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The incidences of 22q11.2 microdeletion syndrome in congenital heart diseases.

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Abstract

Using classical cytogenetic (G-banding karyotyping) techniques and Fluorescence In Situ Hybridization (FISH) incidences of 22q11.2 microdeletion syndrome were studied in Western Indian population. A total of 78 cases were reported for diagnosis, of which 10 (12.8%) were found positive for 22q11.2 microdeletion syndrome. FISH analysis for 22q11.2 should be performed on children having heart defects and related diseases.

Keywords: 22q11.2, microdeletion syndrome, classical cytogenetic, FISH, Western India

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Introduction

The prevalence of 22q11.2 microdeletion syndrome is approximately 1 in 4000 births and accounts for 5 – 30% of all heart defects. Congenital heart defects (CHDs) are most common of all birth defects. CHD may be an isolated malformation or may be part of a syndrome. One of the common syndromes associated with CHDs includes DiGeorge Syndrome (DGS) or Veloconfacial syndrome (CVF). The clinical features associated with 22q11.2 deletion include contruncal cardiac defect, thymic hypoplasia, cleft palate and hypocalcemia.

Cytogenetically del22q11.2 syndrome is when the affected individual carries deletion only in one of chromosome 22. So it is presumed to be gene haploinsufficiency syndrome [1]. Most people with 22q11.2 deletion syndrome are missing about 3 million base pair on one copy of chromosome 22 in each cell. The deletion occurs near the middle of the chromosome at location designated as q11.2. This region contains 30 to 40 genes. The particular lost gene is thought to be responsible for many characteristics features of 22q11.2. In most cases the deletion occurs *de novo* but in about 10% cases it is inherited form parents affected mildly.

Previous studies on the presence of 22q11.2 microdeletion in patients with CHDs have been reported from different parts of the world [2, 3, 4, 5].However, isolated and regional studies from India have been conducted with regard to incidence of 22q11.2 [6, 7, 8].

Materials and Methods

From September, 2009 to February, 2014, a total of 78 cases of cardiac anomalies were referred to our laboratory from various parts of Western India for diagnosis of 22q11.2 microdeletion syndrome.

The age range of patients varied from 1 day to 37 years, the mean age being 6.6 years. There were 44 males and 34 females.

Peripheral blood samples were obtained from each patient after informed concent, for karyotype and FISH analysis. Chromosome analysis was carried out using standard protocol with slight modification. Minimum of 25 metaphases were analysed per patient.

G-banded metaphase chromosomes were screened at 550 band stages according to the Int. System for Human Cytogenetic Nomenclature [9]. The automatic scanning system (Axiomerger Z_2–Carl-Zeiss) and karyotyping software (IKAROS, Germany) were used to make karyotypes.

Molecular cytogenetic study was carried out on blood cells with FISH analysis. FISH was performed on interphase cells and metaphase chromosome spread using Vysis SI DiGeorge syndrome probe which maps to the TUPLE1 region i.e. 22q11.2 (spectrum orange) combined with 22q11.3(spectrum green) region control probe according to manufacturer's instructions.

Results and Discussion

Cytogenetic analysis of all the 78 patients revealed a normal G-banded karyotpic pattern with no additional chromosome defects at 550 band stages (Fig. 1). However, FISH analysis of 78 patients showed 68 had a normal FISH pattern (Fig. 2a) while only 10 (Table 1) showed del22q11.2 which is depicted in Fig. 2b.

Table 1. *Shows patients with 22q11.2 microdeletion (n =10)*

Case	Age	Gender	Defects*	Interphase FISH results
1	11 months	M	Family history of congenital cardiac defects	94% with interphase with Microdeletion
2	09 months	M	Not known	96% with interphase with Microdeletion
3	06 months	F	Ventricular septal defect	98% with interphase with Microdeletion
4	18 months	F	Truncusarteriosus	96% with interphase with Microdeletion
5	03 years	M	Atrial septal defect	96% with interphase with Microdeletion
6	07 years	M	Tetralogy of fallot	92% with interphase with Microdeletion
7	06 years	F	Non-conotruncal congenital cardiac defect	96% with interphase with Microdeletion
8	02 years	M	Ventricular septal defect	93% with interphase with Microdeletion
9	04 days	M	Not known	96% with interphase with Microdeletion
10	06 months	F	Atrial septal defect and ventricular septal defect	96% with interphase with Microdeletion

