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Original Article

Congenital heart disease in 37,294 births in Tunisia: birth prevalence and mortality rate

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Abstract *Aim:* To investigate the previously unknown birth incidence, treatment, and mortality of children with congenital heart disease in Tunisia. *Methods:* We undertook a retrospective review of medical records of all patients who were born in 2010 and 2011, and were diagnosed in Sfax (Tunisia) with congenital heart defect. *Results:* Among 37,294 births, 255 children were detected to have congenital heart disease, yielding a birth incidence of 6.8 per 1000. The most frequently occurring conditions were ventricular septal defects (31%), ostium secundum atrial septal defects (12.9%), and pulmonary valve abnormalities (12%). Coarctation of the aorta, tetralogy of Fallot, univentricular physiology, pulmonary atresia with ventricular septal defect, and transposition of the great arteries were found in 4.3%, 6.2%, 3.4%, 2.7%, and 2.7%, respectively. During the follow-up of 1 year, 23% of the children died. About three-quarters of those deaths happened before surgery. *Conclusion:* The present study is in line with the general estimates in the world. It has revealed a high case of mortality among the patients awaiting corrective surgery. These children need more facilities.

Keywords: Congenital heart defects; epidemiology; developing countries; mortality

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CONGENITAL HEART DEFECTS ARE SERIOUS ANOMALIES that account for nearly one-third of all major congenital anomalies[1] and have a major impact on paediatric morbidity, mortality, and health-care costs.[2] The internationally accepted birth incidence of congenital heart disease is 8‰, although large variations in data occur across studies.[3] In general, it is argued that the birth incidence of congenital heart disease has remained stable over time.[3,4]

In developing countries, congenital heart disease may go unrecognised, resulting in serious morbidity and high mortality rate.[5]

Tunisia is considered among the emerging countries, and since 1970 the government has focused on rheumatic fever, which benefited from an outreach programme. Thus, the incidence of rheumatic fever decreased dramatically. On the contrary, congenital heart defects are diagnosed more frequently, and the number of operated children is increasing. Unfortunately, surgical treatment of neonatal and complex congenital heart disease in Tunisia remains limited.[6]

Indeed, congenital heart defects represent a public health concern with a heavy economic burden owing to the cost of surgery sometimes carried out repeatedly.

In Tunisia, unfortunately, we do not have precise data of the incidence of congenital heart disease due to the lack of a national registry. Therefore, we continue to ignore those data in our population.

Through this study, we aimed to investigate the birth incidence and mortality rate among children with congenital heart disease born in 2010 and 2011 in Sfax.

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Methods

Study population

This population-based study was conducted in Sfax. Sfax is the second largest city in Tunisia with a high population density – 944,500 inhabitants. In our city, 60% of children are born in hospitals and receive a systematic check up from a physician before discharge and when they are 40 days old.

There is only one tertiary care public centre for cardiology that includes paediatric cardiology. Thus, the cases of children with congenital heart disease in Sfax have been evaluated by a paediatric cardiologist either in our public hospital or in the private sector. Hence, all patients registered in our database and those whose cases have been evaluated by our colleagues in the private sector were eligible for inclusion.

Unfortunately, the stillbirths have not been autopsied systematically. However, we included cases of stillbirth with foetal diagnosis of severe congenital heart disease and also cases of antenatal diagnosis of heart defect with postnatal death of within a few hours.

We also asked the department of forensic medicine for cases of children with congenital heart disease.

Definitions

Data were retrospectively retrieved from the medical records. We included gender, date of birth, address, cardiac diagnosis, interventions, and eventual death.

Patients with the following defects were excluded: isolated patent foramen ovale not requiring closure; rhythm disturbances without structural defects; isolated mild peripheral pulmonary stenosis; isolated patent ductus arteriosus not requiring closure; patent ductus arteriosus in preterm infants and in neonates with delay of closure; hereditary disorders without cardiac consequences; and malpositioning of the heart without structural defects. On the other hand, isolated patent ductus arteriosus requiring either a surgical closure or percutaneous closure are included.

