Congenital heart disease in Saudi Arabia: current epidemiology and future projections

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الداء القلبي الخلقي في المملكة العربية السعودية: الوبائيات الحالية والتوقعات المستقبلية

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الخلاصة: تم تقييم نتائج الدراسات الوبائية التي أُجريت في أربع مناطق في المملكة العربية السعودية (آب/أغسطس 1988 – شباط/فبراير 2000) وشملت 2604 شخصاً يعانون من الداء القلبي الخلقي، بُغْيَةَ إعطاء لمحة عامة عن وبائيات هذا الداء. وأثبتت الدراسة أن عيب الحاجز البطيني يمثِّل أكثر الآفات شيوعاً (33.9٪)، يليه عيوب الحاجز الأذيني (18.1٪). وثبت بوجه عام، وجود نوع من التشابه في توزُّع المرض بين الجنسَيْن، وإن كان إصابة الذكور أكبر من الإناث في ثلاث حالات. فمن بين 2269 حالة (59٪) تجلّت منذ السنة الأولى من الحياة، وجد أن 566 (25٪) يعانون من داء قلبي خلقي وليدي، وكانت متلازمة داون أكثر الأسباب شيوعاً. ووُجِد أن توزُّع آفات معيَّنة والتوزُّع بين الجنسَيْن يتشابه مع نتائج أجزاء أخرى من العالم؛ وإن كان المعدل التراكمي لاكتشاف الداء منسوباً للعمر عند تجلّي الأعراض أقلّ.

ABSTRACT To provide an overview of the epidemiology of congenital heart disease, the results of epidemiological studies done in 4 regions of Saudi Arabia (August 1988–February 2000) and 2604 individuals with congenital heart disease were evaluated. Ventricular septal defect was the commonest lesion (33.9%) followed by atrial septal defect (18.1%). Overall, sex distribution was similar; for 3 conditions, more males than females were affected. Of 2269 (59%) presenting in the first year of life, 566 (24.9%) had neonatal congenital heart disease. Down syndrome was the commonest cause. Distribution of specific lesions and sex distribution was similar to findings from other parts of the world; however, the overall detection rate at 1 year of age was lower.

La cardiopathie congénitale en Arabie saoudite : épidémiologie actuelle et projections futures

RÉSUMÉ Afin de décrire l'épidémiologie des cardiopathies congénitales, les résultats des études épidémiologiques réalisées dans quatre régions d'Arabie saoudite (août 1988-février 2000) ont été évalués et 2604 cas de cardiopathie congénitale ont été analysés. La communication interventriculaire était la lésion la plus courante (33,9 %), suivie par la communication interauriculaire (18,1 %). Dans l'ensemble, la répartition par sexe était similaire ; pour trois affections, les garçons étaient plus touchés que les filles. Sur les 2269 cas (59 %) apparaissant dans la première année de vie, 566 (24,9 %) étaient des cas de cardiopathie congénitale néonatale. Le syndrome de Down était la cause la plus fréquente. La répartition des lésions spécifiques et la répartition par sexe étaient similaires à celles observées dans d'autres parties du monde ; le taux global de dépistage à l'âge d'un an était toutefois inférieur.

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Introduction

The epidemiology of congenital heart disease in Saudi Arabia has not been determined, nor has it received the attention it warrants. Only scattered efforts have been made in 4 regions. These were done over different time periods and using different methodologies. This study aimed at utilizing the results of these studies to establish the epidemiology of congenital heart disease in Saudi Arabia. The expected problems resulting from the differences in time, place and methodology in the 4 studies are reflected.

Several previous reports suggest a changing pattern and incidence of congenital heart disease in various geographic locations [*1,2*]. Knowledge of the epidemiology of congenital heart disease is the basis on which investigative efforts will emerge to identify the causes of cardiac dysmorphogenesis and afford opportunities to prevent them [*3*]. Future projections, thought to be critical for the comprehensive and optimum care of congenital heart disease population in Saudi Arabia, are also discussed. These are also considered of pivotal importance for groups which care for patients with congenital heart disease as well as for policymakers.

