Profile and Risk Factors for Congenital Heart Disease

Pages with reference to book, From 78 To 81

Imran Hassan, Abdul Ahad Haleem, Zulfiqar Ahmed Bhutta (Department of Paediatrics, The Aga Khan University Hospital, Karachi.)

Abstract

Congenital heart disease is an important cause of infant mortality and disability. The frequency, spectrum and contributory risk factors for significant cardiovascular malformations among live-births was retrospectively evaluated at the Aga Khan University Hospital. Of a total of 8331 live births between July, 1987 and December, 1992 34babieswere diagnosed to have congenital heart diseasein the neonatalperiod giving a prevalence of 4 per 1000 live births. Ventricular septal defects was the most common (n=10, 29%) abnormality. Eight cases had associated chromosomal abnormality, the most common being Trisomy 21. Maternal abortions, still-births, consanguinity and diabetes mellitus were not found to be significant risk factors for congenital heart disease in this survey (JPMA 47: 78,1997).

Introduction

Congenital heart disease (CHD) includes major structural malfonnations of the heart and/or major vessels present at, or persisting abnormally after birth[1]. The prevalence of congenital heart disease (CHD) atbirthhasbeen relatively variable at 4.05 to 10.4 cases per 1000 live births in different surveys using avariety of case discovery methods[2-4], In a meta analysis using only cases “confinned” by autopsy, surgery, cardiac catheterization or echocardiography, the birth prevalence was nearly constant at approximately 4 per 1000 live births[5].

Despite the importance of CHD as a cause of infant mortality and disability, the exact etiology of these anomalies remans mostly unknown[6]. Approximately 80-90% of these cases have a genetic-environmental interaction[7], Classic Mendelian single gene defects account for about 3-5% and chromosomal defects for 5-8% cases of CHD. The most common defect is Trisomy 21, but Trisomy. 13, Trisomy 18 and the 45X0 (Turners syndrome) can also be involved[2-7]. Pnmaiy environmental factors are the etiological cause in the remaining 2-3% cases[7]. These include the drug Thalidomide and rubella virus as the classical causes of CHD. As a result of cultural and religious factors not permitting autopsies, lack of population studies and limited resources very few reports on, CHD am available, from Asian and African countries including Pakistan. Yet it is important to find out the possible role of various environmental and -genetic factors and to determine antenatal risk factors for CHD in our population. Similarly information on the prevalence and spectrum of CHD is necessary to develop effective paediatnc cardiology services for their management and treatment among Pakistani newborn infants.

Methodology

Retrospective analysis of all live births with CHD delivered at the Aga Khan University Hospital between July, 1987 and December, 1992 were analysed and case control analysis done on CHD cases without chromosomal anomalies. All live births who during the neonatal period (initial hospitalization and first postnatal visit, between 2 1-28 days of age) were clinically suspected to have CHD and subsequently confirmed to have a significant cardiovascular malformation by echocardiography were included. For each case, a control was identified as the next consecutive live birth without any

congenital malformation, matched for sex and weight. Premature infants with patent ductus arteriosus (PDA) were excluded from the study. Maternal and neonatal data was collected from the medical files using data extraction sheets. Data was analyzed using the statistical package for social sciences (SPSS) (Windows 6.1 1994 Chicago, USA). Umvariate methods were used forcalculationof odds ratio and corresponding 96% confidence intervals and analysis of variance employing the two-tailed students t-test was used for evaluation of continuous data, Significance was set at 5%.

Results

A total of 34 new borns were diagnosed to have a significant congenital heart disease (CHD) during the neonatal period out of a total of 8331 live births. The prevalence of CHD in neonates was found to be 4 per 1000 live births. The most common cardiovascular malformation detected was ventricular septal defect(VSD) (n=10) followed by patent ductus arteriosus (PDA) (n=7) (Table I).

Table I. Comparative prevalence of congenital heart disease among different studies.

Congenital defects	Our study[6]		Toronto[6]	Denmark[6]	Minnesota[6]	Liverpool[11]	India[11]	Saudi Arabia[12]	Singapore[13]
	No.	(%)	%	%	%	%	%	%	%
Ventricular septal defect	10	(29)	31	24	34.6	32.5	56	74	28
Patent ductus arteriosus	7	(20)	7.1	12.6	10.6	11.9	-	2	10
Tetralogy of Fallot	3	(9)	8	5.8	5	5.9	-	1	13
Atrial septal defect	2	(6)	11.2	9.4	7.3	5.9	-	8	-
Transposition of great vessels	2	(6)	2.6	4.8	7.8	5	8	-	6
Left hypoplastic heart syndrome	2	(6)	-	3	4.5	2.8	8	-	-
Total pulmonary anomalous venour drainage	2	(6)	-	1.4	2.8	0.8	-	-	-
Pulmonary artery stenosis	2	(6)	10.8	5.9	5	7.6	-	-	-
Atrio ventricular defect	1	(3)	-	2.6	4.5	2.4	-	-	-
Situs inversus	1	(3)	-	-	-	-	-	-	-
Pulmonary atresia	1	(3)	-	-	-	-	-	-	-
Right hypoplastic heart	1	(3)	1.1	1.8	3.4	2.5	-	-	-
Coarctation of aorta	-		3.4	7.0	5.6	6.3	4	1	-
Aortic stenosis	-		8.4	4.7	6.1	5.1	-	-	-
Miscellaneous	-		16.4	15.7	2.8	8	24	14	42

*includes 4 cases of PS with VSD.