Classification of congenital heart disease[7,8]

The left to right shunt includes ventricular septal defects, atrial septal defects, persistence of ductus arteriosus, complete atrioventricular septal defect, atrial septal defect-type Ostium primum, and atrial septal defect-type sinus venosus with or without abnormal venous return.

The cyanotic congenital heart defects include tetralogy of Fallot, pulmonary atresia with ventricular septal defect, transposition of the great arteries, discordant atrioventricular connections, truncus arteriosus, total anomalous pulmonary venous return, tricuspid atresia, Ebstein's anomaly, single ventricle complex, and heterotaxy syndrome.

Left heart obstructive defects include coarctation of the aorta, valvar aortic stenosis, interrupted aortic arch, and hypoplastic left heart syndrome.

Right heart obstructive defects include pulmonary stenosis and pulmonary atresia without ventricular septal defect.

As a considerable number of patients had more than one heart defect, a hierarchic system of classification was adopted, which allowed the inclusion of each patient in only one diagnostic category.[4] We used an anatomical hierarchy, based mainly on anatomical severity, and where there were two or more malformations within the same diagnostic group – left to right shunt especially – we chose the heart defect that required intervention.

To calculate the birth incidence of congenital heart disease and specific heart defects, we needed birth rate information for 2010 and 2011 in Sfax, which was given by the national institute of statistics. Owing to the fact that this study used existing and anonymous data, no informed consent was required.

Results

Birth incidence

In 2010 and 2011, 37,294 births were registered in Sfax. We recorded 255 children with congenital heart disease born in 2010–2011. This yielded a birth incidence of congenital heart disease of 6.8 per 1000 births (Table 1). We also included one case of stillbirth with a foetal diagnosis of hypoplastic left heart syndrome.

By far, the most frequent heart malformation was ventricular septal defect, which accounted for almost 31% of all cases. There were five additional categories of heart malformation – atrial septal defects, atrioventricular septal defect, pulmonary stenosis, coarctation of the aorta, and persistent ductus arteriosus – that occurred in 4–12% of all heart malformations. Hypoplastic left heart, transposition of the great arteries, and tetralogy of Fallot occurred in 1.1%, 2.7%, and 6.2% of all heart defects, respectively. Double-outlet right ventricle was shown to exist in two children (0.78%) and single ventricle/tricuspid atresia in 3.4% of all heart malformations. Truncus arteriosus and pulmonary atresia with intact ventricular septum occurred in 0.4% and 0.7% of heart malformations, respectively.

Of the children with congenital heart disease, 134 were girls (52%) and 121 were boys (48%).

Circumstances of discovery and age at diagnosis of congenital heart disease

Patients with congenital heart disease were referred for many reasons ranging from simple murmur to severe symptoms (Fig 1).

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Table 1. Incidence of congenital heart diseases at birth.

Heart malformation	No. of patients	Mean age at diagnosis (years)	Incidence per 1000 live births	% of all heart malformations
Left to right shunt				
VSD	79		2.1	31%
Large VSD	32	0.24		
Restrictive VSD	47	0.36		
ASD	33	0.46	0.88	12.9%
ASD ostium secondum	29			
ASD sinus venosus	3			
Partial anomalous pulmonary venous return	1			
Atrioventricular septal defect	23	0.23	0.6	9.4%
Complete atrioventricular septal defect	12			
Partial atrioventricular septal defect	5			
Intermediate Atrioventricular septal defect	6			
Patent ductus arteriosus	12	0.68	0.3	4.7%
Cyanotic defects				
Tetralogy of Fallot	16	0.49	0.4	6.2%
Double-outlet right ventricular	2	0.1	0.05	0.78%
Pulmonary atresia with ventricular septal defect	7	0.1	0.18	2.7%
Transposition of the great arteries	7	0.07	0.18	2.7%
Total anomalous pulmonary venous return	1	0.1	0.02	0.4%
Truncus arteriosus	1	0.1	0.02	0.4%
Double discordance	2	0.19	0.04	0.7%
Single ventricle/tricuspid atresia	6/3	0.15	0.16/0.08	2.3%/1.1%
Heterotaxy	1	0	0.02	0.4%
Ebstein's anomaly	1	1.1	0.02	0.4
Left heart obstructive defects				
Coarctation of the aorta	11	0.12	0.3	4.3
Valvar aortic stenosis	3	0.27	0.08	1.1
Interrupted aortic arch	3	0.01	0.08	1.1
Hypoplastic left heart syndrome	3	0.02	0.08	1.1
Mitral stenosis	1	0.01	0.02	0.4
Right heart obstructive defects				
Pulmonary stenosis	30	0.44	0.8	11.7
Pulmonary atresia without ventricular septal defect	2	0.04	0.04	0.7
Others				
Complex heart disease	6	0.48	0.16	2.3
CHD with Marfan syndrome	1	0.2	0.02	0.4
Cantrell syndrome	1	0	0.02	0.4
Total	255			100

