Review Article

The genetic implication of scoliosis in osteogenesis imperfecta: a review

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Abstract: Osteogenesis imperfecta (OI) is a kind of heritable connective tissue disorder, including blue sclerae, hearing loss, skeletal dysplasia causing bone fragility and deformities. It is typically caused by collagen related gene mutations, which could lead to bone formation abnormalities. Scoliosis is one of the most common and severe spinal phenotype which has been reported in approximately 26–74.5% of all OI patients. Recent breakthroughs have suggested that OI can be divided into more than 16 types based on genetic mutations with different degrees of scoliosis. In this review, we summarize the etiology of scoliosis in OI, especially the genetic studies of different types. We aim to provide a systematic review of the genetic etiology and clinical suggestions of scoliosis in OI.

Keywords: Osteogenesis imperfecta (OI); scoliosis; bone formation; gene

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Introduction

Osteogenesis imperfecta (OI) is a kind of heritable skeletal dysplasia, which is often called "fragile bone". It affects about 1 in 5,000 to 20,000 births (1), and most cases are caused by mutation of collagen related genes, non-collagen genes account for less than 10% of OI patients (*Table 1*). The classical phenotypes of OI include frequent long bone fractures, vertebral compression fractures, short stature, blue sclera and dentinogenesis imperfecta (DI) (11). Patients can also have other manifestations, such as scoliosis, unilateral spinal anesthesia (12), among which scoliosis is commonly seen.

According to previous investigations, the prevalence of scoliosis in OI varies from 26% to 74.5% (2,3,5-7,11,13,14). The severity and prevalence of scoliosis in different types of OI is various (*Table 1*), and the type III patients often had higher prevalence of severe scoliosis than type I and IV (2,3,6).

The outset years of scoliosis in OI cases ranged from 2 to 65 years (15), always the spinal malformation progresses rapidly after 5 years old or after the spinal curve exceeds

Table 1 Classification of OI types and vertebral malformations

Type (OMIM)	Inheritance (gene)	Locus	Protein defect	Phenotype	Severity	Vertebral anomalies	Scoliosis progression rate	Scoliosis prevalence (total sample size)	Reference
I #166200	AD (*COL1A1* or *COL1A2*)	17q21.33 or 7q21.3	Matrix insufficiency	Fractures, blue sclerae, and hearing loss	Mild, nondeforming	Codfish vertebrae (adults)	1 degrees per year	10 [30]	(2)
								17.6 [244]	(3)
								19 [57]	(4)
								36 [72]	(5)
								39 [159]	(6)
II #166210	AD (*COL1A1* or *COL1A2*)	17q21.33 or 7q21.3	Collagen structure	Fractures, often succumb due to cardiopulmonary causes	Perinatal lethal	Platyspondyly	–	–	–
III #259420	AD (*COL1A1* or *COL1A2*)	17q21.33 or 7q21.3	Collagen structure	Fractures, gray or blue sclerae, short stature, often DI, "popcorn" sign of distal femoral growth plates on radiography	Progressively deforming	Codfish vertebrae; kyphoscoliosis; platyspondyly	6 degrees per year	47 [100]	(3)
								57 [7]	(2)
								100 [8]	(5)
								68 [81]	(6)
								72 [18]	(4)
IV #166220	AD (*COL1A1* or *COL1A2*)	17q21.33 or 7q21.3	Collagen structure	Multiple phenotypes and with or without di, frequent long bone fractures	Moderately severe	Codfish vertebrae	4 degrees per year	31.3 [147]	(3)
								70 [10]	(5)
								54 [59]	(6)
								61 [21]	(4)
V #610967	AD (*IFITM5*)	11p15.5	Bril-marker of osteoblast, critical in bone formation	Variable scleral hue, calcification of forearm interosseous membrane, radiodense metaphyseal band at growth plates of long bones, radial-head dislocation	Moderate to severe	Mild to moderate scoliosis Compression fractures	–	31.3 [16]	(3)
								57 [42]	(7)
								76.5 [17]	(8)
VI #613982	AR (*SERPINF1*)	17p13.3	PEDF	Increased osteoid volume, decreased bone formation parameters	Moderate to severe	Compression fractures; scoliosis	–	27.3 [11]	(3)