There were 8 cases with chromosomal abnormalities, of which there were 7 cases of Trisomy 21 and 1 ofTrisomy 18. Congenital rubella syndrome was the etiological cause in 2 cases, while in the remaining cases no definite etiology could be ascertained.

Table II. Maternal and perinatal risk factors for neonates with congenital heart disease without chromosomal anomalies.

Risk factors	Case		Controls		OR	95% C.I.	p-value
	No.	(%)	No.	(%)			
Abortion	6	(22)	11	(20)	1.10	0.36-3.43	
Still-births	1	(4)	4	(7)	0.48	0.05-4.5	
Consanguinity	6	(22)	14	(26)	0.97	0.69-1.36	
Diabetes	1	(4)	6	(11)	0.30	0.03-2.6	
Apgar 1	6.8±2.0		7.7±1.2				0.021
Apgar 5	8.6±1.3		9.0±0.5				0.01
Gestation (wks)	38.8±1.3		38.4±1.2				0.932
Birth weight (g)	3008.8±527.1		3044.8±483.0				0.610

Data as n (%) or mean±SD
OR = Odds ratio
95%CI = 95% Confidence interval

Table II lists maternal risk factors and neonatal characteristics at birth for non-chromosomal cardiovascular malformations. No association of CHD was found with antenatal conditions such as abortions, still-births and maternal diabetes mellitus. Consanguinity was also not significantly associated with cardiovascular malformations. Affected newborn infants were morç likely to have lowerapgar scores of 1 and 5 minutes at birth however, there was no significant difference in the birth weight or gestation of the cases.

Discussion

The 4 per 1000 live birth prevalence of CHD among Pakistani newborn infants delivered at this hospital may be considered as an under-estimate of the actual figure. Firstly, many cases of CHD such as those with minimal pulmonic stenosis or very small ventricular or atrial defects, may not become clinically evident in the neonatal period and therefore not be diagnosed by ordinary clinical examination[2]. Secondly only 40-50% of cases with CHD are diagnosed in the first week and 50-60% in the first month after birth[2]. Since our study only included cases diagnosed during the neonatal period, a significant number of cases which were diagnosed after the first month of birth, may have been missed. Another important factor in assessing the actual incidence of CHD is the fact that the incidence appears to be approximately 5 times higher in still-born fetuses and abortuses than in live born infants[2]. However, the malformations in abortuses and intrauterine deaths are usually excluded from estimates of prevalence of CHD in birth cohorts. By not considering the incidence of CHD in pre-natal deaths, in children with minimal CHD and those cases detected after the neonatal period, the potential importance of genetic and chromosomal factors is grossly under-estimated. At the same time the importance of environmental teratogens may be incorrectly assessed. However, even though this figure may be an under-estimate of the actual incidence, it still represents a significant thsease'burden on the health system.

The spectrum and incidence of various cardiac lesions in this series is similar to what has been reported elsewhere. According to Hoffman[2] various social, religious and economic factors may prevent infant receiving medical care and autopsies in several Asian and African countries. Therefore, serious cardiac lesions that cause early death and very mild lesions may be under represented in reported series from these countries. This may be one of the possible explanations for the difference in distribution of various cardiac lesions in this study as compared to other reports. For example, the difference in the incidence of the most common lesion i.e., ventricular septal defect (VSD) between different reports, is because clinically inevident defects, only detectable by invasive methods, were included in several of the studies. Differences in the incidence rate of rare lesions can also be due to relatively small numbers of these lesions in each series. However, prevalence rate of CHD reported here is similar to the figures cited from a population based study of live births by Ferencz et al[14], although lower figures have been reported among a review of over a million live births fmm the New England Regional Infant Cardiac Programme[15]. The prevalence of cardiovascular malformations in Trisomy 21 is reported to be about 40~50%[8-10]. While the incidence of Trisomy 21 in reported series of children with CHD ranged from 3.2 to 10.4%, none of them mentioned maternal age, in any detail[2]. In this study of live births with CHD, 20% of the cases had Trisomy 21, whereas the proportion of mothers older than 35 years of age was 6% of the total maternal population. It is therefore difficult to attribute the greater proportion of cases with CHD due to Trisomy 21 in this sample, to agreater number of elderly mothers orto alternative undetermined factors.

