studies on congenital heart disease have indicated a prevalence ranging from 4 to 14 per 1000 live births. The reported incidence of associated extracardiac anomalies ranges from 7% to 45% [27-29].

Here, we formed a study which includes all children with congenital heart disease recognised and treated in 14 paediatric cardiology centres in Croatia, born between October 2002 and October 2007.

The aim of this study is to describe the prevalence of congenital heart disease in live births and its association with other, non-cardiac congenital anomalies in Croatia. This study also compares its results with studies done elsewhere, and puts forward an explanation for wide variations found between studies.

Materials and methods

Congenital heart disease was defined as „a gross structural abnormality of the heart or intrathoracic great vessels that is actually not potentially of functional significance [26]. We excluded functionless abnormalities of great veins, but included congenital arrhythmias and cardiomyopathies. We excluded patent ductus arteriosus as a single defect in preterm infant before three months because it is more often based on abnormal physiology rather than on a structural abnormality [13.21,22], we excluded patent foramen ovale with the tiny left-to-right shunt in the first year of life because of high rate of spontaneous closure [13,14], we excluded isolated partial anomalous pulmonary venous connection because it is rarely reported in reports of the incidence of congenital heart disease[13], mild pulmonic stenosis if the systolic gradient across the valve is under 20 mmHg if showed no progression with time. We also excluded bicuspid aortic valve and mitral valve prolapse and mitral incompetence as isolated congenital lesion because they are not usually reported in the other studies of incidence in this pediatric population [13,14]. For the purpose of this study we excluded abnormalities of coronary arteries, pericardium and AV fistule, aortic arch branch abnormality and vascular ring. We included aortic stenosis if a flow velocity in the ascending aorta exceeded 2 m/s. Information about the patients was obtained from medical records from 14 paediatric cardiology centres that cover the whole country. Diagnosis of congenital heart disease was made by clinical findings, electrocardiography, chest X-ray, echocardiography, catheterisation or autopsy. All cases of congenital heart disease were coded according to European Paediatric Cardiac Code (EPCC) [8].

When a patient had more than one lesion, we considered the defect that required treatment, or the one that caused the greatest hemodynamic effect, to be the main malformation.

For the purpose of this study, we define ‘‘severe’’ congenital heart defects as the following 12 conditions: hypoplastic left heart syndrome (HLHS), single ventricle, tricuspid atresia, common arterial trunk, interrupted aortic arch, pulmonary atresia without ventricular septal defect, complete transposition of great arteries (TGA),

double outlet right ventricle (DORV), atrioventricular septal defects and common AV junction (AVSD), totally anomalous pulmonary venous connection (TAPVR), tetralogy of Fallot, and Epstein's malformation of tricuspid valve [27].

For the purpose of this study, a syndrome was defined as „a recognised pattern of congenital abnormalities whose unique combination of features sets it apart from other patterns [18]. Syndromes were subdivided into recognised chromosomal anomalies and recognised non-chromosomal syndromes or sequences. A malformation was defined as „a permanent change produced by intrinsic abnormality of development in a body structure during prenatal life"[18]. Malformations were subdivided into major and minor malformations following guidelines set out by EUROCAT (European Registers of Congenital Anomalies and Twins) [1]. Only major malformations were included.. Chromosomal analyses were made by using high-resolution banding and fluorescence in situ hybridization.

The study was set up according to the EUROCAT registries principles to cover congenital heart disease in case of late fetal deaths folloving prenatal disanoses of cardiac disesa, livebirths and stillbirths [1,20]. Early fetal deaths or spontaneus abortions are not covered by the study.

All children with congenital heart disease born to Croatian residents between October 1st 2002 and October 1st 2007 were included. Information on patients born during five years study and with the diagnoses of congenital heart defect of 745 through 747 according to the ninth revision, Q20 through Q28 of the tenth revision of the International Classification of Disease, and from 01.01.01 through 09.29.31 according to the European Paediatric Cardiac Code – The Short List [8], was obtained during the period of study, from medical records from 14 paediatric cardiology centres that cover the whole country. The patients and their diagnoses were organised as age cohorts according to the age of birth, with patients and their diagnoses belonging to the year of birth, whenever diagnoses was made.

