RESEARCH BRIEF

Extracardiac Birth Defects in Children with Congenital Heart Defects

SUNIL KARANDE, VARSHA PATIL, ARCHANA KHER AND MAMTA MURANJAN

From Genetic Clinic, Department of Pediatrics, Seth GS Medical College and KEM Hospital, Parel, Mumbai, India.

Correspondence to: Dr Sunil Karande, Professor, Department of Pediatrics, Seth GS Medical College and KEM Hospital, Parel, Mumbai 400 012, India. karandesunil@yahoo.com

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Objective: To assess the proportion and pattern of extracardiac birth defects in children with congenital heart defects referred to a tertiary care institute.

Methods: Cross-sectional observational study from January 2010 to June 2011.

Results: Out of 560 children with congenital heart defects, 98 (17.5%) had extracardiac birth defects. Fifty-six had multiple congenital defects; 36 were syndromic cases and 6 had laterality defects. A total of 386 extracardiac birth defects (103 major and 283 minor) were documented, with craniofacial and skeletal birth defects being the commonest.

Conclusion: Extracardiac birth defects are common in children with congenital heart defects.

Keywords: *Congenital heart disease, Craniofacial abnormalities, Syndrome.*

Congenital heart defects (CHDs) are a common variety of birth defects, with an overall prevalence of 8.1/1000 births [1]. They account for approximately one third of all congenital anomalies, and are the single largest contributor to infant mortality attributable to birth defects [2]. Clinical studies have reported that up to 30% of children with CHDs may have additional extracardiac birth defects that may further add to the morbidity and mortality [3,4]. Data regarding proportion and pattern of these defects in Indian children with CHDs are scarce. We planned this study to assess the proportion and profile of extracardiac birth defects in children with CHDs to referred to a tertiary care hospital in Mumbai, India.

METHODS

This cross-sectional observational study was conducted at a tertiary care institute in Mumbai after approval from its Institutional Ethics Committee. The study was conducted over a period of 18 months (from January 2010 to June 2011). Children (age 1 day to 12 years) with CHDs from pediatric outpatient department, genetic clinic, pediatric wards, pediatric and neonatal intensive care units; and cardiology and cardiovascular and thoracic surgery outpatient departments and wards), both symptomatic and those incidentally detected, were examined for extracardiac defects . The CHDs were diagnosed on basis of detailed clinical examination, chest *X*-ray, and electrocardiography (ECG); and confirmed by 2D-echocardiography or cardiac catheterization.

The extracardiac defects were diagnosed based on standard definitions [5-11]. Wherever indicated, further investigations like ultrasound (abdomen/skull), computed tomography (CT), audiometry, ophthalmologic evaluation and thyroid hormone profile were done. G-banded karyotype and fluorescence in situ hybridization (FISH) studies (for microdeletions) were performed whenever indicated. Defects were termed as 'major' if they had medical or surgical significance, or serious cosmetic significance [6]. 'Minor' defects were defined as unusual morphologic features not having any serious medical, surgical or cosmetic significance [6].

Only patients with CHDs having associated extracardiac defects were included as study population and were classified into three distinct groups: (*i*) multiple congenital defects (MCDs), (*ii*) syndromes, and (*iii*) laterality defects. MCDs comprised those having at least one major or three minor extracardiac congenital birth defects [6,12]; were further classified into: (*a*) those having an unrecognized pattern, and (*b*) those having a recognized pattern of unknown etiology [12]. Those with chromosomal anomalies, single-gene defects or teratogenic syndromes were counted among syndromes [6,13]. Children having laterality defects (*e.g*., heterotaxy syndromes) were grouped separately [6,13]. The extracardiac defects documented in this study were also grouped into organ systems [14,15].

RESULTS

Out of a total 560 children diagnosed with CHDs during the study period, 98 (17.5%) (52 boys) had associated extracardiac birth defects. The mean (SD) ages at time of

diagnosis of CHD and at time of enrolment were 6.5 (16.9) months and 24.2 (34) months, respectively. Thirteen (13.3%) patients were born of a third-degree consanguineous marriage; 33 (33.7%) had global developmental delay.

Sixty-four children had acyanotic CHD and 34 had cyanotic CHD (***Table* I**). In the acyanotic CHD, 14 had ventricular septal defect, 11 had atrial septal defect and 10 had patent ductus arteriosus. In the cyanotic CHD group, tetralogy of Fallot was the commonest defect (*n*=23). ***Table* I** presents the profile of extracardiac defects in study children. Patients with 'MCDs with unrecognized patterns' formed the largest group of cases. All six patients of 'MCDs with recognized pattern of unknown etiology' had VACTERL association. The 36 'syndromic cases' included Down syndrome (*n*=25), velocardiofacial syndrome (*n*=3); Noonan syndrome, CHARGE syndrome, Lenz microphthalmia syndrome, CCGE (cleft palate, cardiac defect, genital anomalies, and ectrodactyly) syndrome, achondroplasia and congenital rubella syndrome (1 each); and two children with undefined syndromes with abnormal karyotype patterns. Among the six children with laterality defects, 5 had situs inversus (without polysplenia/asplenia) and one had heterotaxia (asplenia syndrome).

A total of 386 extracardiac birth defects (103 major and 283 minor) were documented (***Web Table* I**).

DISCUSSION

In the present study, almost one-fifth of children with CHDs had associated extracardiac birth defects. Majority belonged to MCDs group, and craniofacial birth defects were the most frequent. Miller, *et al*. [13] conducted a population based surveillance study of 7984 live-born and stillborn infants and fetuses with CHDs: 1080 (13.5%) had multiple, 1048 (13.1%) had syndromic and 161 (2.0%) had laterality defects [13]. Tennstedt, *et al*. [14] conducted a necropsy study in 815 fetuses; 85 (66%) had extracardiac birth defects with central nervous system birth defects being the most frequent. Gucer, *et al*. [15] conducted autopsies in 305 children with CHDs; 140 (46%) had extracardiac birth defects with craniofacial birth defects being the most frequent.

TABLE I PROFILE OF EXTRACARDIAC BIRTH DEFECTS IN CHILDREN WITH CONGENITAL HEART DEFECTS

Congenital heart defect	Multiple congenital defects *n* (%)		Syndromic *n* (%)	Laterality defects *n* (%)
	Unrecognized pattern	Recognized pattern		
Acyanotic	29 (29.6)	3 (3.1)	28 (28.6)	3 (3.1)
Cyanotic	21 (21.4)	3 (3.1)	8 (8.2)	3 (3.1)

The present study had some potential limitations. The study was based on convenience sampling, and was conducted in a tertiary care hospital setting wherein most of the patients were referred cases. Moreover, we could not do autopsy studies in children with CHDs who died at our institute. Due to financial constraints, small structural cytogenetic abnormalities and single-gene mutations might have remained undiagnosed, resulting in the inadvertent inclusion of some genetically determined cases in the MCDs group.

The treating pediatrician needs to be aware that extracardiac birth defects are common in children with congenital heart defects. Identification of extracardiac birth defects may have implications for clinical practice (such as surgical management of associated anomalies), early intervention therapy for developmental delay, and genetic counseling for future pregnancies.

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