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Review Article

Orthopaedics Section

Osteogenesis Imperfecta: A Narrative Review of Pathogenesis, Clinical Manifestations and Emerging Therapies

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ABSTRACT

Osteogenesis Imperfecta (OI) is a genetic disorder that causes "brittle bone disease" due to defects in type I collagen and other genes that control collagen synthesis and osteoblast activity, resulting in fragile bones, as well as skeletal problems and connective tissue disorders. Individuals with this condition exhibit symptoms ranging from mild intermittent fractures to life-threatening cases, with varying degrees of severity. The genetic condition OI includes primary types (I-IV), which exhibit autosomal dominant traits, whereas newer versions (V-VIII) demonstrate autosomal recessive or unique dominant characteristics. The characteristics of OI include brittleness, which leads to easy fractures, shortened body length, spinal curvature, a bluish ring around the eyes, ear problems, weak teeth and sensitive skin. Diagnosis relies on clinical assessments, imaging tests and genetic testing, as these methods aid in subtype identification and genetic counselling. Physical therapy, along with assistive technology, helps patients manage OI. Bisphosphonates are the primary drugs used for treating OI, accompanied by calcium supplements and vitamin D, which constitute the pharmacological therapy. Surgical interventions, such as intramedullary rodding and spinal fusion, become necessary when severe deformities develop. Future treatments for OI's inherited nature include three promising therapies that combine gene therapy, stem cell therapy and antisclerostin antibody protocols. Advances in genetic testing, alongside new therapeutic developments, unlock new medical possibilities to enhance patient healthcare and increase the need for research into the management of this complex condition.

Keywords: Bisphosphonates, Collagen, Fractures, Mutation, Therapy

INTRODUCTION

People suffering from OI usually develop fragile bones that are prone to breaking, often with little or no trauma [1]. Human bone fragility, along with skeletal abnormalities and connective tissue defects, arises from gene mutations (typically COL1A1 or COL1A2) that affect the production of type I collagen [1]. The diagnostic features of OI include short stature, combined with bone malformations, as well as fragile bones and multiple fractures [2]. Mild forms of OI may remain unidentified until an individual reaches adulthood, while severe cases can result in foetal death during pregnancy [2]. The disease is classified into five widespread forms, with type I being mild and type II being fatal [3]. Patients with types III and IV survive beyond the normal newborn period despite presenting with severe conditions, whereas type V OI exhibits a combination of mild to moderate symptoms, along with interosseous membrane involvement [3]. The decline in normal type I Collagen (Col I) production or the formation of aberrant collagen occurs due to mutations in Col I genes [4]. Mutations in genes that regulate Col I synthesis and processing, as well as the differentiation of osteoblasts, have been reported in cases of OI [4]. OI presents as a global health problem with predominantly autosomal dominant patterns, though rare autosomal recessive forms also exist [1,3].

Types and Characteristics of Osteogenesis Imperfecta (OI)

OI exhibits four traditional primary forms (I-IV), which are classified based on genetic aetiology, inheritance patterns and clinical severity levels [2]. Type I OI is the mildest and most commonly occurring form of the condition, manifesting as blue sclera and hearing deficits, along with numerous bone fractures throughout life [5]. This genetic condition arises from mutations in the COL1A1 or COL1A2 genes, which reduce type I collagen production, and follows an autosomal dominant inheritance pattern [1,5].

Type II OI is the most severe and fatal form of OI, as sufferers typically die either in the womb or shortly after birth due to extreme bone fragility and respiratory complications [6]. The development of significant mutations in collagen genes leads to this condition, which also displays autosomal dominant inheritance [6,7].

Individuals diagnosed with type III OI experience numerous fractures, severe bone abnormalities, short stature and spinal curvature [7]. This form of OI shares similarities with types I and II as an autosomal dominant condition affecting the COL1A1 or COL1A2 genes, causing structural defects in the collagen produced [7].

Type IV OI is characterised by bone fragility and mild to moderate short stature, along with bone abnormalities, representing a moderately severe form of the disease. Patients with type IV OI may exhibit either plain sclerae or a faint blue appearance, which is their only visible differentiator compared to type I [8]. The condition is associated with mutations in collagen genes and follows an autosomal dominant transmission pattern [8].