ASD = atrial septal defect; CHD = congenital heart disease; VSD = ventricular septal defect.

Foetal diagnosis occurred in only 13 cases: three cases of single ventricle, one case of hypoplastic left heart syndrome, one case of transposition of the great arteries, two cases of tetralogy of Fallot, five cases of atrioventricular septal defect, and one case of double-outlet right ventricle.

The mean age of infants at first contact was 0.29 years. About 21% of cardiac anomaly was diagnosed at <1 week of age and 34% at <1 month of age. In all, 54% were diagnosed between 1 month and 1 year of age, and only 11% were diagnosed at >1 year of age.

Treatment

A total of 77 children were born with ventricular septal defect. Only 24 required surgery, that is, 31% of total ventricular septal defects. Of these, 14 patients underwent surgery; 12 cases were successful and two patients died in the post-operative period. There were eight patients with large ventricular septal defect who died before reaching surgery. The reasons for these eight deaths were hospital infections in the majority of cases.

A total of 23 children were born with a complete or incomplete defect of the atrioventricular septum. Down syndrome was present in 13 children (56%). In children with a complete form of this anomaly (12 cases), surgery was performed in five cases, with one death in the post-operative period. Death occurred in six children before surgery.

Tetralogy of Fallot is the most frequent cyanotic congenital heart defect in our study; it was present in 16 cases. There were two children who died in

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the first half year before surgery: one case with very tight pulmonary stenosis and the second case was agenesis of the pulmonary valve in a premature child. In all, six children underwent surgery with success in Tunisia until the end of this study.

Transposition of the great arteries is the second cyanotic congenital heart defect. There were seven children with this anomaly. Only one case had benefited from foetal diagnosis. All patients but one were treated with the Rashkind procedure. The mean age at diagnosis was 24 days (from 1 day to 71 days). The survivors were not operated on in Tunisia, as this surgery is not available in our country.

In all, 11 children were born with coarctation of the aorta, with nine having a neonatal form diagnosed before the age of 2 months. The latter anomaly was associated with ventricular septal defect in six cases. The mortality rate in this congenital heart defect reached 70%. There were five patients with coarctation of the aorta who died within few days after surgery; these surgeries were performed in Tunisia.

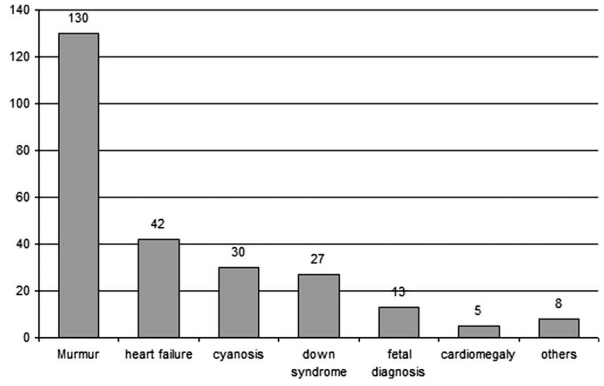

Figure 1.
Circumstances of discovery of congenital heart disease.

Mortality

During the follow-up period of 1 year, 60 children (23.5%) died. The majority of these were boys (52%). Most children in this group died during the first 6 months of life. Table 2 describes the mortality rate according to the primary diagnosis and shows a striking difference in mortality between heart defects. The reasons for deaths were cardiac failure in 24 children, post-operative complications in 12 cases, sudden death in one case, and pulmonary complications, especially respiratory infections, in 21 cases. Infective endocarditis was fatal in two cases: one child with restrictive ventricular septal defect with immunity disorder and another child with successfully operated interruption of the aorta.