We also obtained access to autopsy reports and death certificates of those patients who had died. All pregnant women in Croatia are offered prenatal ultrasonic screening in the nineteenth week of gestation, and they are referred for specialized fetal echocardiography if an abnormality is suspected from the four chamber view obtained at that visit, or if there are other fetal or maternal factors for increased risk. We collected the data obtaining approval for the study from the ethical committee of the University Hospital of Croatia A resident was considered to be anyone who had lived in Croatia for one year or more.

Statistics

For relevant findings, we primarily used descriptive statistics. Ninety-five percent confidence intervals for rates were calculated using binomial distribution. Means and standard deviations were calculated for continuous variables. Significance of difference in congenital heart defects distribution by gender was tested by multiple logistic regression. To measure association for categorical variables Pearson's Chi square test was used. Official Croatian publications were used to obtain total live birth from October 1st 2002 to October 1st 2007. All data were collected in File Maker pro 5, and then exported to the Microsoft Office Excel. For statistical analysis we used Statistical Package for Social Sciences 13.0 (SPSS Inc., Chicago, IL, USA).

Results:

From October 1st 2002 to October 1st 2007, there were 205 051 live births. Congenital heart disease had been diagnosed in 1480 children, 700 girls (47%) and 780 boys (53%), giving a prevalence of 0.72%. The yearly incidence varied from 8.14 ‰ of live-born children in 2002 to 6.59‰ in 2007 (Table 1).

Ventricular septal defect was the most common heart defect, diagnosed in 513 children, accounting one third of the total number (34.6%). Atrial septal defect was diagnosed in 235 children (15.9%), 145 had patency of arterial duct (9.8%), 73 pulmonary valvar stenosis (4.9%), 49 tetralogy of Fallot (3.3%), 49 transposed great arteries (3.3%), 49 aortic stenosis (3.3%), 47 aortic coarctation (3.2%), 64 had atrioventricular septal defect and common atrioventricular orifice (4.3%), 34 had hypoplastic left heart syndrome (2.3%), 26 with cardiomyopathy (1.8%), 73 rhythm disturbances (4.9%), and 123 (8.3%) with other severe defects (excluding hypoplastic left heart syndrome, atrioventricular septal defects, tetralogy of Fallot and transposition of great arteries). Table 2. lists the distribution of the specific lesions and gender of the patients. For coarctation of aorta (OR 2.17, CI 1.15-4.09, $p<0.05$) and aortic stenosis (OR 1.89, CI 1.03-3.47, $p<0.05$) the ratio was significantly increased in favour of males, and for the atrial septal defect (OR 1.32, CI 1.0-1.75, $p=0.05$) the ratio was significantly increased in favour of females.

Table 3 shows prevalence of defects during the study period with significantly increasing trend ($p<0.05$) observed only for coarctation of aorta. For the purpose of reduction of potential bias by the number of patients who could be diagnosed later in live, years 2006 and 2007 were excluded from the study of changing prevalence of specific defects, with calculated statistical significance as a deviation from the rectangular distribution only for the period 2003-2005.

The average age in the time of diagnoses is 70.41 days (SD 188.13), with median age of 4 days (Q1-Q3: 1-37), with average time of diagnoses of severe heart defects, 9.6 days (SD 32.52) and median age of 1 day (Q1-Q3: 0-4). Prenatal diagnoses was made in 3% of all children. No case of late fetal death or abortion due to severe cardiac disease were documented during the study.