Table 1 *(continued)*

Table 1 *(continued)*

Type (OMIM)	Inheritance (gene)	Locus	Protein defect	Phenotype	Severity	Vertebral anomalies	Scoliosis progression rate	Scoliosis prevalence (total sample size)	Reference
VII #610682	AR (*CRTAP*)	3p22.3	CRTAP	Neonatal fractures, osteochondrodysplasia with rhizomelia, broad undertubulated long bones, frail ribs. White or rarely, light gray sclerae	Severe to lethal	Severe scoliosis	–	40 [5]	(3)
VIII #610915	AR (*LEPRE1*)	1p34.2	P3H1	Neonatal fractures, osteochondrodysplasia with rhizomelia, broad undertubulated long bones, frail ribs. White or rarely, light gray sclerae	Severe to lethal	Severe scoliosis; could be similar to OI type II/III	–	–	–
IX #259440	AR (*PPIB*)	15q22.31	CyPB	Neonatal fractures, osteochondrodysplasia without rhizomelia, broad undertubulated long bones, frail ribs. White or rarely, light gray sclerae	Severe to lethal	Kyphoscoliosis; may not have compression fractures; range of skeletal features similar to OI type II/III/IV	–	–	–
X #613848	AR (*SERPINH1*)	11q13.5	HSP47: collagen chaperone defects, delayed secretion rate	Blue sclerae, skin blisters and bullae at birth, inguinal hernia	Severe	–	–	–	–
XI #610968	AR (*FKBP10*)	17q21.2	FKBP65	Phenotypes broadened, with Bruck syndrome I	Moderately severe	–	–	63 [38]	(9)
XII #613849	AR (*SP7*)	12q13.13	Protein osterix: regulate osteoblast differentiation	Delayed tooth eruption, midface hypoplasia, normal sclerae	Moderate	–	–	–	–

Table 1 *(continued)*

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Type (OMIM)	Inheritance (gene)	Locus	Protein defect	Phenotype	Severity	Vertebral anomalies	Scoliosis progression rate	Scoliosis prevalence (total sample size)	Reference
XIII #614856	AR (*BMP1*)	8p21.3	C-Propeptide cleavage enzyme	Long bone deformities, wrists, elbows and interphalangeal joints hyperextensibility.	Severe	–	–	–	–
XIV #615066	AR (*TMEM38B*)	9q31.2	TRICB: regulate calcium release	Normal or blue sclerae, osteoporosis	Moderate to severe	–	–	–	–
XV #615220	AR (*WNT1*)	12q13.12	–	Early-onset osteoporosis	Moderately severe, progressively deforming	–	–	–	–
	AD (*WNT1*)	12q13.12				–	–	–	–
XVI #616229	AR (*CREB3L1*)	11p11.2	DGKZ isoforms 1 in fiberblasts	Fractures in utero and after birth, beaded ribs, callus formation	Severe to lethal	–	–	–	–
XVII #616507	AR (*SPARC*)	5q33.1	SPARC	Bone fractures, joint hyperlaxity, underdeveloped and weak muscles of the lower extremities, and bowing of both humeri, expressive and comprehensive speech delay, soft skin	–	Vertebral compression fractures, platyspondyly	–	100 [2]	(10)
Others #300131	XL (*PLS3*)	Xq23	Plastin	–	Mild	–	–	–	–
Others #601865	AR (*PLOD2*)	3q24	Lysyl hydroxylase 2	Progressive joint contractures	Progressively deforming	–	–	–	–

OI, osteogenesis imperfecta; DI, dentinogenesis imperfecta; AD, autosomal dominant; AR, autosomal recessive; XL, x-linked; COL1A1, collagen, type I, alpha-1; COL1A2, collagen, type I, alpha-2; CRTAP, cartilage-associated protein; IFITM5, interferon-induced transmembrane protein 5; SERPINF1, serpin peptidase inhibitor, clade F, member 1; LEPRE1, leucine- and proline-enriched proteoglycan 1; PPIB, peptidyl-prolyl isomerase B; SERPINH1, serpin peptidase inhibitor, clade H, member 1; FKBP10, FK506-binding protein 10; P3H1, prolyl3-hydroxylase 1; CyPB, cyclophilin B; Bril, bone-restricted ifitm-like protein; PEDF, pigment epithelium-derived factor; TRICB, trimeric intracellular cation channel type B; SPARC, secreted protein, acidic, cysteine-rich; OMIM, online Mendelian inheritance in man.

