



Osteogenesis Imperfecta, Type I

Alternative Names

OI, Type I
Osteogenesis Imperfecta Tarda
OIT
Osteogenesis Imperfecta with Blue Sclerae

WHO International Classification of Diseases

Congenital malformations, deformations and chromosomal abnormalities

OMIM Number

166200

Mode of Inheritance

Autosomal dominant

Gene Map Locus

17q21.31-q22, 7q22.1

Description

Osteogenesis imperfecta is a group of rare disorders affecting the connective tissue and characterized by extremely fragile bones that break easily often without any apparent cause. This disorder is due to failure of maturation and organization of collagen fibers, defect in collagen leading to decreased collagen secretion, and there may be an inability to form normal bone due to a defect in osteoblastic function. The disorder is currently classified into seven types based on differences in clinical presentation and bone architecture.

Type I osteogenesis imperfecta tends to be milder than the other types of osteogenesis imperfecta and is most common type of the disorder occurring with a frequency of about 1 in 15,000 to 20,000 people. It is usually transmitted as an autosomal dominant trait with variable penetrance. The clinical manifestations of the disorder can be skeletal (bone fragility, hyperextensible joints and ligaments), cutaneous (thin and translucent skin), ocular (keratoconus, megalocornea), and dental (hypoplasia of dentin and pulp). Hearing loss

occurs in at least half of people with type I osteogenesis imperfecta, usually beginning in the late teens or early adulthood. Decreased hearing is usually caused by problems with the middle ear bones (conductive hearing loss), but in some cases the inner ear and nerves from the ear to the brain also become involved (mixed conductive and sensorineural hearing loss). Inguinal and umbilical hernia secondary to poor muscular development, capillary fragility, small stature with short limbs, and triangular-shaped head, may occur.

Molecular Genetics

More than 90% of individuals with osteogenesis imperfecta have mutations in one of the two genes, COL1A1 and COL1A2, that encode the chains of type I procollagen, the major protein in bone and most other connective tissues. The two general outcomes of these mutations are either a decrease in the amount of type I procollagen produced or the production of some abnormal type I procollagen molecules.

In the vast majority of instances, osteogenesis imperfecta type I results from mutations in the COL1A1 gene that result in premature termination codons. The majority of these mutations are deletions or insertions of a small number of nucleotides, a number not divisible by three, in the coding sequences of exons throughout the gene. These mutations, single codon changes that introduce premature termination codons, and some splice-site mutations that lead to exclusive use of cryptic sites and generation of out-of-frame transcripts all lead to premature termination codons. The presence of a premature termination codon that is separated by one or more introns in the gene leads to marked instability of the mRNA derived from the mutant allele. As a consequence, the amount of COL1A1 mRNA is reduced to half the normal amount, with no compensation by the other allele. Type I procollagen is a trimer that must contain at least



two pro alpha1 chains. With a reduction in the COL1A1 mRNA, an obligatory decrease in the production of type I procollagen occurs, although the protein produced is structurally normal. The diminished amount of type I collagen in bone appears to reduce the amount of bone that can be made and leads to brittle bones.

Epidemiology in the Arab World

United Arab Emirates

Al Talabani et al. (1998) studied the pattern of major congenital malformations in 24,233 consecutive live and stillbirth at Corniche hospital, which is the only maternity hospital in Abu Dhabi, between January 1992 to January 1995. A total of 401 babies (16.6/1,000), including 289 Arabs, were seen with major malformation. Single gene disorders accounted for 24% of the cases, 76% were due to autosomal recessive disorders. In their study, Al

Talabani et al. (1998) observed six cases of type I osteogenesis imperfecta (tarda) in families from the United Arab Emirates. Recurrence and consanguinity were reported in these families. Al Talabani et al. (1998) concluded that their study is very close to representing the true incidence of congenital abnormalities in the whole United Arab Emirates, as this study included over 98% of deliveries in Abu Dhabi, the capital of United Arab Emirates.

References

Al Talabani J, Shubbar AI, Mustafa KE. Major congenital malformations in United Arab Emirates (UAE): need for genetic counselling. *Ann Hum Genet.* 1998; 62 (Pt 5):411-8.

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