Of all 1480 patients with congenital cardiac malformations, 215 (14.5%) had associated non cardiac anomalies (Table 4). Of these, 50.2% had chromosomal defects, 14.4 % syndromes and 35.3% other major congenital anomalies (Table 5). Down syndrome accounted for 89.8% of all chromosomal anomalies, with a birth prevalence of Down syndrome associated with cardiac anomaly of about 0.47/1000 live births. The most common non-chromosomal syndrome was diGeorge syndrome with a proportion of 35.5%, followed by Williams-Beuren, Noonan, Ivemark, Alagille and other (Table 5). Syndromes are divided according to the most frequent genetic basis of development [29,31]. The most common major non–cardiac malformations were gastrointestinal anomalies.

The most common cardiac anomaly associated with Down syndrome is atrioventricular septal defect, with a percentage of 41.2 %.

Of the 1480 children born during the period of study, 430 needed an operation. Among 553 cardiac surgeries performed, 202 were done in two institutions in Croatia and 351 were done in 7 institutions abroad. Case complexity was analysed using both the Aristotle Basic Complexity Score and the Risk Adjustment for Congenital Heart Surgery methodology, The methodological details of each system are described in the respective references [17,19] The average complexity for cardiac procedures done in Croatia according to the Aristotle Basic Complexity Score (ABC score) was 6.1 and the average complexity for procedures done abroad according to the Aristotle Basic Score was 9.2 with statistically significant difference ($p<0.001$). The average complexity for cardiac procedures done in Croatia according to the RACHS-1 methodology was 2.2 and the average for procedures done abroad according to the RACHS-1 methodology was 3.1 with statistically significant difference ($p<0.001$). Among 202 procedures done in Croatia, death occurred after 10 procedures

with mortality rate at disharge of 5 %, on the other hand, among 351 procedures done abroad death occurred after 14 procedures with calculated mortality rate at discharge of 4%. During the study 57 children died, 24 children who died were operated, other died because of a cardiac anomaly or other related problems. Mortality related to congenital cardiac defects was thus 3.85 %.

Discussion:

Early studies of the incidence of congenital heart disease produced low incidence of about 4 per 1000 live births, but this figure has been rising steadily until recently when incidences of 12 to 14/1000 live births, or higher, have been reported in the literature [2,3,6,7,10,13,14, 23,28,33]. Older studies were hampered by lack of non-invasive diagnostic technique, with mild lesions diagnosed on clinical grounds only, some mild lesions may not have been included if spontaneous resolution occurred on follow-up with disappearance of clinical signs. On the other hand, improving diagnostic capability with colour Doppler echocardiography has allowed more confident diagnoses of minor lesions and increased the number of diagnoses of small degrees of aortic stenosis, pulmonary stenosis and atrial septal defects. There are also, more reasons for a low incidence, a few studies were restricted to infancy and so missed some patient who present later in life, some studies bases their data on the results of foetal echocardiography in populations, these studies will not detect patients with a small ventricular or atrial septal defects, an abnormal patent ductus arteriosus or many with coarctation of aorta. In certain communities the increasing use of foetal echocardiography also leads to abortion and can substantially reduce the incidence of specific lesions or the total incidence. By contrast, high incidences were found in those studies that examined all or almost all newborns, because they detected large numbers of small ventricular septal defects, foramen ovale apertum, tiny arterial ducts or other trivial lesions. If studies includes bicuspid aortic valves, isolated lobar anomalous pulmonary veins connection, so called pulmonary or aortal stenosis with gradient across the valve less than 20 mmHg, the prevalence should be increased by 20/1000 live births.

Actual prevalence of congenital heart disease for the five years period in Croatia is 7.2 per 1000 live births and is comparable with similar studies. The rates of specific cardiac defects in our study are generally comparable with those reported from the Baltimore-Washington study by Ferencz et al and from EUROCAT registry [1,6,7]. As expected, the most frequent diagnosis was ventricular septal defect, followed by atrial septal defect, patent arterial duct, pulmonary stenosis, and atrioventricular septal defects. These five diagnoses accounted for more than 60% of all cases.