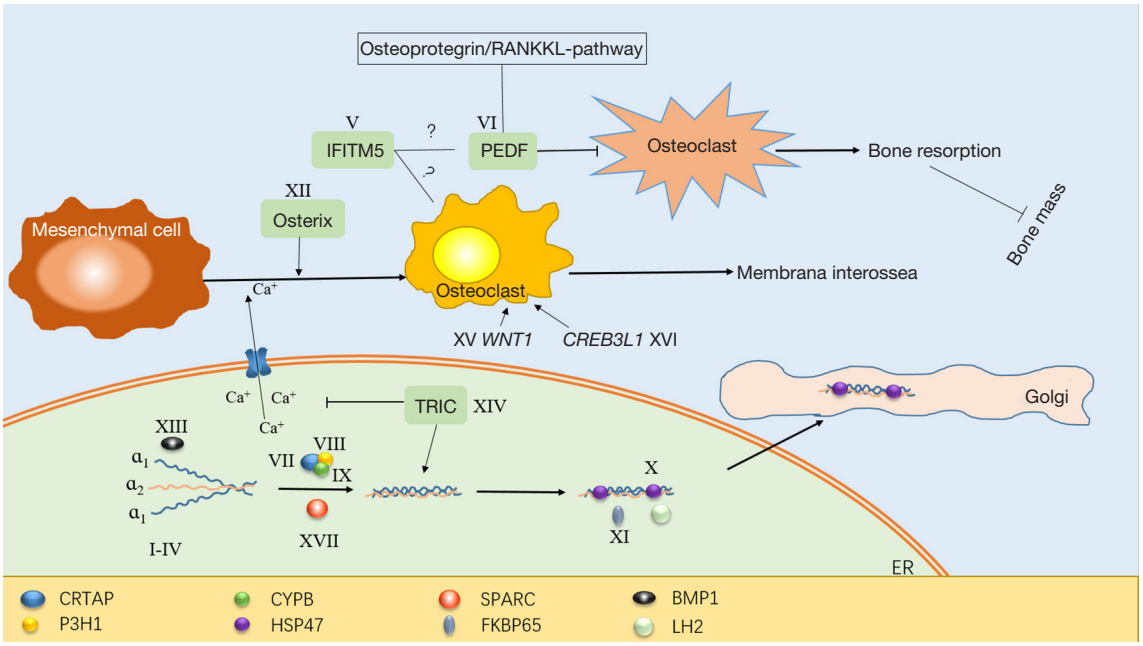

Figure 1 The pathogenesis of different types of OI with scoliosis. OI, osteogenesis imperfecta; CyPB, cyclophilin B; SPARC, secreted protein, acidic, cysteine-rich; FKBP, FK506-binding protein; P3H1, prolyl3-hydroxylase 1; CRTAP, cartilage-associated protein; PEDF, pigment epithelium-derived factor; IFITM5, interferon-induced transmembrane protein 5.

50 degrees (16). Although scoliosis was rare before 6 years of age (17), some types of OI can also have scoliosis just after born (18).

The curvature of scoliosis in OI was different varying from 7 to 105 degrees (19). According to a national cross-sectional study by Karbowski (14), 73.7% was mainly mild (<40 degrees), while 10.5% showed moderate (<60 degrees), 9.2% severe (<80 degrees) and 6.6% very severe deformity (>80 degrees). The vertebral deformities included codfish or wedge-shaped vertebrae (20) which were mostly common, and platyspondylia. Another study indicated that there were four types of vertebral body deformities including biconcave, flattened, wedged and unclassifiable vertebrae. The number of biconcave vertebrae (normally six or more) may indicate the severity and possibility of scoliosis (21).