Methods

The findings of epidemiological studies conducted in 4 different regions of Saudi Arabia were examined. The areas were: east area [*3*] (Al-Hasaa region, estimated population 1.2 million), south-west area [*4*] (Aseer, estimated population, 2 million), west area [*5*] (Al-Madina region, estimated population 2 million) and north central area [*6*] (Al-Qaseem region, estimated population 1.5 million). These studies were commissioned over different periods between August 1988 and February 2000, some overlapping, as follows: January 1990–December 1992 in Al-Qaseem, March 1992–February 1995 in Al-Madina, July 1994–June 1996 in Aseer and March 1997–February 2000 in Al Hasaa.

The studies were implemented in 4 related institutes, which are the only referral centres in those regions to which children suspected of having congenital heart disease are referred from both government and private hospitals and primary health care centres. These amount to 10–15 secondary hospitals and 30–50 primary health care centres in the 4 areas.

A total of 2604 patients, 1299 males and 1305 females, age range 0–13 years, were evaluated in the studies. The principal authors of these studies (qualified paediatric cardiologists) aided by qualified paediatric specialists made the diagnostic decisions after carrying out a full physical examination, plain chest radiography, electrocardiography and echocardiography. All patients were finally diagnosed in the main referral institutes.

A significant number of referrals (234 of 974, i.e. around 24% in the Al Hasaa study) were normal and excluded from the study. Patients with acquired heart disease such as rheumatic fever were also excluded. Down syndrome patients need karyotyping for confirming diagnosis of trisomy 21; this was done through further chromosomal analysis of blood samples at Damman Central Hospital laboratories for the patients from Al Hasaa.

Congenital heart disease was subcategorized into 9 major lesion types, the most common defects, plus a group which included the rare complex lesions. This classification is an internationally accepted practice. When there was > 1 cardiac lesion, the dominant lesion structurally and haemodynamically was used for the diagnosis.

This is also the most accepted practice in such situations.

Briefly, the diagnostic criteria of each type of cardiac lesion (based on echocardiography/Doppler examination) were:

- ventricular septal defect: communication between the 2 ventricles (perimembranous, membranous, mid-muscular, outlet, inlet or basal);
- atrial septal defect: communication between the 2 atria (primum, secundum or sinus venosus);
- pulmonary stenosis: narrowing of right ventricular outflow tract (valvular, subvalvular, supravalvular);
- patent ductus arteriosus: patency of ductus arteriosus;
- atrioventricular septal defect: defect in the atrioventricular septum with common atrioventricular valve (complete) or 2 distinct valves (partial);
- tetralogy of Fallot: large non-restrictive outlet ventricular septal defect and infundibular stenosis with aortic overriding and secondary right ventricular hypertrophy;
- aortic stenosis: narrowing of left ventricular outflow tract (valvular, subvalvular, supravalvular);
- coarctation of aorta: narrowing of the aortic arch at the isthmus;
- dextro-transposition of great arteries: ventriculoarterial discordance;
- other: all other congenital heart lesions, such as pulmonary atresia, tricuspid atresia, double outlet right ventricle, etc.

Data collection in these cases included proportion and sex distribution. Three studies [*3,5,6*] included age at presentation. The total number of individuals referred due to suspicion of heart disease was noted in 3 studies [*3–5*]. Neonatal congenital heart disease was examined in 3 studies [*3,5,6*], covering 1566 neonates from a total of 2269. Incidence of congenital heart disease and details of congenital heart disease in Down syndrome, as well as confidence limits of sex affected with each lesion were documented in 1 study [*3*].

Results

In the 4 studies, 2604 patients were diagnosed with congenital heart disease. The distribution of the various cardiac defects in each region is shown in Table 1. Ventricular septal defect was the commonest disorder in all 4 studies, accounting for 33.9% of congenital heart disease overall. The second most common lesion was atrial septal defect, accounting for 18.1% of all congenital heart disease. Left-sided obstructive lesion (aortic stenosis and coarctation of aorta) was documented in 4.8% of all congenital heart disease. The overall incidence of total anomalous pulmonary venous drainage was 0.3%.

