Prevalence and distribution of children with congenital heart diseases in the central Anatolian region, Turkey

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SUMMARY: Başpınar O, Karaaslan S, Oran B, Baysal T, Elmacı AM, Yorulmaz A. Prevalence and distribution of children with congenital heart diseases in the central Anatolian region, Turkey. Turk J Pediatr 2006; 48: 237-243.

Congenital heart diseases (CHD) are the most frequent malformation at birth. The aims of this study were to assess the prevalence of congenital heart disease, their different types, and the detection rate among children in the central Anatolian region in Turkey.

The study was conducted during an eight-year period (March 1995-December 2002). The prevalence of CHD in a large tertiary care hospital in the central Anatolian region in Turkey was studied. The diagnosis of a structural defect was based on echocardiographic study. The following age groups were considered: neonates, infants and toddlers, preschool children, schoolchildren, and adolescents.

In the study period, 1,693 children were found to have CHD; 1,253 patients were neonates and infants. Total prevalence of CHD over the study period was 7.77 per 1,000 live-born. The prevalence increased from 6.35 to 9.65 per 1,000 live births between 1995 and 2002 ($p<0.05$). The average age at diagnosis was 2.2±3.64 years (1 day to 18 years, median 5 months). There were 863 (51%) boys and 830 (49%) girls, with a male/female ratio of 1:1. Isolated ventricular septal defect (32.6%) was the most frequent acyanotic anomaly, and tetralogy of Fallot (5.8%) was the most frequent cyanotic anomaly. The commonest non-cardiac anomalies with CHD were musculoskeletal anomalies. Down syndrome was determined in 83 patients (78.3%) from all syndromic CHD cases.

Congenital heart disease is a very significant health problem. It requires urgent measures in terms of organization of early diagnosis and proper management. The prevalence rate is comparable to that of similar developed countries. Increasing incidence of CHD might be attributed to more diagnoses with new technologic development or it may indicate a real increase in the defects.

***Key words**: congenital heart disease, echocardiography, prevalence.*

Congenital heart diseases (CHD) comprise the most common group of congenital malformations. Despite recent developments in interventional and surgical techniques, heart disease in children continues to be an important cause of morbidity and mortality[1]. Population-based epidemiological studies on CHD have indicated a prevalence ranging from 4.6 to 12.2 per 1,000 live births[2-6]. Most of the studies were documented data from the 1970s and 1980s. The current study was undertaken to evaluate the spread of CHD in the central Anatolian region in Turkey. There has been no population-based study on CHD in Turkey. The worldwide incidence of CHD is known to the extent that ethnic occurrence can be reasonably predicted, but variations occur and may provide clues to etiology[7].

Konya is a central-Anatolian region with a total population of around 1,827,113 and a birth rate of around 12.04‰ deliveries in 2002[8]. This study aimed at establishing the

frequency and prevalence of CHD in children referred to a tertiary care center of pediatric cardiology.

Material and Methods

Definitions

Congenital heart diseases were defined as a structural abnormality of the heart or intrathoracic great vessels that is actually or potentially of functional significance[1]. The classification was based on sequential analysis of the heart performed on the echocardiogram, following nomenclature of the European Pediatric Cardiac Code[9]. The following conditions were excluded: cardiac arrhythmias, patent ductus arteriosus in premature newborns and before one month of age in newborns, bicuspid aortic valve, mitral valve prolapsus, mirror-image dextrocardia, patent foramen ovale, acquired heart disease, cardiac tumors and thrombus, persistent left superior vena cava, right aortic arch, cardiomyopathy of infants of diabetic mothers and other cardiomyopathies. Complex CHD were classified as tricuspid atresia, truncus arterious, pulmonary atresia and severe hypoplasia, heterotaxy syndromes, common atrium, hypoplastic left-heart syndromes, single ventricle and/or double inlet ventricle, corrected transposition of the great arteries, dextrocardia with CHD, and severe Ebstein anomaly.