In this study certain maternal conditions of the cases without chromosomal abnormalities during the previous and current pregnancies were investigated to evaluate their association with CHD. Of these factors maternal abortions, still-births, consanguinity and maternal diabetes inellitus[16] were not

associated with a significant risk of CHD. However, newborns with CHD were overall found to be more depressed at birth in our study in comparison with controls. Several other workers have also failed to identify any clear etiological factors for CHD[17]. The intake of drugs during early pregnancy is hazardous because they are responsible for 1.5% of all congenital anomalies and most drugs have not been tested in humans[5]. Known cardiogenic teratogens include lithium, hydantoin, retinoic acid, amphetamines and maternal hormonal therapy[5]. Several reports have suggested that amphetamines and salicylate intakes could also cause cardiovascular malformations[15,16]. Maternal drug intake could not be ascertained as a possible risk factor in this series because of incomplete documentation in the medical record. It is important to monitor and document all maternal drug intake during the antenatal period and to avoid unnecessary use of drugs, especially during the first trimester. This survey from a well defined obstetric population with neonatal follow-up suggests that CHD represents a significant burden of congenital malformations. The present data does represent some differences from the pattern of congenital heart disease among referred children in other series fmrn Pakistan, which contained mostly older children[18,19]. Thus rates of PDA are proportionately higher in this series than tetralogy of Fallot. Considering the additional children who acquire heart disease from rheumatic fever each year, these data represent a substantial burden of heart disease in the paediatric age group. This has important implications in the future development of paediatric cardiac services including the training of pediatricians inPakistan.It is also essential to carry out further multi-center and population based studies to determine and validate various maternal and neonatal risk factors for CHD in Pakistani population at large.

References

1. Hayward, R. and Swanton, H. Congenital cardiovascular abnormalities. Br. J. Hosp. Med.. 1981;43:211-219.
2. Hoffman, J.I.E. Congenital heart disease: Incidence and inheritance. Pediatr. Clin.North Am., 1990;37:25-43.
3. Mayberry, J.C., William, A. S. and Stanley, J.G. Increased birth prevalence of cardiac defects in Yuma, Arizona. Am. 3. Cardiol., 1990;16:1696-1700.
4. Sadiq, M. and Silove, E.D. A higher prevalence of congenital heart disease in U.K. immigrants of Indian subcontinent; implication in development of pediatriccardiacservices in Pakistan. Pak. Pediatr, J., 1994; 18:153-159.
5. Ferencz, C., Neil, C.A., Boughman, J.A. et al. Congenital cardiovascular malformations associated with chromosome abnormalities. An Epidemiologic study. 3. Pediatr. 1989;114:79- 86,
6. Chandramouli, B. The neonate with congenital heart disease: Diagnosis and management. Indian J.Pediatr., 1991;58:453-469.
7. Tikkanen, J. and Heinonen, OP. Congenital heart disease in the offspring and maternal habits and home exposures during pregnancy. Teratology, 1992,46:447454.
8. Hoe, TS., Chan, K.C. and Boo, N.Y. Cardiovascular malformations in Malaysian neonates with Down's syndrome. Singapore Med. J., 1990;31:474-476.
9. Clark, SB. Congenital cardiovascular defects in infants with Down's syndrome (Commentary). Pediatr.. Rev., 1989;11:99-100.
10. Hoe, T. S., Boo, N.Y. and Clyde, MM. Incidence ofDown's syndrome in a large Malaysian maternity hospital over an 18, month period. Singapore Med. J., 1989;30:24.6-248.
11. Singh, M. and Sharma, N.K. Spectrum of congenital malformation in the newbprn. Indian 3. Pediatr., 1980;4:239-244.
12. Hegazy, SI., Al-Beyari, T.H., Al-Amari, A.H. et al. Congenital malformations in primary health care in Al Qassini region. Ann. Saudi Med., 1995;15:48-53.

13. Thein M.M., Koh, D., Tan, K.L. et al. Descriptive profile of birth defects among live births in Singapore. Teratology, 1992;4.6:277-284.
14. Ferencz, C., Rulein, J.D., MeCarter, R.J, et al. Cardiac and non- cardiac malformations: Observations in a population based study. Teratology, 1987;35:367-78.
15. Fyler, D.C., Buckley, L.P.,Hellenbrand, W. et al. Report of the New England Regional Infant Cardiac Program. Pediatrics, 1980;65(Suppl):377-461.
16. Chung, CS. and Myrianthopoulos, NC. Factors affecting risks of congenital malformations. 1- Analysis of epidemiologic features in congenital malformations: Report from the collaborative perinatal project. Birth Defects, 1975;11:1-22.
17. Pycritz, RE. and Murphy, E.A. Genetics and congenital heart disease: Perspectives and prospective. J. Am. CoIl. Cardiol., 1989; 13:1458-68.
18. Rahirntoola, R.J., Majid, I., Shafqat, H. et al. Congenital heartdisease in children visiting JPMC. Pak. Heart 3., 1980; 13:21.
19. Aziz, K. Incidence of heart disease in children at the National Institute of Cardiovascular Diseases in children. Karachi Shakoorsons, 1991. pp. 1-5.