Compared with Baltimore-Washington study, the rate for patent arterial duct was slightly greater, the possible reason might be excluding patent ductus arteriosus as a single defect in preterm infant before three months, but inclusion of tiny patent arterial duct with can be incidental finding in hemodynamically normal heart. Some studies based on echocardiography have shown that in the term infant the ductus arteriosus is almost always closed by four to seven days after birth [21,22,30], studies done a few days after birth will have recorded a larger number with a „so called“ patent arterial duct. The rate for atrioventricular septal defect is 4.3%, mean percentage with regards to reports from other registries with rates from 1.34% to 7.4% [6,33]. Incidence of atrioventricular septal defects varies in accordance with the age of the involved mothers due to fact that the Down syndrome is more common in mothers who are more than 34 years old, and atrioventricular septal defects are very frequent in those with Down syndrome [5,13]. Because termination of pregnancy is performed if trisomy 21 is discovered, the incidence of atrioventricular septal defects is likely to decrease [13,23]. In Croatia,

the official religion is Roman-Catholic and termination of pregnancy is illegal, so prenatal diagnoses and growing proportion of pregnant women in which foetal echocardiography was done, have no important influence to prevalence of congenital heart defects. Early fetal deaths or spontaneous abortions, according to the literature, are not at present covered by registration system, although they may be of great interest for the study of congenital malformations [20]. Due to the fact that spontaneous abortions and illegal abortions are not systematically reported and because of potential proportion of illegal abortions because of prenatal diagnoses of cardiac heart disease, estimated number of unknown cases could remain high [20] .

The total rates for the 12 severe defects selected did not vary significantly between the studies [27,28]. We counted rhythm disturbances in our current analysis, mostly paroxysmal supraventricular tachycardia and neonatal bradycardia together with congenital atrioventricular block, because of recognized proportion of 4.9% of all congenital heart diseases in our study.

During the five years of study, prevalence of congenital defect as well as the prevalence of specific diagnoses changed in total number. If we look at the prevalence throughout the study, it is possible that prevalence is higher than in 2006 and 2007 due to fact that some children with congenital heart disease born in last years of study have not yet been diagnosed and the number may still rise. The prevalence might also rise because of the fact that some children born in 2007 years and followed up as foramen ovale will be included in the number of children with congenital heart disease as atrial septal defects at the age of 12 months. Increasing trend of coarctation of aorta might be due to continuous improving of early diagnoses.

For all the cardiac defects, the average sex ratio was 1/0.9. The proportion of males and females is similar to reports from other studies [6,27,28]. There were significantly high sex ratios in the groups with left sided opstruction anomalies, aortic stenosis and coarctation of the aorta.

The average time of diagnoses shows that most patients with congenital heart disease are now diagnosed during infant period, with low average time of diagnoses of severe heart defects, near period of discharge from hospital. Potential factor leading to early detection of congenital heart disease could be due to the fact that Croatia is a small country, access to medical specialist is good, detection and follow up of patients is fairly centralised and provided in tertiary medical centres. For these reasons, we think that Croatian population can provide accurate information on the incidence of congenital heart disease, as well as the age of diagnoses.

Patients with cardiac defects often have other congenital anomalies, chromosomal defects and syndromes. The proportion of comorbidity is between 4-45% depending on many factors [4,6,9-11,20,24,27,28,33]. The prevalence of congenital heart disease associated with chromosomal anomalies depends on the maternal age profile in the country, the proportion of chromosomal cases diagnosed prenatally followed by termination of pregnancy. The percentage of chromosomal defects and other anomalies depends on methodology, such as differing inclusion criteria for both congenital heart disease and syndromes and malformation [13]. The increased number of minor defects is diluting the proportion of other anomalies [33].. Distribution of congenital heart disease associated with non-cardiac malformation is higher in autopsied children reaching percentage of 45 % [12,32]. Here we find 215 children (14.5%) with recognised non-cardiac anomalies. Of these, 50.2% had chromosomal defects, 14.4 % syndromes and 35.3% other congenital major anomalies. Heritable syndromes can also be grouped by genetic abnormalities on chromosomal abnormalities, microdeletions, and gene mutations or by developmental similarities on group associated with situs and looping defects, syndromes with cardiofacial

(branchial arch) abnormalities, VACTERL, syndromes with intracardial flow disturbances, sy Noonan, connective tissue disorders, metabolic genetic syndromes.