Ventricular septal defects were classified regarding localization of defect - perimembranous (inlet, outlet, and trabecular) and muscular defects. Isolated ventricular septal defect was defined if there was only one defect. If another defect was present like atrial septal defect, patent ductus arteriosus, pulmonary stenosis, aortic stenosis, or coarctation of the aorta, simple CHD and ventricular septal defect was defined. If tetralogy of Fallot, transposition of the great arteries, atrioventricular septal defect, double outlet right ventricle, double aortic arch, interrupted aortic arch, or pulmonary vascular sling was present, complex CHD combined with ventricular septal defect was defined.

The following age groups were considered: newborns (1-30 days), infant and toddler (1 month to 2 years), preschool children (2 to 6 years), schoolchildren (6 to 12 years), and adolescents (>12 years).

Patients and Population

All cases of CHD that were diagnosed by echocardiography in the Meram Medical Faculty Hospital during the period March 1995-December 2002 and were residing in Konya were included. During the study period, 10,941 patients with different problems were seen at our unit. All known cases of CHD were entered retrospectively from lists of patients seen at the center, with their pediatric echocardiogram reports.

Each child was given general and cardiovascular examinations by a pediatric cardiologist. Any child showing an abnormal heart condition such as central cyanosis, cardiac murmur, cardiomegaly, or arrhythmia was given a 12-lead electrocardiogram and chest X-ray, and complete echocardiographic examinations.

Echocardiography examination was conducted using M-mode, two-dimensional and color, pulse and continuous wave Doppler echocardiogram. Two-dimensional echocardiographic pictures were recorded in standard parasternal long-axis, short-axis, apical four chamber, subcostal and suprasternal views. The presence and severity of any cardiac defect was analyzed as per recommendations of the American Society of Echocardiography[10]. Cardiac catheterization and invasive procedures were performed in some patients.

Data regarding estimated population, live births rate and pediatric populations were obtained from the official regional bureau[8].

Statistics

Exploratory data analysis was performed using descriptive measures. All mean ages reported are mean ages calculated at first examination. Data are expressed as mean ± SD. Prevalence rates were calculated. The population at risk in the study was obtained from the records of the official regional bureau[8]. The Statistical Package for Social Sciences 11.0 (SPSS, Inc., Chicago, IL, USA) and Medcalc version 7.3.0.1 for Windows were used for analysis. The two-tailed chi-square test (χ^2) was used for detecting differences among the yearly prevalence rates. A p value of <0.05 was considered significant.

Results

A total of 10,941 children (aged 1 day to 18 years) attended the Pediatric Cardiology clinic during the eight-year study period. A

total of 1,693 patients with CHD meeting inclusion criteria were studied. There were 863 males (51%) and 830 females (49%) (M/F ratio of 1:1), with a mean age of 2.2±3.64 years (median 5 months) and body weight of 9.3±9.6 kg (1.3 to 7.7 kg). The mean follow-up period was 20.9±22.9 months (1 month-13.8 years, median 12 months), and 969 patients (57.2%) could be followed.

The most frequent diagnosis made was isolated ventricular septal defect (553 patients) representing 32.6% of the total cardiac anomalies. There were 279 males and 274 females (M/F, 1:1), mean age 22.38±39.94 months (median 3.5 months, 1 day to 16 years), and mean body weight 8.62±8.67 kg (median 5, 1.3 to 52 k). The next most frequent diseases were patent ductus arteriosus in 270 patients (15.9%), isolated atrial septal defect in 222 (13.1%), isolated pulmonary stenosis in 134 (7.9%), and tetralogy of Fallot in 99 (5.8%), followed by others. The relative frequency and sex difference of the defects are shown in Table I.

defects in 189 children were associated with atrial septal defect in 101 patients, patent ductus arteriosus in 60, pulmonary stenosis in 52, and coarctation of the aorta in 17.

Excluding complex CHD patients, ventricular septal defects were small in 450 (60.6%), moderate in 207, and big in 85. Multiple defects were present in 41 patients (7.4%). Perimembranous defects were encountered in 501 patients (outlet in 359, inlet 115, trabecular 56) and muscular in 256 patients. Spontaneous closure was documented in 68 patients (8.7%) at a mean of 15.2 months and occurred most frequently in muscular defects (95.5%).