Although scoliosis develops indolently, once the malformations evolve, they tend to be progressive and have numerous influence on the patients' life, such as pulmonary function and height (22). The treatment is ineffective in severely affected individuals who have minimal cortical bone (23), so it is necessary to prevent spinal curvature progression before severe complications arise (16,17). We are going to explore the tendency and severity of scoliosis, and give some interventions before scoliosis progressing in different types of OI (24). This review will be the first to give an integrated genetic landscape and aim to provide a basic knowledge of scoliosis in OI (25).

Genetic variants and pathogenesis

There are 19 types of OI according to genetic variants, the pathogenesis is not fully understood yet as shown in *Figure 1*. Based on the mechanism, OI can be divided into five groups (26). According to previous research, all of the groups and 16 types of the 19 types were reported to be manifest with scoliosis.

In the first group, OI is mainly caused by defects in collagen synthesis, structure, or processing including type I–IV and XIII. Most of OI patients have mutations in type I collagen related genes. Based on severity, OI is classified into four types (27). As shown in *Table 1*, patients with OI type I to IV always have variants in either collagen, type I, alpha-1 (*COL1A1*) or collagen, type I, alpha-2 (*COL1A2*). The production of type 1 collagen α1 or α2 chains would decrease. Patients with type I OI always have lower bone mineral density (BMD), thinner cortexes and reduced trabecular number (28) which would cause vertebra compression fracture. Together with joint hypermobility,

patients manifested with scoliosis as shown in *Table 2*. Type II OI is also caused by mutations in *COL1A1* or *COL1A2*, but this type is always too lethal to observe bone change and scoliosis. Type III has severely deforming and higher prevalence of scoliosis with vertebra compression and platyspondyly. Bisphosphonate treatment could decrease Cobb angle progression rates in type III at early age (24). Type IV can also have vertebra compression and severe scoliosis. OI type XIII is mainly caused by *BMP1* defects which leads to retention of the C-propeptide (61). Scoliosis with umbilical hernia and platyspondyly were reported at early age (58).

In the second group, OI is mainly caused by defects in collagen modification including type VII–IX, XIV and XVII. The collagen prolyl 3-hydroxylation complex which consisted of three proteins in a 1:1:1 ratio of prolyl3-hydroxylase 1 (P3H1), cartilage-associated protein (CRTAP), and cyclophilin B (CyPB) has a significant collagen post-translational over-modification role (62). Each of those protein is encoded by *CRTAP*, *LEPRE1* and *PPIB*. Defects of these three genes which cause delay of collagen helix folding could lead to OI type VII, VIII and IX (63). Defects of secreted protein, acidic, cysteine-rich (SPARC) which encoded by *SPARC* also could lead to delay of collagen folding, this type OI is considered to be type XVII (10). Type XIV is caused by *TMEM38B* mutations. The mechanism has not been completely elucidated. According to recent studies, *TMEM38B* mutations could inhibit calcium release, abnormal calcium signaling would decrease osteoblast growth and differentiation (64). Meanwhile post-translational modification of collagen would be influenced by calcium alteration of endoplasmic reticulum (26). In those types, patients with scoliosis always have low BMD as shown in *Table 2*.

In the third group, OI is mainly caused by defects in collagen folding and cross-linking including type X, XI and type caused by *PLOD2* mutation. OI type X is mainly caused by mutation of *SERPINH1* which encodes HSP47. HSP47 is important in stabilizing folded collagen and transferring to Golgi (49). This type of OI could lead to platyspondyly and scoliosis at early age. Like *SERPINH1*, *FKBP10* is another important gene in procollagen modification (9). Its deficiency could lead to OI type XI. Associated with *FKBP10*, *PLOD2* which encodes LH2 is another gene which could cause OI (54). Scoliosis is also very common in both types.

In the fourth group, OI is mainly caused by defects in bone mineralisation including type V and VI. Mutations of interferon-induced transmembrane protein 5 (*IFITM5*) could cause autosomal-dominant OI V. IFITM5 has close relationship with osteoblast, which may elucidate hyperplastic callus formation and membrana interossea ossification of forearms after injury (65). Patients with scoliosis could have cystic lesions vertebral bodies or vedge-shaped compression fractures (41). Connected with *IFITM5*, *SERPINF1* which underlying OI type VI encodes protein pigment epithelium-derived factor (PEDF) (41). PEDF plays an important role in osteoprotegerin/RANKLE-pathway (66). Some studies had shown that decreased PEDF level may lead to activated osteoclast increased and thus induced bone resorption (67,68). This type OI could have severe scoliosis (33).

