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ABOUT US

Chromosome Disorder Outreach provides support and information to anyone diagnosed with a rare chromosome change, rearrangement or disorder. CDO actively promotes research and a positive community understanding of all chromosome disorders.

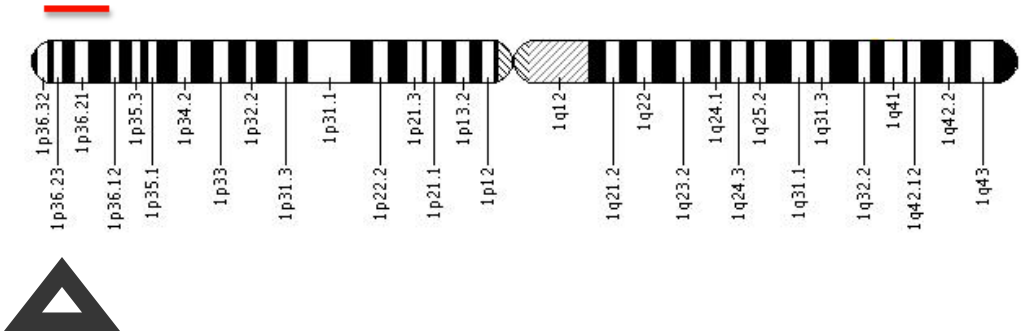
CDO is a 501c3 organization founded in 1992.

1p36 Deletion Syndrome

(Monosomy 1p36)

1p36 Deletion Syndrome

Occurring in 1 out of 5,000-10,000 live births, monosomy 1p36 is the most common subtelomeric deletion syndrome in humans (1). The first reports of individuals with partial monosomy of chromosome 1p36 were published in the early 1980s (2). Identifying patients with monosomy 1p36 may be difficult because characteristic dysmorphic features are sometimes subtle or missing, congenital anomalies are numerous, and none seem to be pathognomonic or systematically present (3).



Common features associated with this syndrome include developmental delay (severe to profound in a majority), hypotonia (low muscle tone), microcephaly (abnormally small head), and characteristic dysmorphic facial features consisting of midface hypoplasia (underdevelopment), broad nasal root, deep-set eyes, straight eyebrows, pointed chin, large, late-closing anterior fontanelle (1). Developmental delays are variable but present in all individuals (2). Brachydactyly (short fingers and toes) and short feet are also common (3). Hypotonia and seizures are seen in more than one-half of affected patients (4). Nearly all patients have EEG abnormalities but only 44%-58% have clinical seizures (5). Hearing loss and vision problems are seen in one-half of individuals, and renal abnormalities are seen in one-quarter (4).

Significant part of patients with deletion 1p36 has heart defects – both structural and functional. Spectrum of structural heart defects is similar to the same in general population, most of them are not life threatening. At least ¼ of patients have cardiomyopathies – functional defects which may be found both in persons with and without structural heart abnormalities. The most common form is left ventricular noncompaction (LVNC). Association of LVNC with increased size of heart ventricles and diminished systolic function may lead to dilated cardiomyopathy (DCM). Although PRDM16 gene is considered the main player for DCM in patients with 1p36 deletion (6), other genes in this area may also contribute to the development of this condition (7).

Most genes contributing to the phenotypic features of 1p36 deletion syndrome are located distal to marker D1S2870 (chr1:6,289,764–6,289,973), this region is subsequently referred to as the distal or classical critical region (2). Some of the most strongly implicated 1p36 genes include MMP23B, GABRD, SKI, PRDM16,KCNAB2, RERE, UBE4B, CASZ1, PDPN, SPEN, ECE1,HSPG2, and LUZP1 (2). Although, genes that contribute to most 1p36-related phenotypes have yet to be identified, many 1p36-related phenotypes may arise from haploinsufficiency (only one copy of a gene) for more than one gene within a particular genomic region (2).

There is marked variability in the deletions of 1p36 , with no common breakpoints or deletion sizes (1). Although a majority (52%) of deletions are pure terminal deletions, interstitial deletions (29%), complex rearrangements with multiple deletions and/or duplications (12%), and unbalanced translocations (exchange of chromosome material causing extra or missing genes) (7%) are also seen (1). Despite this genotypic variability, there is a relatively consistent phenotypic presentation, and patients with non-overlapping deletions have been reported to have similar features (1). Affected children are particularly weak at language expression (speech). Behavioral disorders are present in 50% of affected individuals (5). These include poor social interaction, temper tantrums, self-biting, stereotypies and less commonly hyperphagia (abnormally increased appetite for food) (5).

According to the published clinical studies, brain abnormalities occur in 60-88% of the patients (3). The most frequent findings indicating brain mal- or dysformation include diffuse (generalized) brain atrophy (degeneration), cortical atrophy, micropolygyria (neuronal migration disorder), focal pachygyria, and enlargement of the lateral ventricles (3). In some cases, brain imaging demonstrated shared findings of white matter abnormalities involving periventricular and subcortical areas emerging in different ages predominantly in the parietal lobes (related to sensory processing) (3).

Because deletions 1p36 in significant part of patients are caused by parental rearrangements (translocations or more complex abnormalities) examination of the parental karyotypes is necessary, especially for the families planning further children. Prenatal diagnosis may require molecular cytogenetic examination of the fetus, because “standard” cytogenetic tests may be not sensitive enough to detect deletion 1p36.