Delineation of association by developmental events may clarify the etiology of congenital heart disease. Well-designed family studies could identify individuals at increased risk and provide a scientific basis for genetic counselling of at-risk families [29].

Surgery was performed on 29% of all infants with congenital heart disease. Out of 553 cardiac surgeries performed, 202 were done in Croatia and 351 were done abroad. Among children who were operated, during the study, 24 died, giving the all-cause mortality in patients who underwent cardiac surgery of 5.6 %. As it could be seen after stratification for complexity, majority of complex operations, is still performed in medical centers abroad. Of all 1480 children with congenital heart disease, during the period of study 57 died (3.85%) because of heart or other related reasons. Although mortality rate is near reports from other more developed centers [15], it is not satisfying, especially having in mind that majority of complex surgery procedures is still perforfmed in centers abroad Improvements in the medical care of patients with congenital heart disease, including early diagnoses, diagnostic procedures, neonatal care, intensive care units was not followed by advance in surgical development. Further analysis should reveal potential problems and additional improvement in the care of children with congenital heart disease will further diminish the mortality of this common group of congenital disorders [14].

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Tables

Table 1. Prevalence of congenital heart disease in Croatia from October 1st 2002 to October 1st 2007

Time period	Live-born children	Children with CHD[a]	Prevalence (per 1000 live-born)
1.10-31.12.2002	9704	79	8.14
2003	39 668	314	7.92
2004	40 307	289	7.17
2005	42 492	314	7.39
2006	41 446	277	6.68
1.1-1.10.2007	31 434	207	6.59
1.10.2002-1.10.2007	205051	1480	0.72

[a] congenital heart disease

Table 2. Distribution of congenital heart defects and the ratio of males and females in children born in Croatia from 1st 2002 to October 1st 2007

Congenital heart disease	Number	(%)	Male/Female
Ventricular septal defect	513	(34,6)	1/0.97
Atrial septal defect	235	(15.9)	1/1.14
Patent arterial duct	145	(9.8)	1/1.16
Pulmonary valvar stenosis	73	(4.9)	1/0.97
Tetralogy of Fallot	49	(3.3)	1/0.78
Transposed great arteries	49	(3.3)	1/0.58
Aortic stenosis	49	(3.3)	1/0.48
Coarctation	47	(3.2)	1/0.42
Atrioventricular septal defect	64	(4.3)	1/1.2
Hypoplastic left heart syndrome	34	(2.3)	1/0.62
Cardiomyopathy	26	(1.8)	1/0.86
Rhythm disturbances	73	(4.9)	1/0.59
Severe heart defect (excluding TF[a], HLHS[b], AVSD[c], TGA[d])	123	(8.3)	1/0.73
Total	1480	(100,0)	1/0.90

[a] tetralogy of Fallot, [b] hypoplastic left heart syndrome, [c] atrioventricular septal defect and common AV junction, [d] transposition of great arteries