In the fifth group, OI is mainly caused by defects in osteoblast development with collagen insufficiency including type XII, XV and XVI. *SP7* which encodes protein Osterix is target gene of Wnt pathway. Scoliosis in OI type XII with *SP7* mutation was also reported (57), osteoblast development defects were considered to happen in this progress. Both heterozygous and homozygous *WNT1* mutations could lead to OI type XV. As a member of Wnt family, mutations of *WNT1* could cause complex signaling pathway defects in bone formation. In this type, scoliosis with early onset osteoporosis was reported (18). Just like *WNT1*, *CREB3L1* mutation could also influence osteoblast development which may cause OI type XVI (69). But no scoliosis was reported yet. As OI type XVI, *PLS3* mutation could lead to OI manifesting with osteoporosis and fractures (70). The exact mechanism is not known and report with scoliosis was not found yet.

Mechanism of scoliosis

The mechanism of scoliosis in OI has not been clarified, it is thought that there are some triggering factors such as vertebral microfractures caused by vertebral growth plates injuries or bone fragility. Some other factors like length inequality, pelvic obliquity, ligamentous laxity and inter-vertebral disc abnormalities would lead to scoliotic progression.

The vertebral body malformation may cause abnormal spinal curve in OI. Wedged vertebrae had been reported in OI patients representing kyphosis and quadriparesis (71). Fragile bone and fracture could lead to deformities in some severe OI forms, for example scoliosis (72). Although this is very common in OI, scoliosis patients can have no spinal fracture (32,59).

Osteopenia is also very common in OI patients which

Table 2 Gene variants in different types of OI with scoliosis

Chromosome region	Gene	Mutation location	Function	Inheritance	OI type	Vertebral anomalies	Onset age (years)	Overlap phenotype	Reference
17q21.33	*COL1A1*	c.700delG	Frameshift	Heterozygous	I	Vertebra compression fracture	13	Joint hypermobility	Wang *et al.* 2015 (29)
17q21.31-q22	*COL1A1*	IVS26DS, G-A, +1	Splicing	Heterozygous	I	Mild, <10°	28	Ligamentous laxity	Stover *et al.* 1993 (30)
17q21.3	*COL1A1*	c.4358_4362delAATTC	Frameshift	Heterozygous	I	Mild	33	–	Willing *et al.* 1990 (31)
17q21.3	*COL1A1*	c.661G>T	Missense	Heterozygous	I	Mild	38	Hypermobile joints	Shapiro *et al.* 1992 (32)
17q21.3	*COL1A1*	c.3421C>T	Missense	Heterozygous	I	Mild	22	–	Venturi *et al.* 2006 (33)
17q21.3	*COL1A1*	IVS17+1G>A	Splicing	Heterozygous	I	–	5	Joint laxity	
17q21.31-q22	*COL1A1*	562-BP DEL	Frameshift	Heterozygous	III	Vertebra compression fracture, 40°	9	Basilar invagination	Wang *et al.* 1996 (34)
7q22.1	*COL1A2*	V255del	Deletion	Heterozygous	III	Vertebra compression, minimal scoliosis	2	Marked osteopenia	Molyneux *et al.* 1993 (35)
17q21.3	*COL1A1*	c.4391T>C	Missense	Heterozygous	III	Moderate	3	Joint laxity	Oliver *et al.* 1996 (36)
17q21.3	*COL1A1*	c.994G>A	Missense	Heterozygous	III	Marked	12	–	Pruchno *et al.* 1991 (37)
17q21.3	*COL1A1*	c.2461G>A	Missense	Heterozygous	III	Platyspondyly	40	–	Venturi *et al.* 2006 (33)
17q21.3	*COL1A1*	c.2503G>T	Missense	Heterozygous	III	–	3	–	
17q21.31-q22	*COL1A1*	c.1964_1966del	Frameshift	Heterozygous	IV	Severe, prominent	19	Hypermobility	Lund *et al.* 1996 (38)
17q21.3	*COL1A1*	c.3028G>A	Missense	Heterozygous	IV	Mild	5	–	Marini *et al.* 1989 (39)
		c.1588G>A				Vertebra compression	6.5		Marini *et al.* 1993 (40)
11p15.5	*IFITM5*	c.119C>T	Missense	Heterozygous	V	Small cystic lesions vertebral bodies	10	Regurgitation of the tricuspid	Farber *et al.* 2014 (41)
11p15.5	*IFITM5*	c.-14C>T	5' prime UTR	Heterozygous	V	Wedge–shaped compression fractures	>5	Joint hypermobility	Semler *et al.* 2012 (42); Cho *et al.* 2012 (43); Shapiro *et al.* 2013 (8) Rauch *et al.* 2013 (7)
–	–	–	–	–	VI	Severe	3	–	Venturi *et al.* 2006 (33)