Table 2 shows the distribution of various cardiac defects in Saudi Arabia compared with other geographic regions of the world [*1,7–14*]. Ventricular septal defect was consistently the commonest congenital heart condition worldwide, although a wide variation in frequency was noted (24.0% in Denmark, 60.0% in Japan). The low frequency of left-sided obstructive lesion in Asian countries such as Saudi Arabia (4.8%) [*1*] and Japan (3.7%) [*7*] contrasted with the higher figures from Europe, e.g. Denmark (11.7%) [*8*], Sweden (15.2%) [*9*] and Hungary (17.0%) [*10*]. Dextro-transposition of great arteries was relatively rare in Saudi Arabia compared to the other studies. Occurrence of atrioventricular septal defect varied from a low of 1.8% in Japan [*7*] to a high of 7.4% in the United Kingdom study [*11*].

Table 1 **Frequency of cardiac lesions in 2604 patients with congenital heart disease in 4 regions of Saudi Arabia [*3–6*]**

Lesion	Al Hassa		South east		North central		West		Overall	
	No.	%	No.	%	No.	%	No.	%	No.	%
VSD	292	39.5	109	32.5	123	38.4	359	29.7	883	33.9
ASD	85	11.5	35	10.4	37	11.6	314	26.0	471	18.1
PS	66	8.9	34	10.1	29	9.1	195	16.1	324	12.4
PDA	64	8.6	53	15.8	25	7.8	159	13.2	301	11.6
AVSD	26	3.5	12	3.6	16	5.0	38	3.1	92	3.5
TOF	31	4.2	18	5.4	15	4.7	26	2.2	90	3.5
AS	26	3.5	9	2.7	9	2.8	20	1.6	64	2.5
COA	20	2.7	11	3.3	6	1.9	23	1.9	60	2.3
D-TGA	14	1.9	5	1.5	14	4.4	22	1.8	55	2.1
Other	116	15.7	49	14.6	46	14.4	53	4.4	264	10.1
Total	740	100.0	335	100.0	320	100.0	1209	100.0	2604	100.0

VSD = ventricular septal defect; ASD = atrial septal defect; PS = pulmonary stenosis; PDA = patent ductus arteriosus; AVSD = atrioventricular septal defect; TOF = tetralogy of Fallot; AS = aortic stenosis; COA = coarctation of aorta; D-TGA = dextro-transposition of great arteries.

Distribution according to sex, male: female ratio, standard error and 95% confidence intervals (CI) for each cardiac lesion are illustrated in Table 3. For congenital heart disease in general, frequency was almost the same for males and females. Female predominance was seen in patent ductus arteriosus (95% CI: 56.2–61.8). A significant male predominance was clear in left-sided obstructive lesions [aortic stenosis (95% CI: 69.6–80.4), coarctation of aorta (95% CI: 66.2–77.8)] and dextro-transposition of great arteries (95% CI: 64.9–77.1).

The age distribution of patients presenting with congenital heart disease for each type of cardiac lesion in 3 centres (87% of all centres) is shown in Table 4. The cumulative detection rate at 1 year of age for all lesions was 59%. Age at presentation for specific lesions showed wide variation. Ventricular outflow tract obstruction such as aortic stenosis had a cumulative detection rate at 1 year of only 40%, while for cyanotic heart disease such as dextro-transposition of great arteries, 83% were diagnosed in the first 4 weeks and 98% in the first year of life.

The incidence of various cardiac defects in neonates (infants ≤ 28 days old) in the same 3 centres is shown in Table 5. Ventricular septal defect was the commonest (29.0%). Patent ductus arteriosus accounted for 17.3% of neonatal congenital heart disease. The 87 (15.4%) neonates included under others, the more complex congenital heart conditions such as pulmonary atresia with and without ventricular septal defect, tricuspid atresia, univentricular heart and heterotaxy syndrome, constituted the fourth largest group. Of 3786 patients referred for evaluation of congenital heart disease in 3 centres 60% had congenital heart disease; the remainder were normal or had acquired heart disease.