Aortic stenoses, coarctation of the aorta and hypoplastic left-heart syndrome were more common among boys. Tricuspid and pulmonary atresia had a male predominance. Patent ductus arteriosus, pulmonary stenosis, and atrial septal defect occurred more frequently in girls, except in atrioventricular septal defect (Table I).

The ages at diagnosis were different, with 507/1693 (30%) studied in the neonatal period (Group I), 746 (44%) in infant and toddler

Table I. Relative Frequency of Some of the Congenital Heart Diseases and Sex Difference

Heart disease	n	%	boys	girls	M/F
Isolated ventricular septal defect	553	32.6	279	274	1:1
Patent ductus arteriosus	270	15.9	127	143	1:1.1
Isolated atrial septal defect	222	13.1	90	132	1:1.4
Simple CHD* and ventricular septal defect	189	11.1	97	92	1:1
Isolated pulmonary valve stenosis	134	7.9	64	70	1:1.1
Tetralogy of Fallot	99	5.8	59	40	1.4:1
Coarctation of the aorta	82	4.8	52	30	1.7:1
Atrioventricular septal defect	62	3.6	32	30	1:1
Isolated aortic valve stenosis	77	4.5	55	22	2.5:1
Transposition of the great arteries	52	3.0	34	18	1.8:1
Dextrocardia (situs solitus 65.5%, inversus 27.6%, ambiguous 6.9%)	29	1.7	14	15	1:1
Double outlet right ventricle	18	1.0	14	10	1.4:1
Pulmonary atresia or severe pulmonary hypoplasia	16	0.9	9	7	1.2:1
Hypoplastic left heart syndrome and/or aorta-mitral hypoplasia	15	0.8	10	5	2:1
Tricuspid atresia	13	0.7	8	5	1.6:1
Single ventricle and/or double inlet left-right ventricle	12	0.7	2	10	1:5
Common atrium	10	0.5	3	7	1:2.3
Truncus arteriosus	8	0.4	2	6	1:3
Heterotaxy syndromes	5	0.3	4	1	4:1
Corrected transposition of the great arteries	4	0.2	3	1	3:1
Ebstein anomaly	3	0.1	1	2	1:2

Simple CHD*: Ventricular septal defect ± atrial septal defect ± pulmonary stenosis ± aortic stenosis ± patent ductus arteriosus ± coarctation of the aorta.

One thousand and two patients had ventricular septal defect-526 male, 476 female (M/F, 1.1:1), mean age 19.64±38.01 months (median 3), mean weight 7.94±8.38 kg (median 4.8, 1.3 to 62). Simple CHD and ventricular septal

period (Group II), 204 (12%) in preschool age (Group III), 187 (11%) in school-aged children (Group IV), and 49 (3%) in adolescents (Group V). Distribution of the various cardiac anomalies and age at diagnosis are given in Table II and Fig. 1.

Table II. Congenital Heart Diseases and Age at Diagnosis

Patient characteristics	Group I	Group II	Group III	Group IV	Group V	Total
Patient number (%)	507 (30)	746 (44)	204 (12)	187 (11)	49 (3)	1693
Boy/girl (M/F)	254/253 (1:1)	356/390 (1:1.1)	115/89 (1.3:1)	103/84 (1.2:1)	35/14 (2.5:1)	863/830 (1:1)
Isolated ventricular septal defect (%)	182 (32.9)	248 (44.8)	59 (10.7)	53 (9.6)	11 (2)	553
Isolated atrial septal defect (%)	49 (22.1)	111 (50)	24 (10.8)	32 (14.4)	6 (2.7)	222
Isolated patent ductus arteriosus (%)	29 (25.2)	51 (44.3)	18 (15.7)	12 (10.4)	5 (4.3)	115
Isolated pulmonary stenosis (%)	12 (9)	64 (47.7)	22 (16.4)	32 (23.9)	4 (3)	134
Tetralogy of Fallot (%)	23 (23.2)	44 (44.4)	15 (15.2)	13 (13.1)	4 (4)	99
Isolated aortic stenosis (%)	8 (10.4)	15 (19.5)	22 (28.5)	20 (26)	12 (15.6)	77
Atrioventricular septal defect (%)	21 (33.9)	28 (45.2)	11 (17.7)	2 (3.2)	–	62
Transposition of the great arteries (%)	32 (61.5)	14 (26.9)	3 (5.8)	2 (3.8)	1 (2)	52
Double outlet right ventricle (%)	3 (12.5)	19 (79.1)	–	1 (4.2)	1 (4.2)	24
Coarctation of the aorta	34 (41.5)	26 (31.7)	14 (17.1)	7 (8.5)	1 (1.2)	82
Complex congenital heart diseases*	41 (44.6)	40 (43.5)	4 (4.3)	6 (6.5)	1 (1.1)	92