Table 2 *(continued)*

Table 2 *(continued)*

Chromosome region	Gene	Mutation location	Function	Inheritance	OI type	Vertebral anomalies	Onset age (years)	Overlap phenotype	Reference
3p22.3	*CRTAP*	c.118G>T	Nonsense	Homozygous	VII	Vertebra compression fracture, mild	7	Osteopenia	Balasubramanian *et al.* 2015 (44)
3p22.3	*CRTAP*	c.804_809delAGAAGT	Deletion	Homozygous	VII	Vertebra compression fracture	4.2	Low BMD	Amor *et al.* 2011 (45)
1p34	*LEPRE1*	c.2055+18G>A	Splicing	Homozygous	VIII	Platyspondyly	13*	Osteopenia	Willaert *et al.* 2009 (46)
		c.1102C>T	Nonsense	Heterozygous					
1p34	*LEPRE1*	c.1656C>A	Nonsense	Homozygous	VIII	Platyspondyly	6	Osteopenia	Cabral *et al.* 2007 (47)
15q21-q22	*PPIB*	c.451C>T	Nonsense	Homozygous	IX	Severe	4.5	Hypermobility	Van Dijk *et al.* 2009 (48)
		c.556_559delAAGA	Frameshift						
11q13.5	*SERPINH1*	c.233T>C	Missense	Homozygous	X	Platyspondyly	1	Osteopenia	Christiansen *et al.* 2010 (49)
17q21.2	*FKBP10*	c.122_156del	Frameshift	Homozygous	XI	Na	22	Growth retardation	Kelley *et al.* 2011 (50)
17q21.2	*FKBP10*	c.321_353del	Deletion	Homozygous	XI	Wedge vertebrae	–	Severe osteopenia	Alanay *et al.* 2010 (51)
		c.831_832insC	Frameshift	Homozygous					
17q21.2	*FKBP10*	c.743dupC	Frameshift	Homozygous	XI	Severe scoliosis	6*	Osteopenia	Shaheen *et al.* 2011 (52); Schwarze *et al.* 2013 (9)
17q21.2	*FKBP10*	c.1271_1272delCCinsA	Frameshift	Homozygous	XI	Compression	6	Osteopenia, wormian bones	Barnes *et al.* 2012 (53); Puig-Hervás *et al.* 2012 (54)
17q21.2	*FKBP10*	c.948dupT	Frameshift	Homozygous	XI	–	13	Wormian bones	Schwarze *et al.* 2013 (9)
		c.14delG	Frameshift	Homozygous		–	11	–	
		c.337G>A	–	Homozygous		Vertebrae fracture	–	–	
		c.344G>A	Missense	Homozygous			7	–	
		c.831dupC	Frameshift	Homozygous		Vertebrae fracture	14	–	
		c.831dupC+c.948dupT	Frameshift	Compound heterozygous		–	–	–	
		c.1330C>T	–	Homozygous		–	8	–	