Discussion

Several epidemiological studies on congenital heart disease in children have been completed to date. The majority of these studies relied on data

Table 2. Description of mortality cases according to the primary diagnosis.

Heart malformation	No. of patients	No. of deaths (mortality in each malformation)	No. of patients who died before surgery
Large VSD	32	10 (31%)	8
Infective endocarditis complicating VSD	1	1	1
Partial anomalous pulmonary venous return with or without sinus venosus ASD	4	1 (25%)	1
Complete atrioventricular septal defect	12	6 (50%)	5
Tetralogy of Fallot	16	2 (12.5%)	2
Double-outlet right ventricular	2	2 (100%)	2
Pulmonary atresia with or without ventricular septal defect	9	6 (66%)	5
Transposition of the great arteries	7	3 (42%)	3
Total anomalous pulmonary venous return	1	0	0
Truncus arteriosus	1	1 (100%)	1
Univentricular physiology	9	6 (66%)	5
Heterotaxy	1	1 (100%)	1
Coarctation of the aorta	11	8 (72%)	3
Critical valvar aortic stenosis	1	1 (100%)	1
Interrupted aortic arch	3	3 (100%)	2
Hypoplastic left heart syndrome	3	3 (100%)	3
Mitral stenosis	1	1 (100%)	1
Critical pulmonary stenosis	2	0	0
Complex heart disease	6	4 (66%)	4
Double discordance	2	1 (50%)	0
Total	124	60	48

ASD = atrial septal defect; VSD = ventricular septal defect.

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collected by national registries in developed countries. In Tunisia, and with regard to the extent of coronary artery disease, congenital heart disease seems to be orphan. Thus, this study has the merit to be the first one that gives an estimation of the incidence of congenital heart disease. This was possible, first, because of computerisation of all reports of echocardiography in our tertiary department, and second because of a real collaboration between cardiologists in both public and private sectors.

Epidemiological data

The birth incidence of congenital heart disease of 6.8 per 1000 births in the present study is in line with the general estimates in the world.[3] Nonetheless, this incidence is lower than that usually found in Europe,[9] for which the average incidence is 8‰. It would be closer to those found in other developing countries,[10,11] where the lack of national registry and population-based surveys hampers such a comparison.

To determine the birth prevalence of congenital heart disease in our sample, we included young patients who were diagnosed within their first 2 years of life (2010–2011). Therefore, with this approach, we definitely missed about 8% of heart defects that diagnosed after the age of 5.[12] It is obvious that the prevalence found in our study is an underestimate one.

The prevalence of heart defects found in our study is consistent with that of previous reports. As in other studies, ventricular septal defects, atrial septal defects, and pulmonary valve abnormalities were the most frequently occurring heart defects.[11,13–16] Ventricular septal defects was the most prevalent heart defect in our study, accounting for 31%. The high prevalence of ventricular septal defects in our study and in other reports might be due to the fact that they show clinical signs and symptoms, for example heart murmur.

Comparing our rates with those in the meta-analysis of Hoffman,[3] it may be noted that frequencies of coarctation of the aorta (4.3 versus 4.09) and transposition of the great arteries (2.7 versus 3.1) are consistent with those reported. However, atrioventricular septal defect (9.7 versus 3.4), tetralogy of Fallot (6.2 versus 4.2), pulmonary atresia (3.4 versus 1.3), and univentricular physiology (3.4 versus 1.7) exceeded the rates observed. These high rates could be explained by some overriding risk factors in our city such as consanguinity, diabetes, and above all air pollution. In fact, Sfax is an industrialised city with high exposure to air pollutants – nitrogen dioxide (NO_2), sulfur dioxide (SO_2), particulate matter (PM10) and ozone (O_3).[17] Pollution has been recognised as a congenital heart defect risk factor in some recent studies.[18,19]