Group I: newborns, II: infant and toddlers, III: preschool children, IV: school children, V: adolescents.
Complex CHD*: tricuspid atresia, truncus arterious, pulmonary atresia and severe hypoplasia, heterotaxy syndromes, common atrium, hypoplastic left-heart syndromes, single ventricle and/or double inlet ventricle, corrected transposition of the great arteries, dextrocardia with CHD, Ebstein anomaly.

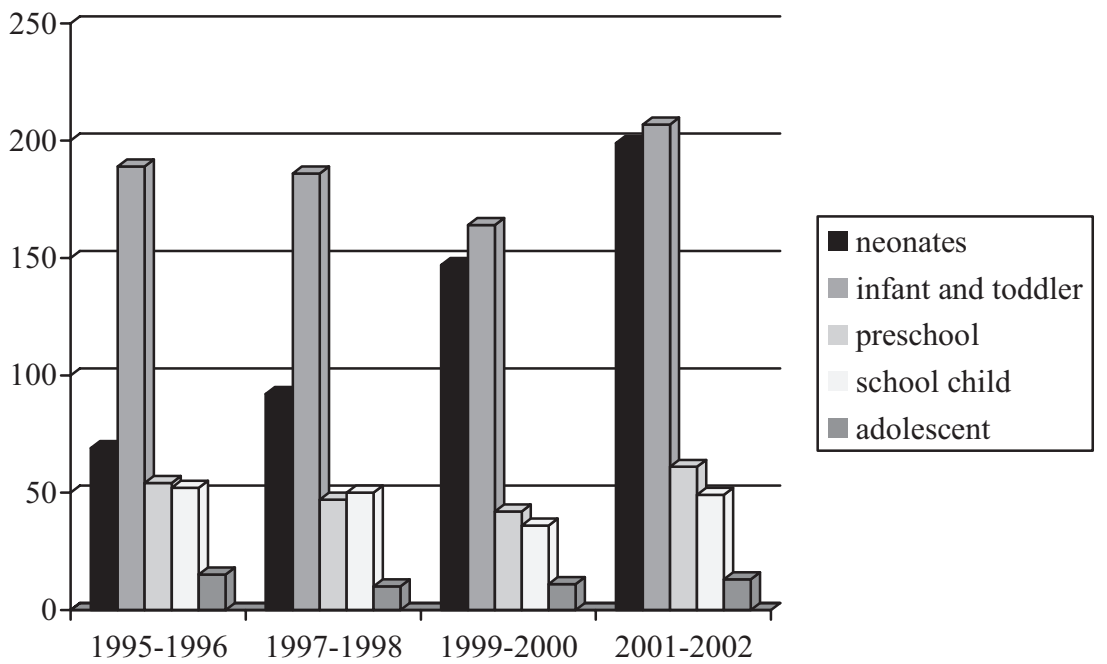

Fig. 1. Congenital heart disease and application age by the time.