Congenital heart disease in Down syndrome was specifically studied in Al Hassa

Table 2 **Distribution of cardiac lesions in Saudi Arabia and in 8 other countries [*1,7–14*]**

Lesion	Saudi Arabia % (*n* = 2604)	Sweden[a] % (*n* = 369)	USA[b] % (*n* = 163)	Nigeria % (*n* = 635)	Denmark % (*n* = 5249)	USA[c] % (*n* = 420)	UK[d] % (*n* = 338)	Canada[e] % (*n* = 464)	Japan % (*n* = 773)	Hungary % (*n* = 43)
VSD	33.9	27.1	31.3	35.0	24.0	32.1	28.1	31.0	60.0	20.9
ASD	18.1	4.3	6.1	7.5	9.4	7.4	8.3	11.2	5.3	10.4
PS	12.4	3.8	13.5	9.0	5.9	8.6	2.7	10.8	9.6	10.4
PDA	11.6	9.5	5.5	22.0	12.6	8.3	6.5	7.1	3.6	11.9
AVSD	3.5	3.0	3.7	–	2.6	3.6	7.4	–	1.8	4.5
TOF	3.5	4.1	3.7	10.0	5.8	5.0	8.6	8.0	5.8	4.5
AS	2.5	5.4	3.7	0.6	4.7	3.8	4.1	8.4	1.0	11.0
COA	2.3	9.8	5.5	2.0	7.0	6.7	5.6	3.4	2.7	6.0
D-TGA	2.1	6.0	3.7	4.5	4.8	2.6	5.6	2.6	2.2	4.5
Other	10.1	27.0	23.3	9.4	23.2	22.0	23.1	17.5	9.5	15.9

[a]Gothenburg; [b]California; [c]Multi-centre; [d]Blackpool; [e]Toronto.
VSD = ventricular septal defect; ASD = atrial septal defect; PS = pulmonary stenosis; PDA = patent ductus arteriosus; AVSD = atrioventricular septal defect; TOF = tetralogy of Fallot; AS = aortic stenosis; COA = coarctation of aorta; D-TGA = dextro-transposition of great arteries.
– = not measured.

[*3*]. Of a total of 740 patients, 44 were diagnosed with Down syndrome. Ventricular septal defect was the commonest acyanotic congenital heart condition in this group. Tetralogy of Fallot was the commonest cyanotic heart lesion (Table 6).

Discussion

Echocardiography became a common diagnostic tool for congenital heart disease only in the mid-80s of the last century. Its increasing accuracy as a superior diagnostic tool resulted in increased values for incidence of congenital heart disease by uncovering commonly-overlooked lesions such as muscular ventricular septal defect, small patent ductus arteriosus and coronary artery fistulae to cardiac chambers before the development of the colour flow mapping technique. Knowledge of the incidence of various types of congenital heart disease and their clustering in time or place may aid in understanding what caused them [*13*].

Generally speaking, determination of the true incidence of congenital heart disease requires accurate diagnosis of all affected individuals in the study area; consequently, underestimation is the rule since children at the extremes of the disease are inevitably not counted. This includes babies who die soon after birth with undiagnosed, severe, complex congenital heart disease and those with asymptomatic lesions. As the cardiac units in the 3 studies were the only referral centres for their respective regions, children suspected or known to have congenital heart disease of wide-ranging severity are referred to these units. This situation is thought to reflect the pattern rather than the incidence of congenital heart disease in Saudi Arabia.

Table 3 **Distribution of lesions in 2604 patients with congenital heart disease according to sex [*3–6*]**

Lesion	Total	Males			Females			M:F ratio
		No.	%	CI	No.	%	CI	
VSD	883	442	50.1	48.3–57.7	441	49.9	48.3–51.7	1:1
ASD	471	224	47.6	45.7–50.7	247	52.4	49.7–54.3	0.9:1
PS	324	155	47.8	45.2–50.8	169	52.2	49.2–54.8	0.9:1
PDA	301	122	40.5	38.2–43.8	179	59.5	56.2–61.8	0.7:1
AVSD	92	44	47.8	42.8–53.2	48	52.2	46.8–57.2	0.9:1
TOF	90	45	50.0	44.7–55.3	45	50.0	44.7–55.3	1:1
AS	64	48	75.0	69.6–80.4	16	25.0	19.6–30.4	3:1
COA	60	43	71.7	66.2–77.8	17	28.3	22.2–33.8	2.5:1
D-TGA	55	39	70.9	64.9–77.1	16	29.1	22.9–35.1	2.4:1
Other	264	137	51.9	48.9–55.1	127	48.1	44.9–51.1	1.1:1
Total	2604	1299	49.9	49–51	1305	50.1	49–51	1:1

CI = confidence interval.
VSD = ventricular septal defect; ASD = atrial septal defect; PS = pulmonary stenosis; PDA = patent ductus arteriosus; AVSD = atrioventricular septal defect; TOF = tetralogy of Fallot; AS = aortic stenosis; COA = coarctation of aorta; D-TGA = dextro-transposition of great arteries.

