Pattern of congenital heart disease in Southern Yemeni children referred for echocardiography

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ABSTRACT

الأهداف: دراسة توزيع السن، نوع الجنس والتكرار المتناسب لعيوب القلب الخلقية في وقت التشخيص لدى الأطفال بجنوب اليمن.

الطريقة: أُجريت دراسة إستعادية تم فيها التركيز على نتائج تصوير أصداء القلب لعدد 393 طفل مصابين بعيوب خلقية في القلب، بينة الأعراض. أُجريت هذه الدراسة بقسم تخطيط أصداء القلب بمستشفى تحويلي بمدينة عدن – اليمن، خلال الفترة ما بين يناير 2001م وحتى ديسمبر 2005م.

النتائج: من بين 987 طفل محول، كان هناك 393 (39.8%) يعانون من عيب خلقي في القلب، بلغ متوسط العمر 4±3.45 عام، وكانت نسبة الذكور (48%) والإناث (52%). كما كانت نسبة الغير مصابين بالازرقاق (85%)، المصابين بالازرقاق (15%)، حديثي الولادة 5 (1.3%)، الرضع تحت عام واحد 156 (39.7%) وبلغ عدد الذين يزيد عمرهم عن عام واحد 232 (59%). حضر معظم الأطفال المرضى المصابين بالازرقاق (66%) خلال عامهم الأول من العمر، فقط (8.5%) كانوا من الرضع. حضر معظم المرضى غير المصابين بالازرقاق (64%) بعد عامهم الأول من العمر (متوسط العمر 3.9 عام)، لم يكن أي منهم حديث الولادة. كانت أكثر العيوب شيوعاً وتكراراً تلك التي لاتحدث ازرقاق: عيب الحاجز البطيني بنسبة (26.5%)، التضييق الرئوي بنسبة (17.6%) ، القناة الشريانية المفتوحة بنسبة (17.3%)، عيب في الحاجز الاذيني بنسبة (15.8%). أما أكثر التشوهات التي تحدث ازرقاق فقد كانت رباعية فالوت بنسبة (8.9%) وتغير في وضع الأوعية الكبيرة بنسبة (3.1%).

خاتمة: يتميز نموذج أمراض القلب الخلقية لدى الأطفال في جنوب اليمن بعيوب بسيطة قابلة للتصحيح، تدني تمثيل التشوهات التي تسبب الازرقاق، وغياب العيوب الحرجة التي تحدث ارتفاع في معدل الوفيات خلال مرحلة الرضاعة.

Objectives: To study the distribution of age, gender, and the relative frequency of congenital heart defects at the time of the diagnosis in Southern Yemeni children.

Methods: This retrospective study focused on echocardiographic findings of 393 symptomatic children affected by congenital heart disease. It was conducted in the Echocardiography Department of a referral hospital for Aden city and surrounding governorates, Yemen, from January 2001 to December 2005.

Results: Out of 987 referred children, congenital heart defects were detected in 393 (39.8%); mean age was 3.45 ± 4 years; of them, 48% males and 52% females. They were 85% non-cyanotic and 15% cyanotic. Patients comprised neonates, 5 (1.3%); infants under one year, 156 (39.7%), and children more than one year, 232 (59%). Most cyanotic patients (66%) presented during their first year of life, but only 8.5% were neonates. Most non-cyanotic (64%) presented after their first year (mean age 3.9 years), none of them were neonates. The most frequent defects were: ventricular septal defect (26.5%), pulmonary stenosis (17.6%), patent ductus arteriosus (17.3%), and atrial septal defect (15.8%). Tetralogy of Fallot (8.9%) and transposition of great vessels (3.1%) were the most frequent cyanotic defects.

Conclusion: The pattern of congenital heart diseases in Southern Yemen, is characterized by simple, potentially correctable heart defects, under-representation of cyanotic, and absence of critical defects that provokes high mortality during infancy.