Therefore, the diagnosis of different types of congenital heart disease was made not only for most common ones, but also for the complex anomalies and less frequent ones despite the socio-economic level of the population of developing countries. Unfortunately, prenatal diagnosis occurred in only 5%, which is far inferior to that observed at the European study (20.2%).[9]

Treatment and mortality

Data on mortality from congenital heart disease must be interpreted in the context of the medical and surgical care available in the region studied.[20]

The differences in mortality between the industrialised countries and third-world countries are striking, from 3–7% to 20%, respectively. The mortality rate in Belgium did not exceed 4% in a recent study.[16] Significantly high mortality rates have been found in recent reports from African countries.[20,21] The case fatality rate in our study was high, about 23%, which corresponds to the habitual rate found in the developing countries such as Guatemala and Sri Lanka.[22,23] However, it must be considered that with improvement in diagnostic methods the total number of congenital heart disease cases has increased to include less serious or subclinical defects, thus decreasing the relative, but not absolute, mortality.[20] Furthermore, the mortality from congenital heart disease is possibly under-reported in third-world nations because access to diagnosis is more difficult, and the great majority of studies only report data from patients in tertiary centres.[20]

Among the 23% of mortality cases, about three-quarters were observed before undergoing surgery. It may be explained by the initially severe clinical presentation of the patient, which evolved rapidly to death. In addition, socio-economic status and the parents' educational level can influence the consultation time and the speed of the management of the child's case. However, the lack of a near and well-equipped cardiothoracic surgical centre could be a reason for this striking rate of death. In fact, malnourished and hypotrophic children are exposed to respiratory infections while awaiting surgery. In addition, the surgical delay can affect the patient's clinical condition and worsen the prognosis. For example, larger defects – ventricular septal defect – may lead to congestive heart failure, and infants succumb in the early months of life either to cardiac failure or to superimposed respiratory infection.

The reduction in mortality from congenital heart disease, which has been described in the western countries in the last 25 years, can be largely ascribed to three main factors: (1) an increase in prenatal diagnosis of serious disorders and subsequent

terminations[24]; (2) better early diagnosis and access to tertiary care centre of severe congenital heart disease; and (3) large advances in therapeutics, both medical and surgical. This could be a lesson for the governments in developing countries such as ours.

Limitations

Our study has several limitations, and results should be interpreted with caution. First, we included live births in which congenital heart disease was detected – only one stillbirth was included because a known diagnosis of hypoplastic left heart syndrome. In fact, stillbirths are not consistently autopsied, and the frequency of congenital heart disease in this subgroup is unknown. Second, subclinical heart defects are missed as a systematic screening of the entire population is not done. In fact, with high frequency of consanguinity, we could expect higher incidence than industrialised countries, this discrepancy could be explained by misdiagnosed cases. Third, our study included young children, and thus we missed about 8% of congenital heart disease generally diagnosed after the age of 5 years.[12]

Conclusion

Through this study, we have shown a birth prevalence of congenital heart disease of 6.8 per 1000 births. Both the birth prevalence of congenital heart disease and the prevalence of specific heart defects are consistent with international data. However, the mortality rate is striking. Hence, there is an urgent need for the government to establish a well-equipped cardiothoracic surgical and paediatric cardiology unit.[25] Moreover, foetal and neonatal outreach programmes should be implemented, especially in less-favoured regions in the country.

Finally, there is a need to properly identify the extent of this global health problem by determining its true incidence. This can be done by conducting a national study or national registry. This kind of a database will be definitely more convincing.