Table 4 **Distribution of various cardiac lesions in 3 areas of Saudi Arabia according to age at presentation [*3,5,6*]**

Lesion	Al Hassa				Al Qaseem				Al Madina				Overall			
	≤ 1 yr		1 yr		≤ 1 yr		1 yr		≤ 1 yr		1 yr		≤ 1 yr		1 yr	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
VSD	147	50	145	50	72	59	51	41	231	64	128	36	450	58	324	42
ASD	55	65	30	35	20	54	17	46	185	59	129	41	260	60	176	40
PS	36	55	30	45	13	45	16	55	77	40	118	60	126	43	164	57
PDA	48	75	16	25	14	56	11	44	122	77	37	23	184	74	64	26
TOF	24	77	7	23	10	67	5	33	16	62	10	38	50	69	22	31
AS	10	38	16	62	3	33	6	67	9	45	11	55	22	40	33	60
COA	13	65	7	35	3	50	3	50	17	74	6	26	33	67	16	33
D-TGA	14	100	0	–	13	93	1	7	22	100	–	0	49	98	1	2
Other[a]	43	30	99	70	46	74	16	26	75	82	16	18	164	56	131	44
Total	390	53	350	47	194	61	126	39	754	62	455	38	1338	59	931	41

VSD = ventricular septal defect; ASD = atrial septal defect; PS = pulmonary stenosis; PDA = patent ductus arteriosus; TOF = tetralogy of Fallot; AS = aortic stenosis; COA = coarctation of aorta; D-TGA = dextro-transposition of great arteries.
[a]Including atrioventricular septal defect.

Table 5 **Distribution of cardiac lesions in 566 patients with neonatal congenital heart disease in 3 areas of Saudi Arabia [*3,5,6*]**

Lesion	Al Hassa		Al Qaseem		Al Madina		Overall	
	No.	%	No.	%	No.	%	No.	%
VSD	63	35.4	30	32.3	71	24.1	164	29.0
ASD	19	10.7	10	10.8	65	22.0	94	16.6
PS	10	5.6	3	3.2	16	5.4	29	5.1
PDA	17	9.6	8	8.6	73	24.7	98	17.3
AVSD	7	3.9	9	9.7	10	3.4	26	4.6
TOF	8	4.5	3	3.2	5	1.7	16	2.8
AS	3	1.7	0	–	0	–	3	0.5
COA	8	4.5	0	–	9	3.1	17	3.0
D-TGA	8	4.5	9	9.7	15	5.1	32	5.7
Other	35	19.7	21	22.6	31	10.5	87	15.4
Total	178	100.0	93	100.0	295	100.0	566	100.0

VSD = ventricular septal defect; ASD = atrial septal defect; PS = pulmonary stenosis; PDA = patent ductus arteriosus; AVSD = atrioventricular septal defect; TOF = tetralogy of Fallot; COA = coarctation of aorta; D-TGA = dextro-transposition of great arteries; AS = aortic stenosis.

The changing incidence in different reports may be attributed to differences in the definition of congenital heart disease, study methodology, diagnostic accuracy, genetic predisposition, calcium bioavailability and other environmental factors. Lack of rigorous definition of congenital heart disease, with the emphasis on certain exclusions has a negative impact on accurate calculation of incidence. Patent ductus arteriosus in premature babies, smaller atrial septal defects which eventually close, persistent left superior vena cava and azygous continuity in structurally normal heart are among other lesions with no potential haemodynamic significance, so their exclusion in future studies may improve incidence figures for congenital heart disease.