**Defects were as reported in case paper*

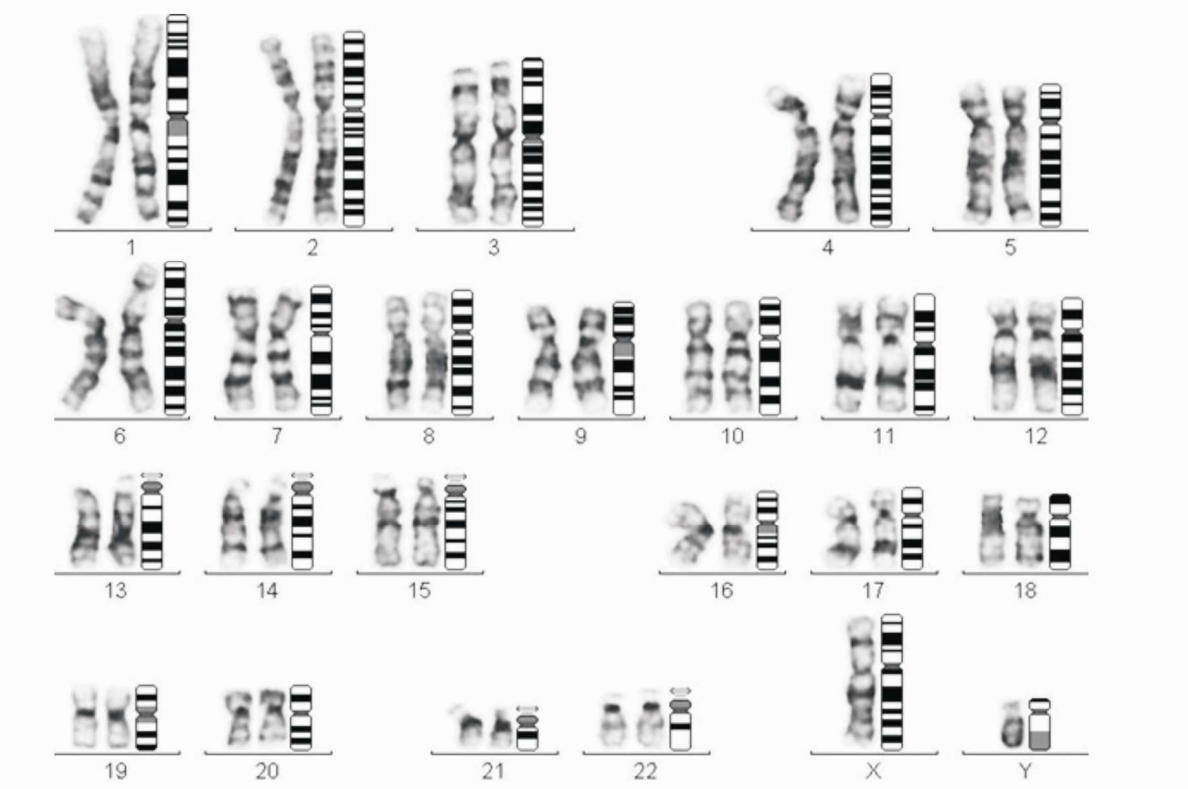

Figure 1. *G-banded karyotype of male patient shows no deletion in chromosome# 22*

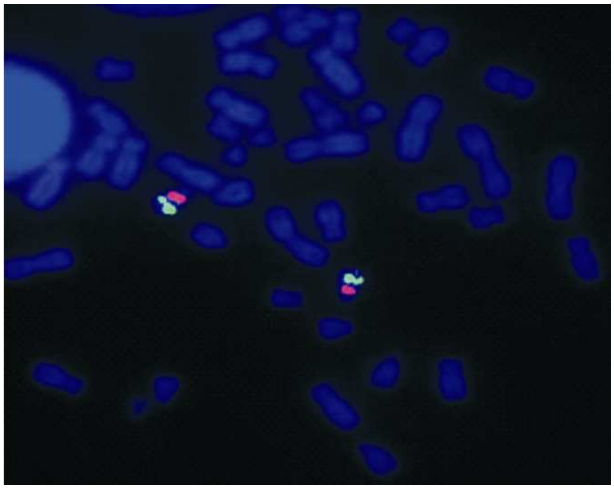

Figure 2a: *Shows spectrum orange on both chromosome 22indicating normal status of the chromosome*

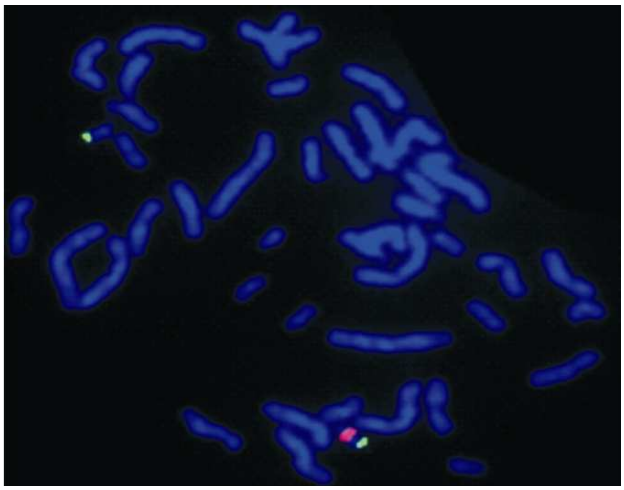

Figure 2a: *Shows absence of spectrum orange on one of the chromosome 22 indicates deletion e chromosome*

The present study was carried out to account for microdeletion of 22q11.2 in isolated Indian population. In our investigation, karyotype analysis did not reveal del 22q11.2in any of the 78 cases referred to our laboratory for diagnosis.

However, FISH analysis using TUPLE1 probe on 78 patients revealed microdeletion in 10 (12.8%) mostly with congenital heart defects. Few studies carried out have suggested a correlation between 22q11.2 and isolated heart defects [2, 3, 4,5]. However, Gawdeet. al.,[6] have studied 105 patients and found del 22q11.2 deletion in 6 patients. They have further suggested that testing for microdeletion 22q11.2 in isolated non-syndromic patients using FISH technique should be mandatory. SimilarlyManji et al., [7] have reported microdeletion of 22q11.2 in 6 individuals from 46 cases. In addition,Halder et al.,[8] have also reported 9 positive cases of microdeletion 22q11.2 from 146 cases.

In our study, out of 78 referred cases we found 10 with del 22q11.2 i.e. 12.8% from Western India.

In summary, we propose that FISH analysis for 22q11.2 microdeletion offers the advantage of planning neonatal care and decision regarding cardiac surgery, if needed.

Conflict of interest:
The authors declare that they have no competing interest.

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