There were 161,241 live births in Konya from 1995 to 2002. Incidence of CHD over this period was 7.77/1,000 live births. Yearly incidence of CHD varied from 6.35 to 9.65 per 1,000 live births, $p<0.05$ (Table III). The prevalence of total ventricular septal defect was 6.2, and for tetralogy of Fallot was 0.62. Complex CHD was found in 92 children or 0.57 per 1,000 live-born. Frequency of simple combined CHD and ventricular septal defect, patent ductus arteriosus, coarctation of the aorta, atrial septal defect, isolated pulmonary stenosis, transposition of the great arteries and complex CHD increased over time ($p<0.05$). Prevalence of isolated ventricular septal defect, atrioventricular septal defect, aortic stenosis,

Table III. Prevalence of Congenital Heart Disease in Live-Born Children

Year	Live birth*	n**	n/1000	χ^2	p
1995-1996	40,594	258	6.35		
1997-1998	41,400	278	6.71		
1999-2000	37,212	311	8.35		
2001-2002	42,035	406	9.65		
Totally	161,241	1253	7.77	37.02	0.0001†

* Live-born children as accounted for by city population and birth rate.
** n: Neonates, infants and toddlers with CHD in these years.
† Statistically significant.

tetralogy of Fallot, and of double outlet right ventricle did not change over time (p>0.05). (Table IV).

One thousand one hundred and fifty-six cases (68.2%) of CHD occurred as single lesions and 538 (31.8%) as multiple cardiac lesions. Two hundred patients had extracardiac anomalies or syndromes. Chromosomal anomalies and recognizable syndromes were diagnosed in 105 patients (52.5%). Down syndrome accounted for 83 (78.3%) of all syndromic congenital heart disease patients (Table V). The commonest non-cardiac anomalies with CHD were musculoskeletal anomalies. Finally, the brother/sister of six patients and mother of one patient had CHD (total 0.4%).

Discussion

Epidemiological studies have shown varied frequency and prevalence of CHD. The incidence of CHD has varied between 4.05 and 12.35/1,000[2-7,11-16]. Our survey reveals an incidence of 7.77/1,000 live births, which falls in the range of the reported studies. Distribution of cardiac defects in our children was not very different from the reported series[1, 11-17]. Botto and Boneva et al.[18,19] have documented variability in the prevalence of CHD by race. No race or ethnic group differences in the prevalence of CHD have been found in previous studies. Ventricular septal defect, pulmonary stenosis and atrial septal defect were reported as the most frequent CHDs[2,3,13]. The results of our study indicate that ventricular septal defect was the most frequent type of CHD in Konya, followed by patent ductus arteriosus and atrial septal defect.

Sex predominance for the more frequent heart defects was also not different from the literature, except for atrioventricular septal defect, for which there was no female predominance, in contrast to reported studies[1,2].

Increased occurrence of some CHDs over time was observed in our study. Zierler et al.[20] found that detectable arsenic levels in the water were associated with a three- to four-fold increase

Table IV. Prevalence of Some Congenital Heart Diseases in Live-Born Children

Congenital heart diseases	1995 1996	Prevalence	1997 1998	Prevalence	1999 2000	Prevalence	2001 2002	Prevalence	Total	Total Prevalence	χ^2	p
Combined CHD* and ventricular septal defect	122	3.00	154	3.72	163	4.38	164	3.90	603	3.74	10.27	0.01†
Isolated ventricular septal defect	86	2.12	114	2.75	113	3.03	117	2.78	430	2.67	6.83	0.07
Atrial septal defect	75	1.85	60	1.45	83	2.23	102	2.43	320	1.98	11.66	0.01†
Isolated atrial septal defect	41	1.01	26	0.63	30	0.80	63	1.50	160	0.99	17.73	0.005†
Patent ductus arteriosus	35	0.86	41	0.99	72	1.93	79	1.88	227	1.41	27.72	0.01†
Isolated pulmonary stenosis	18	0.44	13	0.31	12	0.32	33	0.79	76	0.47	12.77	0.008†
Complex CHD**	18	0.44	12	0.28	21	0.56	30	0.71	81	0.50	8.02	0.04†
Atrioventricular septal defect	11	0.27	13	0.31	9	0.24	16	0.38	49	0.30	1.44	0.69
Coarctation of the aorta	10	0.25	13	0.31	11	0.30	26	0.62	60	0.37	9.55	0.02†
Aortic stenosis	9	0.21	8	0.19	9	0.24	13	0.31	39	0.24	1.26	0.73
Tetralogy of Fallot	9	0.21	18	0.43	15	0.40	25	0.59	67	0.41	6.97	0.07
Transposition of the great arteries	8	0.20	5	0.12	14	0.38	19	0.45	46	0.29	10.21	0.01†
Double outlet right ventricle	5	0.12	6	0.14	7	0.19	5	0.12	23	0.14	0.81	0.84