Table 2 *(continued)*

Table 2 *(continued)*

Chromosome region	Gene	Mutation location	Function	Inheritance	OI type	Vertebral anomalies	Onset age (years)	Overlap phenotype	Reference
17q21.2	*FKBP10*	c.1207C>T	Nonsense	Homozygous	XI	–	43	Hypermobile joints	Steinlein *et al.* 2011 (55)
17q21.2	*FKBP10*	c.976delA	Frameshift	Homozygous	XI	Kyphoscoliosis	7	Joint contracture	Seyedhassani *et al.* 2016 (56)
12q13.13	*SP7*	c.1052delA	Frameshift	Homozygous	XII	Mild scoliosis	8	Pectus carinatum, wormian occipital bone	Lapunzina *et al.* 2010 (57)
8p21	*BMP1*	c.747C>G	Missense	Homozygous	XIII	Platyspondyly	15 & 5	Umbilical hernia, hyperextensibility of elbow, decreased bone density, wormian bones	Martínez-Glez *et al.* 2012 (58)
8p21.3	*BMP1*	c.808A>G c.1297G>T	Missense	Compound heterozygous	XIII	Mild	12*	Umbilical hernia	Cho *et al.* 2015 (59)
9q31.2	*TMEM38B*	c.455-7T>G	Splicing	Homozygous	XIV	Slight	4.5	Osteoporosis	Lv *et al.* 2016 (60)
12q13.1	*WNT1*	c.893T>G c.884C>A	Missense Nonsense	Homozygous	XV	–	2*	Fractures	Pyott *et al.* 2013 (18)
5q33.1	*SPARC*	c.497G>A c.787G>A	Missense	Homozygous	XVII	Vertebra compression fracture	19* 5	Joint hypermobility, decreased BMD	Mendoza-Londono *et al.* 2015 (10)
3q24	*PLOD2*	c.1856G>A	Missense	Homozygous	others	–	–	–	Puig-Hervás *et al.* 2012 (54)

*, month. OI, osteogenesis imperfecta; COL1A1, collagen, type I, alpha-1; COL1A2, collagen, type I, alpha-2; CRTAP, cartilage-associated protein; IFITM5, interferon-induced transmembrane protein 5; LEPRE1, leucine- and proline-enriched proteoglycan 1; PPIB, peptidyl-prolyl isomerase B; SERPINH1, serpin peptidase inhibitor, clade H, member 1; FKBP10, FK506-binding protein 10; SPARC, secreted protein, acidic, cysteine-rich; BMD, bone mineral density.

might be the pathology of scoliosis because of vertebral fragility (73). Some studies have shown the positive correlation of scoliosis with Z-score BMD and BMI (74). In *Col1a1*^{Jrt}/+ mice model with OI and Ehlers-Danlos Syndrome (EDS) (75), the scoliosis mice had lower BMD and bone mineral content (BMC) compared with age-matched +/+ littermates which may lead to the early and rapid progressive malformation of vertebrae body.

There were many other factors which may influence scoliosis in OI. According to a retrospective study (11), scoliosis was significantly associated with age, whereas other clinical characteristics such as gender, weight, SDI were not. In some cases (76), scoliosis and vertebral body compression only happened during growth. Engelbert (4) found that the age of first achieving scoliosis was associated with the age of anti-gravity motor milestone, such as "supported sitting". The connection may be caused by mechanical loads change. Some other studies also shown that the prevalence of scoliosis at maturity was not influenced by bisphosphonate treatment history although the treatment could decrease the progression (24).

Another important reason is increased mechanical strains during childhood. Mechanical loads with osteopenia can cause bone remodeling and progressive deformations, and the pedicle elongation is the most common result. Some OI cases with severe hyperlordosis had been reported to be caused by lumbar pedicle elongation and spondylolisthesis (77). Some other researchers proposed mechanostat model to illustrate bone deformations cause by mechanical forces (78).

Joint hyperlaxity can lead to scoliosis and chest malformations (73). In a subset of OI (79), patients with OI/EDS can have scoliosis because of ligamentous laxity, dislocations of other joints and mild osteopenia, with a few fractures. This may be caused by mutation of exon 6 fromαchain which lead to N-propeptide retention.

Conclusions

Most of the types OI could manifest with scoliosis, with type III patients have higher prevalence and type XV has the earliest scoliosis onset age. The exact mechanism of scoliosis in OI is complex and has not been fully elucidated. Based on current studies, scoliosis is mainly influenced by OI type, osteopenia, age, BMD, BMC, mechanical strains and ligamentous laxity.

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Footnote

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