Frequency of 22q11.2 deletion in Congenital Heart Disease (CHD) cases

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Introduction

Congenital heart disease (CHD) is a classic symptom associated with 22q11.2 deletion syndrome (DiGeorge syndrome, named after Angelo DiGeorge, an Italian-American paediatric endocrinologist). 22q11.2 deletion syndrome has an estimated prevalence of 1 in 4000-6,000 live births. Heart defects may include a hole between the lower chambers of the heart (ventricular septal defect); only one large vessel, rather than two vessels, leading out of the heart (truncus arteriosus); or a combination of four abnormal heart structures (tetralogy of Fallot). 22q11.2 deletion syndrome can cause hypoparathyroidism which leads to low levels of calcium and high levels of phosphorus in the blood. Poor immune function, frequent; severe infections, typical facial characteristics, cleft palate, learning, social, developmental or behavioral problems, attention-deficit/hyperactivity disorder (ADHD) or autism spectrum disorder, increased risk of autoimmune disorders, such as rheumatoid arthritis or Graves' disease, hearing impairment, poor vision, breathing problems, poor kidney function etc are some common symptoms associated with the 22q11.2 deletion. Patients with heart anomalies (tetralogy of Fallot, truncus arteriosus, interrupted aortic arch type B, conoventricular septal defects, and isolated aortic arch anomalies) should be screened for a 22q11.2 deletion, according to new guidelines. In this paper, we report the results of 22q11.2 deletion tests in children who attended the Genetic clinic of SAT Hospital, Kerala with one or more of the above symptoms along with CHD.

Study population

Infants who attended the Genetic clinic of SAT Hospital during 2016 to 2020 (5 years) , presented with CHD along with other symptoms such as truncus arteriosus, TOF, pulmonary atresia, multiple cardiac anomalies, hypocalcemia, facial dysmorphism were screened for the presence of 22q11 deletion. All patients underwent cardiac as well as clinical genetics evaluation, and the relevant information was noted. We evaluate 69 patients all of whom had met the clinical criteria for the deletion was done FISH (Fluorescence In Situ Hybridization).

Peripheral blood sample (2-3ml) were collected from patients (>17 years) with informed consent from their parents. Peripheral blood lymphocyte microculture method was carried out and FISH was performed with a critical region probe for the DiGeorge syndrome chromosome region of chromosome 22 (22q11.2). FISH image were captured through Cytovision software (Germany). A total of atleast 1000 interphase nuclei and atleast 10 metaphase nuclei were scored from each case. Presence of two signals was considered as normal and demonstration of one signal was considered as microdeletion positive. When presence of both one and two signals in interphase as well as in metaphase cells was observed, the case was considered to have mosaicism.

Results

Among the cases, 36 were male and 33 were female childrens. The mean age of the cases was one and half years ranging from 1 month to 10 years. Among the 69, 61 patients had conotruncal heart defect including tetralogy of fallot (TOF) [37 (53.62%)], pulmonary atresia with ventricular septal defect (PA-VSD) [16 (23.19%)], truncus arteriosus (TA) [6 (8.69%)], interrupted aortic arch (IAA) [2 (2.9%)] and the remaining had non-conotruncal heart defect like VSD [5(7.2%)], ASD [3(4.3%)], AVSD, PDA, pulmonary stenosis and two or more combinations of these non-conotruncal anomalies [8 (11.5%)]cases.

Fifteen patients **(21.74%)** were found to have a 22q11.2 microdeletion. The prevalence for each diagnosis was TOF (16.21%), PA/VSD (12.5%), IAA (50%) and TA (66.67%).

Discussion

Cardiac patients with a 22q11.2 deletion do not generally experience higher mortality upon surgical intervention but suffer more peri-operative complications than their non-syndromic counterparts. Early identification of a 22q11.2 deletion in the neonate or infant when other syndromic features may not be apparent allows for timely parental screening for reproductive counseling and anticipatory evaluation of cardiac and non cardiac features. Timely diagnosis of this condition can alert the treating physician about the possibility of the associated comorbities known to occur with this disease. This in turn can help to develop a surveillance plan for these patients. Proactive prevention of the secondary complications and a watchful "system-wise" surveillance plan can go a long way in ensuring a healthy life for most of these individuals.