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Congenital heart disease (CHD) is a structural or functional abnormality of the heart or great vessels that is present at birth.[1,2] It is one of the major diseases among children, the most common birth defect, and the

main cause of infant death from congenital defects.[1,3] It is estimated that two-thirds of affected patients are critical in the first year of life, and only few of them can reach adulthood either by natural selection or by successful palliative or curative surgery.[1,4] Its etiology is unknown, but it seems to be multifactorial, mainly related to the interaction between genetic and environmental factors. Congenital heart disease is an important cause of infant death in developed and undeveloped countries. In developed countries, the number of babies born with CHD has been reduced after timely therapeutic abortion, and survival has improved after surgical correction. Contrary, in undeveloped countries where health services are insufficient or accessible only for wealthy people, the vast majority of patients die or are left undiagnosed. Yemen is an undeveloped country. It is the poorest and the most populated country in the Arabian Peninsula. The majority of its population is illiterate, the fertility and birth rate are one of the highest in the world, and the majority of births occur at home.[5,6] There is a shortage of health services, prenatal and postnatal services are not available in hospitals, and control of CHD is not a health priority yet. Therefore, a high mortality rate is expected, a large number of patients are undiagnosed or lately diagnosed, with few opportunities for surgical intervention. There is insufficient statistics and information regarding this disease. As far as we know, unfortunately, there are neither community-based data nor publications regarding the prevalence, incidence, pattern, and mortality rate of CHD in any city of Yemen. Hospital's statistic data and experts' estimation are insufficient and unreliable. Estimation is based on criteria of non-specialized staff; patient's data is not properly collected, and generally incomplete. Therefore, professionals and health authorities underestimate the true burden of this disease. Echocardiography was introduced in Aden city at the ends of 1999 to provide services for the Southern Yemeni governorates. This accurate, non invasive, and economic method, which has revolutionized the diagnosis and management of heart diseases, allowed the establishment of the pattern of cardiovascular disease in this region for the first time.[7] The CHD ranked the third most common heart disease among referred patients, the second among young, and the first among children. The aim of this research is to assess the distribution of age, gender, and the relative frequency of congenital heart defects in Southern Yemeni children at the time of the diagnosis. The results will help to appreciate the burden of this disease in Yemen, and alert the authorities and professionals of its seriousness.

Methods. This is a retrospective study based on echocardiographic finding. The study was carried out from January 2001 to December 2005, in the sole referral echocardiography department located in the regional hospital (Algamhuria Teaching Hospital) that attends the Southern Yemeni governorates (Aden, Lahij, Dala, Abyan, and Shabwa). Ethical approval was obtained from the Ethics Committee of Aden Faculty of Medicine. Patient consent was obtained from patient's parents before echocardiography. A total of 987 children (aged from birth to 15 years) with suspicion of heart disease were referred for echocardiography from the community or local hospitals by general practitioners or pediatricians. They had never been seen by a cardiologist. The main referral reasons were clinical signs (heart murmur, cyanosis) or symptoms suggesting CHD. Transthoracic M-mode, 2D, and Doppler echocardiography (pulsed, continuous-wave, and color flow mapping) were performed in different views. Standard diagnostic echocardiographic criteria were used to identify the congenital defects according to their structural characteristics and/or hemodynamic effects. The CHD was classified into cyanotic or non-cyanotic according to the standards established.[8] The diagnosis was considered delayed in the following conditions: when it was not recognized before patient referral, children delivered at home without physician supervision, cyanotic patients after being discharged from the birth clinic, patient with systolic murmur discovered during routine investigations, and children who were diagnosed when symptoms or hemodynamic changes appeared. Patients with more than one heart defect were classified according to the malformation that precipitated the presentation and produced the major hemodynamic disturbance. Severity of CHD was considered 'complex' when a valve or chamber was atretic or hypoplastic, 'significant' when treatment was mandatory, and 'minor' when surgical intervention was unnecessary.[9] Patients aged more than 15 years and those that had mitral valve prolapse, minor abnormalities of the great veins or branches of the aortic arch, congenital arrhythmias, hypertrophic or dilated cardiomyopathy, rheumatic heart disease, and bicuspid aortic valve without stenosis or regurgitation were excluded. Congenital anomalies were classified according to the International Classification of Disease (ICD-10).[10] Echocardiography findings were recorded into a computerized database and retrospectively analyzed.