Emerging types of Osteogenesis Imperfecta (OI): The four prominent types of OI remain fundamental for classification, despite newly identified forms, including Type V and later types, displaying distinctive genetic, radiological features and clinical manifestations [9]. Type V OI is characterised by white scleral eyes, interosseous membrane calcification and hypertrophic callus formation due to mutations in the IFITM5 gene [9,10]. Type VI OI is caused by mutations in the SERPINF1 gene, resulting in extreme bone fragility and normal fish-scale bone patterns [10]. Genetic mutations affecting the CRTAP gene lead to Type VII OI, which manifests as rhizomelia and moderate to severe bone fragility [11,12]. The presence of abnormalities in the LEPRE1 gene causes Type VIII OI, resulting in severe or fatal underdevelopment of skeletal structures throughout the body [11,12].

Clinical manifestations vary among activity-related OI types caused by mutations in genes such as PPIB, SERPINH1, FKBP10, SP7/OSX, and other genes due to their unique genetic patterns [13]. Recent forms of OI exhibit an autosomal recessive inheritance pattern, contrasting with the dominant inheritance observed in

types I-IV [13]. Genetic testing has gained new significance through these discoveries, as scientists now have a better understanding of OI genetics, which opens up treatment possibilities for patients [1,11]. The types and characteristics of OI are detailed in [Table/Fig-1] [1,5-13].

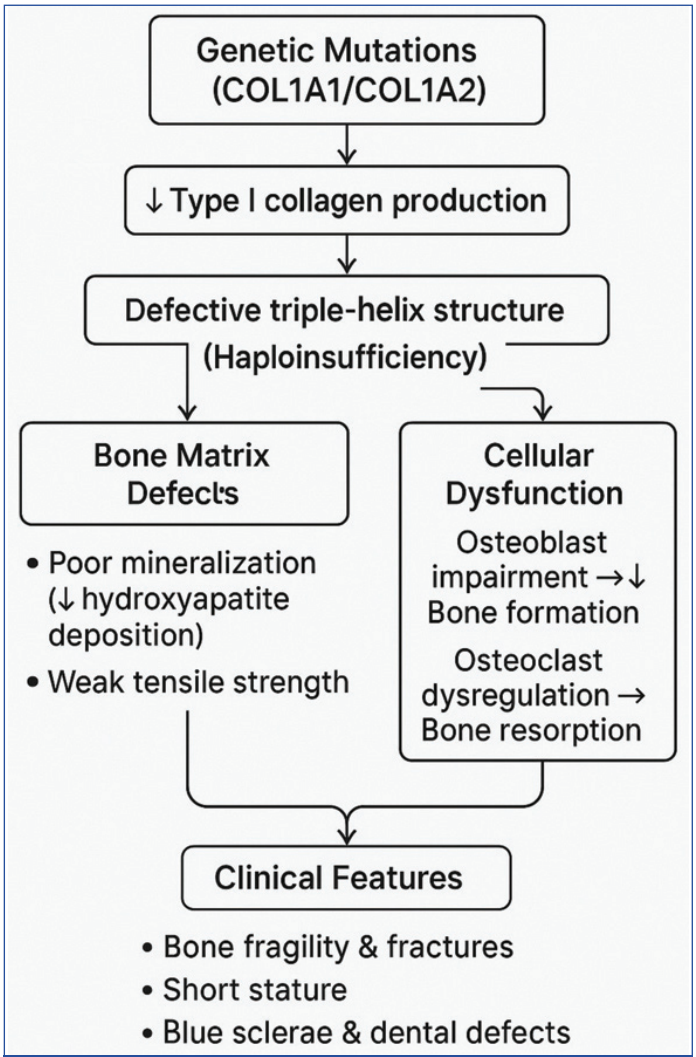
OI type	Characteristics	Genetic basis	Inheritance pattern	References
Type I	Mildest form, blue sclera, hearing deficits, multiple fractures	COL1A1 or COL1A2 mutation reduces type I collagen production	Autosomal dominant	[1,5]
Type II	Most severe, often fatal before or shortly after birth due to extreme bone fragility and respiratory issues	Severe collagen gene mutations	Autosomal dominant	[6,7]
Type III	Severe bone abnormalities, multiple fractures, short stature, spinal curvature	COL1A1 or COL1A2 mutation causing structural collagen defects	Autosomal dominant	[7]
Type IV	Moderate severity, mild-to-moderate short stature, bone abnormalities, normal or faint blue sclera	Collagen gene mutations	Autosomal dominant	[8]
Type V	White sclera, interosseous membrane calcification, hypertrophic callus formation	IFITM5 mutation	Autosomal dominant	[9,10]
Type VI	Extreme bone fragility, fish-scale bone pattern	SERPINF1 mutation	Autosomal recessive	[10]
Type VII	Rhizomelia, moderate to severe bone fragility	CRTAP mutation	Autosomal recessive	[11,12]
Type VIII	Severe or fatal skeletal underdevelopment	LEPRE1 mutation	Autosomal recessive	[11,12]
Other emerging types	Various bone fragility and deformities	PPIB, SERPINH1, FKBP10, SP7/OSX mutations	Autosomal recessive	[13]

[Table/Fig-1]: Types and characteristics of Osteogenesis Imperfecta (OI) [1,5-13].

Pathogenesis of Osteogenesis Imperfecta (OI)

The organic bone matrix is composed primarily of 90% type I collagen, as this protein acts as the main structural component of bone tissue [14]. The bonding of two α1 chains with one α2 chain results in a triple-helix structure that provides bones with tensile strength and flexibility [14,15]. The resistance to compression and stiffness of bones is largely due to collagen serving as a scaffold for the deposition of crystal hydroxyapatite [15]. When osteoblasts produce type I collagen during bone formation, this protein material is integrated into the bone matrix through mineralisation [16]. Osteoblasts and osteoclasts utilise collagen fibres to carry out bone remodelling tasks, as these fibres provide favourable attachment surfaces [16]. The hierarchical structure of collagen fibres enhances bone flexibility and toughness, thereby enabling bones to absorb energy effectively when facing fractures [15]. Proper cross-linking of collagen molecules is necessary to maintain their mechanical properties [14,15].

OI develops primarily due to genetic variations that affect the genes coding for type I collagen. Bone fragility arises from these genetic changes, which hinder type I collagen from performing its normal synthesis and maintaining its standard structural composition [17]. Haploinsufficiency occurs when one specific allele becomes non functional due to mutated genetic sequences, leading to a decreased amount of normal collagen [16,17]. This collagen deficiency weakens the bone structure. Improper collagen structure creates difficulties for bone mineralisation, resulting in poor bone density because it disrupts the alignment of hydroxyapatite crystals during deposition [8]. The altered bone collagen structure diminishes both osteoclast resorption activity and osteoblast function, contributing to increased bone fragility [4,18]. Bone deformities and brittle bones, which are easily fractured, coincide with short stature in patients exhibiting these conditions, along with connective tissue abnormalities that include blue sclerae and dental complications in OI [18]. The pathogenesis of OI is illustrated in [Table/Fig-2].



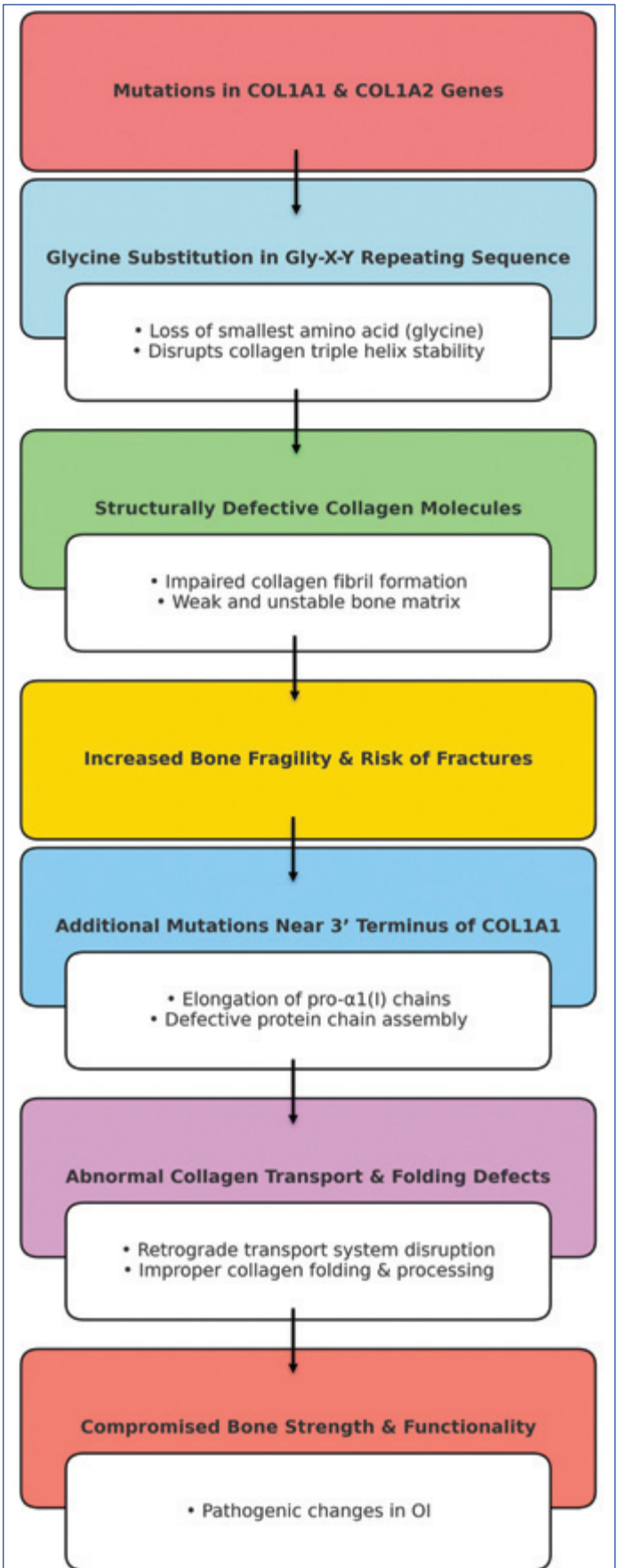
[Table/Fig-2]: Pathogenesis of Osteogenesis Imperfecta (OI).

Molecular basis of Osteogenesis Imperfecta (OI)

The COL1A1 and COL1A2 genes primarily cause OI by carrying mutations that affect the pro-α1 (I) and pro-α2 (I) type I procollagen chains [19]. Glycine substitution is a common consequence of mutations in the Gly-X-Y repeating sequence of collagen triple helices [20]. Glycine is critical for the tightness of collagen helices, as it is the smallest amino acid [20]. Replacing glycine with larger amino acids renders the helical structure unstable, resulting in structural defects within collagen molecules [20]. This instability in the structure of collagen fibrils leads to a weakened bone matrix, which increases the risk of fractures [20].

Expansions that occur near the 3' terminus of the COL1A1 gene, along with glycine substitutions due to mutations, cause excessive elongation of the pro-α1 (I) chains [21]. Abnormal protein chains create barriers to assembly, worsening the quality of the bone matrix tissue [21]. Researchers have found that defects in collagen transport systems result in mutations within the body [21]. Deficiencies in elements of retrograde transport systems prevent proper collagen folding and processing, creating a pathogenic situation in OI [16]. The precise processes of collagen biosynthesis and assembly are crucial for bone strength, as disruptions at the molecular level compromise both the structure and functionality

of bone tissue [20,21]. The molecular basis of OI is illustrated in [Table/Fig-3].



[Table/Fig-3]: Molecular basis of Osteogenesis Imperfecta (OI).

Clinical Manifestations of Osteogenesis Imperfecta (OI)

OI is known as "brittle bone disease" because patients have bones that become brittle, which can break easily during daily activities without evident injuries or trauma [22]. The primary medical sign of this condition is an increased susceptibility to fractures, ranging from moderate to severe levels, depending on the OI subtype [22]. Long bones, particularly the femur, tibia and humerus, experience the majority of fractures associated with this condition [22,23].

Skeletal abnormalities and growth impairments: The main skeletal abnormalities of OI arise from abnormal bone growth and the occurrence of multiple fractures throughout the condition [23]. The most frequently recognised issues in patients with OI affect spinal structure, leading to conditions such as kyphosis or scoliosis, while also deforming the long bones of the limbs, from the arms to the legs [24]. Spinal curvature and chest wall abnormalities may cause breathing difficulties that impact lung capacity and increase the risk of respiratory insufficiency and recurrent lung infections [24]. The abnormal bone growth in OI patients results in diminished stature and shortened height [1,11]. The poor development and growth issues in bones become even more severe with repeated fractures and skeletal abnormalities [3,23].

Ocular, auditory, and dental manifestations: A bluish tint to the whites of the eyes, known as blue sclera, represents a distinctive clinical pattern of OI, as it arises from the thinness of collagen-rich connective tissue, which exposes the visibility of blood vessels [12,25]. The most frequently observed health issue is hearing loss, with manifestations typically beginning in early adulthood and gradually deteriorating over time [26]. Anomalies in the middle ear bones are usually the underlying cause of this condition [26].

Dentinogenesis imperfecta is a common oral condition affecting individuals with OI, as it results in brittle teeth that exhibit discolouration and lead to dental fragility [27]. The development of defective dentin within the teeth gives rise to specific dental anomalies [27]. The connective tissue weakness in individuals with OI results in thin and delicate skin, making them prone to frequent bruising due to underlying tissue fragility [4,5]. These clinical characteristics collectively indicate that OI affects multiple body systems, influencing both skeletal structures and other connective tissues throughout the entire body [1,9]. The clinical features of OI are detailed in [Table/Fig-4] [1,3-5,9,11,12,22-27].

Clinical features	Description	References
Fracture susceptibility	OI leads to brittle bones that break easily without trauma. Long bones like the femur, tibia and humerus are most affected.	[22,23]
Skeletal abnormalities	Includes spinal deformities (kyphosis, scoliosis), limb deformities and chest wall abnormalities that can lead to respiratory issues.	[23,24]
Growth impairments	Abnormal bone growth results in short stature, worsened by repeated fractures.	[1,3,11,23]
Ocular manifestations	Blue sclera due to thin collagen-rich connective tissue revealing blood vessels.	[12,25]
Auditory issues	Hearing loss, typically starting in early adulthood, due to middle ear bone anomalies.	[26]
Dental issues	Dentinogenesis imperfecta causes brittle, discoloured teeth with weak dentin structure.	[27]
Skin fragility	Thin, delicate skin with frequent bruising due to connective tissue weakness.	[4,5]
Systemic impact	OI affects multiple body systems, impacting skeletal structures and connective tissues.	[1,9]

[Table/Fig-4]: Clinical features of Osteogenesis Imperfecta (OI) [1,3-5,9,11,12,22-27].
OI: Osteogenesis imperfecta

Diagnostic Approach to Osteogenesis Imperfecta (OI)

The clinical characteristics of OI include repeated bone fractures, bone irregularities, blue sclera, dentinogenesis imperfecta and hearing loss, all of which assist in its diagnosis [9,28]. The diagnosis of OI can be confirmed through evaluations of family history since relatives are likely to exhibit similar symptoms of the condition [28]. Healthcare professionals examining individuals with moderate to severe forms of OI must assess their height, as these forms commonly cause reduced stature [28]. A proper diagnosis of OI relies on radiographic imaging [2,28].

Diagnostic features for this condition include osteopenia, fractures at various stages of healing, and wormian bones, which are additional sutural bones in the skull [29]. The frequent occurrence of fractures leads to both bending deformities and physical abnormalities of long bones, which often exhibit a slender and elegant structure [29]. The most severe manifestations can result in spinal curvatures known as scoliosis, along with vertebral crush injuries [24,29].

The diagnosis of OI is made certain through genetic testing, which demonstrates the highest accuracy [1,11,30]. The results of genetic testing help physicians confirm the diagnosis of OI and assist in determining the type and severity of the condition to guide medical treatment and genetic counselling [30]. Multiple medical conditions presenting with osteopenia, bone imperfections, or fragility will be considered when diagnosing OI [30]. The diagnosis of rickets becomes evident through specific radiographic features combined with biochemical markers, as its growth plates expand differently compared to OI [31]. Children with unexplained fractures should be evaluated for possible non accidental injuries, including physical abuse [31].

Treatment and Management Strategies for Osteogenesis Imperfecta (OI)

The primary focus of medical treatment is on dual functions: improving bone strength and preventing fractures [2,28]. Pamidronate and other bisphosphonates can be used as the first-line treatments for OI [2,32]. Bisphosphonates protect bones from resorption while simultaneously increasing bone density, thus reducing the likelihood of fractures [32]. These medications provide relief from bone pain and are particularly beneficial for patients with moderate to severe forms of OI [32]. