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## Description of clinical signs of Brazilian patients with the 22q11.2 Deletion Syndrome and comparison with different populations.

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### Abstract

22q11.2 Deletion Syndrome (22q11.2DS) is the most common microdeletion among humans. This syndrome presents several clinical manifestations and symptoms, which hampers its clinical diagnosis. In addition to a wide range of signs/symptoms, recent studies have indicated that the clinical presentation has been observed variable among different population groups. This study aimed to describe the main clinical signs of patients with 22q11.2 DS registered in the Brazilian Database on Craniofacial Anomalies/22q11.2 Deletion Syndrome (BDCA/SDEL22q) and compare the frequency of clinical signs of these with patient groups with the same condition from different populations.

**Key words:** 22q11.2 deletion syndrome, Clinical signs, Different populations.

### Introduction

22q11.2 Deletion Syndrome (22q11.2DS) is the most common microdeletion among humans. This syndrome presents several clinical manifestations and the main signs and symptoms involved are: cardiac malformations, palatal, immunological and neurocognitive alterations, hypocalcemia, psychiatric disorders and facial dysmorphisms<sup>1</sup>. Recent studies have been found heterogeneity of clinical presentation between different ethnic groups<sup>2</sup>. Brazil's Craniofacial Project (BCFP) has an online version of the Clinical and Family Database of Typical Orofacial Clefts, including a specific module for patients with a diagnostic hypothesis of 22q11.2DS. **Objectives:** to describe the main clinical signs of patients with 22q11.2 DS registered in the Brazilian Database on Craniofacial Anomalies/22q11.2 Deletion Syndrome (BDCA/SDEL22q) and compare the frequency of clinical signs of these with patient groups with the same condition from different populations.

### Results and Discussion

**Methods:** Clinical data from 73 patients, with a previous molecular diagnosis, were analyzed using the Excel (Microsoft®) and compared to data from literature (106 patients with this syndrome, including 24 Latin Americans, 27 Asians and 55 Africans). This sample was composed by 45% of males, with age varying from 0 to 32 years old. In view of the prevalence, the five main clinical features should be highlighted: learning problems (97%), palatal abnormalities (84%), developmental delay (83%), immunological diseases (68%) and congenital heart diseases - CHC (62%). Regarding palatal abnormalities, the most frequent symptoms that suggested palatal abnormalities were: nasal voice (91%), nasal reflux (12%) and dysphagia (12%); and anatomical/ functional defects were: velopharyngeal insufficiency (49%), cleft palate (32%) and submucous cleft palate (30%). The most frequent types of congenital heart diseases were: ventricular septal defect (45,2%), atrial septal defect (28,6%), tetralogy of Fallot (14%), and interruption of the aortic arch (14%). Behavioral and psychiatric diseases were found in 48,3% of patients, the most common were attention deficit

hyperactivity disorder (57%), impulsivity (17,9%) and perseveration (10,7%). In addition, 10,7% of the patients had central nervous system structural anomalies; 50% had endocrinological diseases; 46% had hearing loss; 41% had ophthalmologic abnormalities; 18% had genitourinary abnormalities; 48% had gastrointestinal abnormalities; 34% have skeletal abnormalities. Regarding facial dysmorphisms, the most common were: elongated face (58%) alar hypoplasia (49%) dysmorphic ear (44%) and bulbous nose (36%). The frequencies comparison of main clinical features between patients of different populations is described in Table 1.

**Table 1 - Clinical signs of 22q11.2DS in different populations:**

	Kruszka P, Addissie YA, McGinn DE, et al (2017)				Present Study Brazilian
	Global	African	Asian	Latin American	
Number of participants	106	55	27	24	73
Age Range	Infant - 43	1 - 44	Infant - 43	1 - 39	0 - 32
Males	50/106 (47%)	26/55 (44%)	12/27 (44%)	12/24 (50%)	34/73 (47%)
CHD	78/104 (75%)	40/55 (73%)	24/25 (96%)	14/24 (58%)	42/67 (62%)
Learning problems	67/100 (67%)	31/54 (57%)	18/22 (82%)	18/24 (75%)	35/36 (97%)
Developmental delay	39/79 (49%)	20/50 (40%)	9/11 (82%)	10/18 (56%)	50/60 (83%)
Palatal anomalies	46/95 (48%)	13/53 (25%)	14/18 (78%)	19/24 (79%)	53/63 (84%)
Ear anomalies	53/90 (59%)	28/55 (51%)	8/11 (73%)	17/24 (71%)	32/72 (44%)
Psychiatric illness	16/100 (16%)	5/54 (9%)	8/22 (36%)	3/24 (13%)	11/58 (19%)
Immune deficiency	21/42 (50%)	Not examined	8/18 (44%)	13/24 (54%)	37/54 (68%)

### Conclusions

To the best of our knowledge, to date this is the largest sample of Brazilian patients with 22q11.2 DS described. Despite the significant phenotypic variability, these data support the main clinical signs previously reported and shows that some clinical signs present similar frequencies between patients from different populations.

<sup>1</sup> McDonald-McGinn, DM, Sullivan, KE. Chromosome 22q11.2 deletion syndrome (DiGeorge syndrome/velocardiofacial syndrome). *Medicine* (Baltimore). 2011; 90(1):1-18.

<sup>2</sup> Kruszka P, Addissie YA, McGinn DE, et al. 22q11.2 deletion syndrome in diverse populations. *Am J Med Genet Part A*. 2017;173A:879-888. <https://doi.org/10.1002/ajmg.a.38199>.