The Statistical Package for Social Sciences version 10.0 for Windows (SPSS Inc., Chicago, IL., USA) was used for analysis. The results were expressed by percentages and averages (mean ± standard deviation). Medians were compared through Kruskal-Wallis test. A value of $p \leq 0.05$ was considered significant.

Results. Out of 987 referred children (age ranged from birth to 15 years), only 393 (39.8%) were diagnosed as having CHD (mean age, 3.45±4 years; median, 1.3

Table 1 - Distribution between cyanotic and non-cyanotic heart disease according to different age groups.

Age group	Non-cyanotic n (%)		Cyanotic n (%)		Total n (%)	
0-29 days	0	(0.0)	5	(8.5)	**5**	**(1.3)**
1-12 month	122	(36.5)	34	(57.6)	**156**	**(39.7)**
1-5 years	112	(33.5)	20	(33.9)	**132**	**(33.6)**
6-10 years	59	(17.7)	0	(0.0)	**59**	**(15.0)**
11-15 years	41	(12.3)	0	(0.0)	**41**	**(10.4)**
Total	**334**	**(100)**	**59**	**(100)**	**393**	**(100)**

Table 2 - Relative frequency of congenital heart disease (N=393).

Heart defects	n	(%)
Non-cyanotic		
Ventricular septal defect	104	(26.5)
Pulmonary stenosis	69	(17.6)
Patent ductus arteriosus	68	(17.3)
Atrial septal defect	62	(15.8)
Endocardial cushion defect	16	(4.1)
Aortic valve lesions	12	(3.1)
Coarctation of the aorta	3	(0.8)
Total	**334**	**(85.0)**
Cyanotic		
Fallot's tetralogy	35	(8.9)
Transposition of the great arteries	12	(3.1)
Tricuspid atresia	5	(1.3)
Double outlet right ventricle	3	(0.8)
Ebstein's anomaly	2	(0.5)
Truncus arteriosus communis	2	(0.5)
Total	**59**	**(15)**

Table 3 - Gender ratio and mean age at diagnosis of specific congenital heart diseases.

Heart defects	Male: Female ratio	Mean age (months)
Non-cyanotic		
Aortic lesions (stenosis, regurge or both)	1.4:1	58.9
Pulmonary stenosis	1:1	56.7
Atrial septal defect	1.6:1	52.3
Patent ductus arteriosus	0.4:1	45.8
Ventricular septal defect	1.1:1	41.8
Coarctation of the aorta	2:1	36.0
Endocardial cushion defect	0.5:1	17.6
Total of non-cyanotic	**0.9:1**	**47.1**
Cyanotic		
Fallot's tetralogy	0.7:1	13.2
Ebstein's anomaly	1:1	12.0
Double outlet right ventricle	0.5:1	8.0
Truncus arteriosus communis	1:1	7.0
Tricuspid atresia	Male	1.6
Transposition of the great arteries	0.7:1	1.4
Total of cyanotic	**0.8:1**	**9.3**
Overall heart defects	**0.9:1**	**41.4**