Table 3. Prevalence of defects during the period of study

N		Year of birth 2002		2003		2004		2005		2006		2007		p*
		N[a]	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	
513	VSD[b]	30	(38)	112	(35.7)	97	(33.6)	102	(32.5)	92	(33.2)	80	(38.6)	0.570
145	PDA[c]	7	(8.9)	34	(10.8)	36	(12.5)	30	(9.6)	24	(8.7)	14	(6.8)	0.756
235	ASD[d]	5	(6.3)	50	(15.9)	54	(18.7)	48	(15.3)	46	(16.6)	32	(15.5)	0.832
73	PS[e]	6	(7.6)	15	(4.8)	10	(3.5)	17	(5.4)	12	(4.3)	13	(6.3)	0.598
49	Tetralogy of Fallot	3	(3.8)	7	(2.2)	10	(3.5)	16	(5.1)	7	(2.5)	6	(2.9)	0.148
49	TGA[f]	7	(8.9)	12	(3.8)	10	(3.5)	8	(2.6)	7	(2.5)	5	(2.4)	0.670
49	Aortic stenosis	5	(6.3)	10	(3.2)	11	(3.8)	7	(2.2)	6	(2.2)	10	(4.8)	0.629
47	Coarctation	1	(1.3)	3	(1.3)	8	(2.8)	18	(5.7)	14	(5.1)	3	(1.4)	0.002
64	AVSD[g]	1	(1.3)	19	(6.1)	13	(4.5)	15	(4.8)	12	(4.3)	4	(1.9)	0.551
34	HLHS[h]	0	(0.0)	4	(1.3)	7	(2.4)	10	(3.2)	4	(1.4)	9	(4.3)	0.276
26	Cardiomyopathy	3	(3.8)	6	(1.9)	4	(1.4)	6	(1.9)	4	(1.4)	3	(1.4)	0.779
73	Rhythm disturbances	6	(7.6)	16	(5.1)	8	(2.8)	18	(5.7)	16	(5.8)	9	(4.3)	0.135
123	Severe heart defect	5	(6.3)	26	(8.3)	21	(7.3)	19	(6.1)	33	(11.9)	19	(9.2)	0.554
1480	Total	79	(100)	314	(100)	289	(100)	314	(100)	277	(100)	207	100	0.506

*statistical significance: deviation from the rectangular distribution for the period 2003-2005, [a]number of patients, [b]ventricular septal defects, [c]patent arterial duct, [d]atrial septal defect, [e]pulmonary stenosis, [f]tetralogy of Fallot, [g]atrioventricular septal defect and common AV junction. [h]hypoplastic left heart syndrome

Table 4. Number of infants with identified extracardiac anomaly according to cardiac defect type

Congenital heart defect	Extracardiac anomaly Yes	No	Percentage in number of defects
Ventricular septal defect	40	473	7.8
Atrial septal defect	29	206	12.3
Patent arterial duct	13	132	9
Pulmonary valvar stenosis	6	67	8.2
Tetralogy of Fallot	10	39	20.4
Transposed great arteries	6	43	12.2
Aortic stenosis	4	45	8.2
Coarctation	9	38	19.1
Atrioventricular septal defect	43	21	67
Hypoplastic left heart syndrome	6	28	17.6
Cardiomyopathy	4	22	15.4
Rhythm disturbances	4	69	5.5
Severe heart defects (excluding TGA[a], TF[b], AVSD[c], HLHS[d])	41	82	33.3
Total	215	1265	14.5

[a] transposition of great arteries, [b]tetralogy of Fallot, [c] atrioventricular septal defect and common AV junction, [d]hypoplastic left heart syndrome

Table 5. Distribution of congenital heart defects accompanied by syndromes, chromosomal anomalies and other major congenital anomalies.

A. Chromosomal anomaly	Percentage (%)
Down syndrome	45.1
Turner syndrome	2.8
Edwards syndrome	1.4
Patau syndrome	0.9
Total	50.2
B. Syndrome	
Microdeletions	
Di George	5.1
Williams Beuren	2,8
Conotruncal face sy	0.9
Gene mutations	
Noonan	1.4
Ivemark	1.4
Allagile	0.5
Ellis van Creveld	0.5
Jeune	0.5
Klippel-Trenaunay-Weber	0.5
VACTERL	0.9
Total	14.4
C. Other congenital defects	
Gastrointestinal tract	8.4
Cleft palate and/or lip	5.6
Anomalies of head and face	5.6
Neurological and developmental defects	4.7
Genito-urinary tract	4.2
Multiple congenital defects	4.2
Anomalies of other thoracic organs	1.4
Haematological disease	1.4
Total of other congenital defects	35.3

Total	100