Table 6 **Distribution of conditions in 44 individuals with Down syndrome who had congenital heart disease in 1 area of Saudi Arabia [*3*]**

Lesion	No.	%
Non-cyanotic		
VSD	13	30
ASD	7	16
PDA	9	20
AVSD	11	25
Cyanotic		
TOF	2	4
TAPV	2	5

VSD = ventricular septal defect; ASD = atrial septal defect; PS = pulmonary stenosis; PDA = patent ductus arteriosus; AVSD = atrioventricular septal defect; TOF = tetralogy of Fallot; TAPV = total anomalous pulmonary venous return.

As in other parts of the world, ventricular septal defect was the commonest congenital heart disease in the 4 study regions individually and in Saudi Arabia overall (34%). In contrast to many other studies, atrial septal defect was the second most common, 18.1%, compared to 4.3% in Gothenburg (5th most common) [*9*], 5.3% in California, where it was the 3rd most common [*13*] and

10.4% in Hungary, where it was the 4th most common [*10*]. However, atrial septal defect was the second most common condition in 2 studies from North America, a multi-centre study and a study from Toronto, but with lower rates [*1,12*].

The incidence of patent ductus arteriosus was 8.6% overall. In the southeast, a high altitude area, this condition comprised 15.8% of all congenital heart disease. Alzamora-Castro et al. documented the incidence of patent ductus arteriosus to be 30 times greater at high altitudes (4500–5000 m above sea level) [*15*].

The rarity of aortic stenosis and coarctation of aorta in each of the study regions contrasts sharply with European figures (4.8% in Saudi Arabia versus 11% in Hungary) [*10*]. The same was observed in Japan, another Asian country, where aortic stenosis and coarctation of aorta were reported in only 3.7% of all patients with congenital heart disease [*7*]. Studies of ethnic influence on the pattern of congenital heart disease in the United Kingdom revealed a higher frequency of coarctation of aorta in non-Asian (9%) than Asian (3%) infants [*16*]. This might be related to racial and genetic factors.

Atrioventricular septal defect, a characteristic lesion in Down syndrome, accounted for 3.5% of all congenital heart disease in Saudi Arabia with range of 3.1%–5.0%. Fluctuation of incidence of atrioventricular septal defect in different studies is well known. Inclusion of more of the older mothers, in whom the incidence of giving birth to infants with trisomy 21 is increased, would produce higher values [*13*].

As regards cyanotic congenital heart disease, tetralogy of Fallot constitutes 3.5% of all congenital heart disease in Saudi Arabia with a range of 2.2%–5.4%. Most of the other studies reported a higher incidence [*1,7–14*]. Rigorous echocardiographic definition of tetralogy of Fallot is still lacking as some authors still consider double outlet right ventricle with pulmonary stenosis as tetralogy of Fallot, even if most of the aorta emanates from the right ventricle. This will exaggerate the incidence of tetralogy of Fallot.

Transposition of the great arteries was found in 2.1% of all congenital heart disease in Saudi Arabia compared to the studies done by Hoffman and Christian (3.7%) [*2*] and Campbell (4.2%) [*17*]. Nora and Nora suggest that interaction between genetic and environmental factors plays a major role in the etiology of transposition of the great arteries [*18*]. An absence or deficiency of an environmental causative factor or the presence of protective agent might have contributed to the low incidence of this condition in Saudi Arabia.

Total anomalous pulmonary venous drainage was very low overall (0.3%) and was even absent in 1 of the study regions (Al-Ahsa) [*3*]. This is in concordance with the findings of Mitchell, Korones and Bevendes [*1*] and Rose, Boyd and Ashton who reported 0% incidence of total anomalous pulmonary venous drainage [*12*]. These can be compared with the 1.5% incidence of total anomalous pulmonary venous drainage in the Baltimore–Washington infant study [*19*].

Aortic stenosis and coarctation of aorta showed strong male predominance in Saudi Arabia. These findings agreed with the reports of Perry et al. and Rothman and Fyler who reported 64%–78% for aortic stenosis and 57%–65% for coarctation of aorta in boys [*19,20*].

