



## Osteogenesis Imperfecta, Type IIA

### Alternative Names

Brittle Bone Disease  
Glass Bone Disease  
Lobstein Disease  
OI, Type II  
OI, Type IIA  
OI2A  
OIC  
Osteogenesis Imperfecta Congenita  
Osteogenesis Imperfecta Congenita, Neonatal Lethal Form  
Osteogenesis Imperfecta Congenita, Perinatal Lethal Form  
Osteogenesis Imperfecta, Type II  
Vrolik Type of Osteogenesis Imperfecta

### Record Category

Disease phenotype

### WHO-ICD

Congenital malformations, deformations and chromosomal abnormalities > Congenital malformations and deformations of the musculoskeletal system

### Incidence per 100,000 Live Births

6-10

### OMIM Number

166210

### 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 increased bone fragility due to low bone mass giving an increased fracture incidence, affecting more than

1:10,000 individuals. Osteogenesis imperfecta patients present a broad range of clinical severity, ranging from multiple fracturing in utero and perinatal death to normal adult stature and a low fracture incidence. The disorder is currently classified into seven types based on differences in clinical presentation and bone architecture. Osteogenesis imperfecta type I is the most common and the mildest form of the disorder.

Osteogenesis imperfecta congenita or type II osteogenesis imperfecta is the most severe form of the disease. Affected individuals exhibit short limb dwarfism, thin skin, soft skull, unusually large fontanels (soft spots), blue sclera, whites of the eyes, small nose, low nasal bridge, inguinal hernia and numerous bone fractures at birth. There is bowing of limbs due to multiple fractures. More than 60% of affected infants die on the first day; and 80% die within the first week. Survival beyond one year is exceedingly rare and usually involves intensive support such as continuous assisted ventilation. Death usually results from pulmonary insufficiency related to the small thorax, rib fractures, or flail chest because of lack of stable ribs. Those who survive the first few days of life may not be able to take in sufficient calories because of respiratory distress.

### Molecular Genetics

Osteogenesis imperfecta is a dominant autosomal disorder caused by mutations in type I collagen genes, COL1A1 and COL1A2, which are responsible for synthesis of this main protein of bones, skin, ligaments, tendons and most other connective tissues. Those genes encode the alpha 1 and alpha 2 chains of the collagen triple helix, respectively. More than 250 different mutations in the COL1A1 and COL1A2 genes had been characterized. These alterations vary in type and location.

The mild forms of osteogenesis imperfecta are usually caused by mutations that inactivate one allele



of the COL1A1 gene, resulting in a reduced amount of normal type I collagen. The varied clinical characteristics of osteogenesis imperfecta reflect different classes of mutations in different regions of type I collagen genes. Consequently, more than 250 different mutations in the COL1A1 and COL1A2 genes had been characterized. Besides, these alterations vary in type and location, although the most common in COL1 loci are single-base substitutions in the part of the gene coding for the triple helix domain, which result in replacing glycine by an amino acid with a bulkier side chain.

## Epidemiology in the Arab World

### Algeria

Kaplan and Baldino (1953) described a kindred derived from an inbred, Arabic-speaking, polygamous sect called the Mozabites, living in southern Algeria. Nine cases occurred in 4 sibships among the descendants. Kaplan et al. (1958) and Laplane et al. (1959), in a follow-up of the same kindred, described 19 cases.

### Lebanon

Bittar (1998) reported a prospective study of 3,865 consecutive newborns delivered between 1991 and 1993. Major congenital anomalies (MCA) were found in 64 newborns at incidence of 16.5/1000 births. Many of the cases had osteogenesis imperfecta. Among the malformed infants, the rate of low birth weight and the rate of parental first cousin consanguinity were significantly higher than corresponding rates among normal infants in a control group.

### Oman

Sawardekar (2005) conducted a study to establish the prevalence of major congenital malformations in children born during a 10-year period in Nizwa Hospital. Of the 21,988 total births in the hospital, five children were born with osteogenesis imperfecta type 2. Sawardekar (2005) hinted for a possible genetic contribution in these children.

### Sudan

Doumi et al. (1994) reported a prospective study of fractures in 231 children received at Khartoum North Teaching Hospital (KNTH). The incidence of child fracture rated as one per day and it increased from the age of 5 years onwards in boys and between 6 and 8 years in girls. Pathological fractures accounted for 2.2% and were due to bone cysts and osteogenesis imperfecta.

### United Arab Emirates

Al Talabani et al. (1998) studied the pattern of major congenital malformations in 24,233 consecutive live and stillbirth in 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 malformations. Single gene disorders accounted for 24% of the cases, 21% were due to autosomal dominant disorders. In their study, Al Talabani et al. (1998) observed three cases of osteogenesis imperfecta congenita born to first cousin couples from the United Arab Emirates. Recurrence was reported in other members of the families. Al Talabani et al. (1998) concluded that their study was very close to representing the true incidence of congenital abnormalities in the whole United Arab Emirates, as their study included over 98% of deliveries in Abu Dhabi, the capital of United Arab Emirates.

In a 5-year prospective study for newborns at Al Ain Medical District, Al-Gazali et al. (2003) defined the pattern and birth prevalence of the different types of osteochondrodysplasias in the United Arab Emirates. Among the 38,048 births during the study period, 36 (9.46/10,000 births) had some type of skeletal dysplasia of which two, born to non-consanguineous parents, had osteogenesis imperfecta type II (0.52/10,000 births). Al-Gazali et al. (2003) noted that the birth prevalence of osteogenesis imperfecta is higher in the UAE population than those reported for other populations (0.24-0.37/10,000).

## References

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Doumi BA, Ahmed ME, Hassan R, Elnour SH, Kashan A. Fractures in childhood in Khartoum. *East Afr Med J*. 1994; 71(6):354-7. PMID: 7835253

Kaplan M, Baldino C. [Periosteal dysplasia, apparently familial and transmitted according to the recessive Mendelian law.] *Arch Fr Pediatr*. 1953; 10(9):943-50. PMID: 13125648

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Laplane R, Lasfargues G, Debray P. [Attempted genetic classification of osteogenesis imperfecta.] *Presse Med*. 1959; 67(22):893-5. PMID: 13658025

Sawardekar KP. Profile of major congenital malformations at Nizwa Hospital, Oman: 10-year review. *J Paediatr Child Health*. 2005; 41(7):323-30. PMID: 16014135

#### **Related CTGA Records**

Caffey Disease

Osteogenesis Imperfecta, Progressively Deforming, with Normal Sclerae  
Osteogenesis Imperfecta, Type I

#### **External Links**

<http://www.emedicine.com/PED/topic1674.htm>

<http://www.genetests.org/profiles/oi>

<http://www.le.ac.uk/genetics/collagen>

<http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=oi>

<http://www.orpha.net/data/patho/GB/uk-OI.pdf>

[http://www.rarediseases.org/search/rdbdetail\\_abstract.html?disname=Osteogenesis%20Imperfecta](http://www.rarediseases.org/search/rdbdetail_abstract.html?disname=Osteogenesis%20Imperfecta)

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