year); they comprised 189 (48%) males (mean age 3.3±4.0 years), and 204 (52%) females (mean age 3.5 ± 4.0 years). Most patients (59%) were older than one year. The majority of patients (85%) were non-cyanotic, of them 64% were older than one year. Cyanotic defects were detected in 59 patients; approximately 66% were infants less than one year. There were only a few neonates and all of them were cyanotic. The distribution of the patients according to type of lesion (non-cyanotic and cyanotic) and age groups is seen in **Table 1**. **Table 2** shows that ventricular septal defect was the most frequent form of CHD. It was followed in descending order by pulmonary stenosis, patent ductus arteriosus, and atrial septal defect. Tetralogy of Fallot and transposition of great vessels were the most frequent cyanotic defects. The majority of non-cyanotic defects (94%) were isolated. Associated defects were under-represented. The association was mainly between ventricular septal defect with atrial septal defect (8.5%); patent ductus arteriosus (3.8%), and pulmonary stenosis (0.9%). **Table 3** shows that there was no predominance of gender in the overall CHD or in the cyanotic group. However, there was certain predominance of female gender within non-cyanotic defects (p=0.04) and males within those with patent ductus arteriosus (p=0.004). All patients with tricuspid atresia were male.

Patients suspected of CHD were referred late. Cyanotic patients were referred mainly during infancy; most non-cyanotic from early infancy to late childhood, but rarely during the neonatal period. Within the non-cyanotic group, endocardial cushion defect was diagnosed earlier than aortic lesions, pulmonary stenosis, and atrial septal defect. Within the cyanotic defects, transposition of the great arteries and tricuspid atresia were diagnosed during the neonatal period and early infancy, while Fallot's tetralogy and Ebstein's anomaly were diagnosed in later life. Patients with defects of higher risk of death during the first weeks of life (severe coarctation of the aorta, critical aortic stenosis, interrupted aortic arch, hypoplastic left heart syndrome, pulmonary atresia, critical pulmonary stenosis, and total anomalous pulmonary venous connection) did not present. **Table 4** shows that the age at diagnosis of Yemeni children with congenital heart defects was significantly different to other countries (p=0.000).

Discussion. The pattern of CHD varies depending upon patient's age and country development. Studies on patients of different ages reveal that complex defects (hypoplastic left heart syndrome, mitral, and aortic atresia) are common in the autopsy of fetus and neonates;[9] significant defects (transposition of great

Table 4 - Age of patients at diagnosis of congenital heart defects in different countries.

Age	Present study (Yemen) (N=393)	Smitha[22] (India) (N=794)	Alabdulgader[20] (Saudi Arabia) (N=740)	Subramanyan[21] (Oman) (N=992)	Bolisetty[19] (Australia) (N=108)
<1 month	1	17	24	38	73
1–12 months	40	42	53	40	25
1-15 years	59	41	23	22	2
Data are expressed as %					

arteries, Fallot's Tetralogy, and so forth) predominate in neonates and infants,[1,3,4] and minor defects (ventricular septal defect, patent ductus arteriosus, atrial septal defect, and so forth) in older children. In developed countries, this pattern has been modified in such a way that nowadays, CHD is considered a disease of adults as well as of children.[11] The use of echocardiography and routine clinical screening of neonates and infants allow the detection of heart defects at a very early stage, which makes the decision on therapeutic abortion or early surgical correction easier.[12,13] In developing countries, where there is a shortage of health services, however, the pattern still resembles that of the presurgical era.[14] The majority of patients are never diagnosed, those in critical stages die, and survivors are diagnosed too late. In Yemen, there are not prenatal and postnatal medical services, the majority of childbirth occurs at home, and necropsy has not been included within the medical practice yet. Therefore, it is difficult to carry out studies based on neonatal screening in order to ascertain the true pattern of the CHD. However, the introduction of echocardiography in Aden city allowed gathering the first information regarding this disease and concluding that it is one of the most frequent heart diseases.[7,15] The present paper is the first echocardiographic study on CHD carried out in this region. It is limited to findings of transthoracic echocardiocardiography of referred patients; transesophageal echocardiography is not available to confirm the diagnosis of specific lesions. So, rather than establish the real prevalence and incidence of this disease, it will provide preliminary idea on its spectrum and burden. It seems that the majority of patients with CHD in Yemen are never or lately diagnosed. According to this research, symptomatic children are referred generally late. They only have the opportunity to receive medical attention in non-specialized general hospitals or in the sole referral obstetric-pediatric hospital located in Aden, where there are neither proper equipment nor enough nurseries; neither cardiologists, nor neonatologists. Asymptomatic patients or those with mild lesions are rarely diagnosed. Neonates and infants with multiple organs lesions and suspicion of CHD are neglected or occasionally referred. Those with significant and complex defects (high risk of death) die soon after birth.[5,16-18]