Transposition of the great arteries also showed a strong male predominance. Predisposition of the male sex for this condition was first noted by MacMahon et al. in 1953, and has been supported by a number of subsequent studies [*19,21*]. On the other hand,

patent ductus arteriosus showed female predominance (male:female ratio 0.7:1); this is consistent with the reports of Perry et al. and Pradat which documented the predominance of patent ductus arteriosus in girls, range 60%–70% [*19,22*]. Atrial septal defect, pulmonary stenosis and atrioventricular septal defect were reported with slight female predominance in Saudi Arabia (male:female ratio 0.9:1 overall). A stronger female propensity for those lesions has been reported in other studies [*19,20*].

The consistent sex ratio for most of the congenital heart conditions suggests an important causative link that is not well understood. Gensburg, Marshall and Druschel observed that when all isolated lesions are classified by the embryonic timing of disturbed organogenesis, males tend to predominate in those that developed later in gestation [*23*]. The causal implications of this association are yet to be determined.

Premature babies with patent ductus arteriosus were included in some of the study centres, but since most international studies tend to exclude this group, future studies in Saudi Arabia need to do the same to make our data comparable.

Atrial septal defect was the third most frequent neonatal congenital heart condition. One study stressed the fact that atrial septal defect does not give rise to heart murmur in the newborn infant, so it is easily missed, as diagnosis would be made only by echocardiography. The condition was brought to the researcher's attention only because of cardiac and non-cardiac health problems which occurred before 28 days of life [*3*]. This condition is the commonest adult congenital heart disease; it is neglected or not diagnosed in many children. The true incidence can be revealed only by mass echocardiographic screening for all live-born neonates.

The other groups of neonatal congenital heart disease include, predictably, the most complex lesions, which present with haemodynamic instability shortly after birth. For example, 64% of total cases of transposition of the great arteries presented in the neonatal period.

The cumulative detection rate in 3 centres [*3–5*] at 1 year of age was 59%. This is much lower than the rate in a similar British study (82%) [*11*]. Further improvement in case detection by front-line doctors is essential. The impressive network of health institutions in Saudi Arabia should be exploited to give a better future for children with congenital heart disease.

Only 60% of 3786 children referred with suspected heart disease had a congenital heart condition. This burden of unnecessary referrals could be minimized by improving clinical skills for recognizing these conditions.

As in other international studies, the cause of congenital heart disease is largely unknown, but the role of chromosomal anomaly was conspicuous. Down syndrome is the commonest cause of congenital heart disease. There was great success in localizing the cardiac critical region in chromosome 21 to 21q22.2–22.3 region [*24*]. The type of cardiac lesion was determined in 44 patients with Down syndrome. Ventricular septal defect was the commonest lesion in the group, followed by atrioventricular septal defect. Other studies found this specificity of Down syndrome to the lesions listed, as in the Rowe and Uchida prospective study of 184 children [*25*] and a recent study by Abbag, who investigated congenital heart defects in 57 patients with Down syndrome [*26*].

The unprecedented progress of Saudi Arabia in all fields has brought about remarkable advances in medicine, and cardiac

medicine in particular, over the past few decades. Despite this, services are still far from adequate. The availability of paediatric cardiac services in 3 centres within the same region (Riyadh) and an almost complete absence of cardiac centres which investigate congenital heart disease in other regions is a major deficiency which deserves urgent attention from policy makers in Saudi Arabia. Based on the recommendations of the American Academy of Pediatrics, paediatric cardiac centres should be available for a population that generates over 30 000 live births per year [*27*]. Applying these recommendations, Ashmeg and Moheeb concluded that Saudi Arabia optimally required 20 paediatric cardiology centres, but not less than 7 centres [*28*]. There are already 3 centres in Riyadh; 2 are needed in the western region and 1 centre each for the east, south and north.

The availability of sophisticated, state-of-the-art cardiac technology and cardiac surgery in Saudi Arabia created a new group of patients, "adults with operated congenital heart disease" [*3,28*]. They have peculiar anatomy, fluid haemodynamics, complications and special needs. The establishment of adult congenital heart disease teams is critical to continue adequate care for this unique group of patients.

Further knowledge is needed about risk factors (including familial and environmental factors) related to Saudi Arabia. With further research, we look forward to being part of international community, working with sincere efforts to unravel some of mysteries of abnormal cardiogenesis.

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