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References

1. Van der Linde D, Konings EM, Slager MA, et al. Birth prevalence of congenital heart disease worldwide. J Am Coll Cardiol 2011; 58: 2241–2247.
2. Botto LD, Correa A, Erickson JD. Racial and temporal variations in the prevalence of heart defects. Pediatrics 2001; 107: e32.
3. Hoffman JI, Kaplan S. The incidence of congenital heart disease. J Am Coll Cardiol 2002; 39: 1890–1900.
4. Wren C, Richmond S, Donaldson L. Temporal variability in birth prevalence of cardiovascular malformations. Heart 2000; 83: 414–419.
5. Kuehl KS, Loffredo CA, Ferencz C. Failure to diagnose congenital heart disease in infancy. Pediatrics 1999; 103: 743–747.
6. Stolf NA. Congenital heart surgery in a developing country: a few men for a great challenge. Circulation 2007; 116: 1874–1875.
7. Riehle-Colarusso T, Strickland MJ, Reller MD, et al. Improving the quality of surveillance data on congenital heart defects in the metropolitan Atlanta congenital defects program. Birth Defects Res A Clin Mol Teratol 2007; 79: 743–753.
8. Reller MD, Strickland MJ, Riehle-Colarusso T, et al. Prevalence of congenital heart defects in metropolitan Atlanta, 1998–2005. Pediatr 2008; 153: 807–813.
9. Dolk H, Loane MA, Garne E and a European Surveillance of Congenital Anomalies (EUROCAT) Working Group. Congenital heart defects in Europe: prevalence and perinatal mortality, 2000 to 2005. Circulation 2011; 123: 841–849.
10. Vaidyanathan B, Sathish G, Mohanan ST, et al. Clinical screening for congenital heart disease at birth: a prospective study in a community hospital in Kerala. Indian Pediatr 2011; 48: 25–30.
11. Samanek M, Voriskova M. Congenital heart disease among 815,569 children born between 1980 and 1990 and their 14-year survival: a prospective Bohemia survival study. Pediatr Cardiol 1999; 20: 411–417.
12. Wren C, O'Sullivan JJ. Survival with congenital heart disease and need for follow up in adult life. Heart 2001; 85: 438–443.
13. Bosi G, Garani G, Scorrano M, Calzolari E. Temporal variability in birth prevalence of congenital heart defects as recorded by a general birth defects registry. J Pediatr 2003; 142: 690–698.
14. Calzolari E, Garani G, Cocchi G, et al. Congenital heart defects: 15 years of experience of the Emilia-Romagna Registry (Italy). Eur J Epidemiol 2003; 18: 773–780.
15. Marelli AJ, Mackie AS, Ionescu-Ittu R, Rahme E, Pilote L. Congenital heart disease in the general population: changing prevalence and age distribution. Circulation 2007; 115: 163–172.
16. Moons P, Sluysmans T, De Wolf D, et al. Congenital heart disease in 111,225 births in Belgium: birth prevalence, treatment and survival in the 21st century. Acta Pædiatrica 2009 ; 98: 472–477.
17. Annual reports on air pollution in Tunisia: http://www.anpe.nat.tn/index.php?option=com_content&view=article&id=175%3Abulletins-et-rapports&catid=64%3A-pollution-de-lair-&Itemid=184&lang=fr
18. Ritz B, Yu F, Fruin S, Chapa G, Shaw GM, Harris JA. Ambient air pollution and risk of birth defects in Southern California. Am J Epidemiol 2002; 155: 17–25.
19. Vrijheid M, Martinez D, Manzanares S, et al. Ambient air pollution and risk of congenital anomalies: a systematic review and meta-analysis. Environ Health Perspect 2011; 119: 598–606.
20. Mocumbi AO, Lameira E, Yaksh A, Paul L, Ferreira MB, Sidi D. Challenges on the management of congenital heart disease in developing countries. Int J Cardiol 2011; 148: 285–288.
21. Awori MN, Ogendo SW, Gitome SW, Ong'uti SK, Obonyo NG. Management pathway for congenital heart disease at Kennyatta National Hospital, Nairobi. East Afr Med J 2007; 84: 312–317.
22. Trucco SM, Barnoya J, Larrazabal LA, Castañeda A, Teitel DF. Detection rates of congenital heart disease in Guatemala. Cardiol Young 2011; 21: 153–160.
23. Wickramasinghe P, Lamabadusuriya S, Narenthiran S. Prospective study of congenital heart disease in children. Ceylon Med J 2001; 46: 96–98.
24. Kovalchin JP, Silverman NH. The impact of fetal echocardiography. Pediatr Cardiol 2004; 25: 299–306.
25. Yacoub MH. Establishing pediatric cardiovascular services in the developing world. Circulation 2007; 116: 1876–1878.