Taking into consideration that the incidence of CHD reported in different countries[4] is approximately 9/1000, and the official census data in the Southern Yemeni Governorates reports 27,200 live births per year,[5] it is expected that nearly 245 children are born with CHD every year. According to this research, CDH was detected in 393 patients over 5 years, (average 79 per year). So, it is assumable that only 32% of the patients affected with CHD are diagnosed annually in this region of the country. In developed countries (Australia),[19] the majority of patients are diagnosed during the neonatal period. In neighbor rich countries (Saudi Arabia and Oman)[20,21] with similar social and cultural traditions to Yemen, or in countries with similar economic conditions (India),[22] the diagnosis is made mainly during infancy. However, in Yemen the majority of patients are diagnosed after infancy. The relative frequency distribution of heart defects found in this study is similar to that documented in the literature.[1,20,21] Children in Yemen, as in other countries with similar socio-economic conditions, are referred almost always when an evident heart murmur is discovered during clinical examination for other causes rather than CHD or when parents request specialized medical help for symptomatic children. Asymptomatic patients with mild lesions or those mildly symptomatic might not be detected until they are in a critical stage in late childhood or adulthood. Compared to studies carried out in Australia,[19] Saudi Arabia,[20] Oman,[21]and India,[22] in this study there is absence of critical cases and under-representation of cyanotic and multiple defects. Probably, patients are left undiagnosed,[23] neglected, or die during early infancy or neonatal period from duct-dependent lesions,[4] (Prostaglandin E1 is not used yet).

There are various reasons for the late detection of CHD in Yemen. There is no national program for detection and control of the disease; so, referral is not compulsory. The possibility for cardiac surgery locally is scanty. There are only a few cardiologists and pediatricians, and general practitioners are not trained to recognize and manage CHD. Patients fall into hands of unqualified self-proclaimed "cardiologists" or pediatricians that have never been alerted that clinical examination has little diagnostic value while

echocardiography is the key. Parents are not aware of the disease or cannot afford health services. In addition, people's beliefs consider infant mortality as a blessing; after the babies died, they are converted into angels who aid their parents in entering paradise. The mortality rate of children under 5 years in Yemen is one of the highest in the world.[5,6] It is mainly attributed to malnutrition and infectious diseases,[16,24] but less to CHD. It is known that in countries where these diseases are controlled and childbirth has become hospital centered, CHD is the first cause of death.[1,3] On the other hand, routine neonatal examination fails to detect a considerable number of affected children.[17] So, it can be assumed that in Yemen, where deliveries are carried out at home by non-skilled attendants and newborns are not routinely examined by physicians, even in hospitals,[5,23] CHD is a silent major cause of death.

It can be concluded that CHD is a serious health problem for Southern Yemeni children. Neonates and infants are not routinely checked. The diagnosis is made mainly for symptomatic patients who have access to medical services. Its pattern is characterized by simple, potentially correctable heart defects, under-representation of cyanotic, and absence of critical defects that cause higher mortality during infancy. In order to overcome this situation, it is recommended to detect antenatal risk factors, introduce fetal echocardiography, terminate pregnancy in complex cases, and encourage hospital delivery. Also, train the health personnel to carry out routine neonatal and infant examination, including pulse oximetry and refer patients early to the cardiologists. These measurements are the corner stone to reduce the incidence of the disease and the mortality rate, prevent irreversible pulmonary vascular disease, improve the quality of life of patients, and the outcome of those undergoing cardiac surgery.

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