* and **: note legends in Tables I and II.
† statistically significant.

Table V. Syndromes With Associated Congenital Heart Diseases

Syndrome	n	Associated congenital heart diseases
Down syndrome	83	Ventricular septal defect ± atrial septal defect ± patent ductus arteriosus ± coarctation of the aorta in 59 patients, atrioventricular septal defects in 22, tetralogy of Fallot in 2, hypoplastic left-heart syndrome in 1
Williams syndrome	4	Aortic stenosis
Noonan syndrome	2	Pulmonary stenosis
Rubella syndrome	2	Patent ductus arteriosus
Cornelia de Lange syndrome	2	Ventricular septal defect, atrial septal defect
DiGeorge syndrome	2	Truncus arteriosus, interrupted aortic arch
Ellis-van Creveld syndrome	1	Ventricular septal defect
Goldenhar syndrome	1	Ventricular septal defect
Griscelli syndrome	1	Atrial septal defect
Holt-Oram syndrome	1	Atrial septal defect
Klippel-Feil syndrome	1	Atrial septal defect
Marshal-Smith syndrome	1	Atrial septal defect
Pierre Robin sequence	1	Ventricular septal defect – atrial septal defect – aortic stenosis
Rubinstein-Taybi syndrome	1	Atrial septal defect
Russell-Silver syndrome	1	Patent ductus arteriosus
Sturge-Weber syndrome	1	Ventricular septal defect – aortic stenosis
t 6, 18 translocations	1	Ventricular septal defect – atrial septal defect – aortic stenosis

in risk of coarctation of the aorta in offspring. Botto et al.[18] found increasing prevalence of CHD, from 6.2 to 9.0 per 1,000 live births from 1995 through 1997. The causal implications of this increment are yet to be determined. And the apparent increase raises a question - Does this increase represent the change in occurrence? Or does it reflect improved ascertainment and reporting? The technological advances, increased medical insurance system and routine use of echocardiography have contributed to improvement in the establishment of the diagnosis, and therefore to an increase in the prevalence of CHD.

Tetralogy of Fallot and transposition of the great arteries are the most common forms of cyanotic CHD presenting in infancy. Although these can be diagnosed early, unfortunately first diagnosis was made in every age group in our study. Diagnosis of CHD is not usually made in school children in developed countries. An important discrepancy between this study and the literature is the later age of diagnosis[4,12,18,21]. The findings indicate that CHD is an important health problem in Konya, and maybe in Turkey, and one which requires urgent measures aimed at improving both diagnostic and therapeutic facilities.

Down syndrome was found as the commonest syndromic anomaly with cardiac defects[22]. Furthermore, simple cardiac defects might be very common in Down syndrome, aside from atrioventricular septal defect.

In conclusion, ventricular septal defect was the most frequent anomaly and it is commonly associated with a variety of other defects: atrial septal defect, patent ductus arteriosus, etc. The prevalence of CHD is increasing. Whereas most findings likely result from improved case ascertainment and reporting, others might reflect changes in the distribution of risk factors in the population. The declining age at diagnosis predates the introduction of echocardiography, and may be attributed to improvements in social and medical circumstances over the period under study. These include better parental education and better medical training. We suggest that cardiac evaluation be performed at birth in postnatal clinics and in immunization centers, in order to facilitate early detection and treatment of CHD. Potential sources of error in this study include its retrospective nature. In addition, this study only included live births because autopsy data on still-births is not routinely collected in this region; thus, the complex CHD rate may be higher than observed in the study.

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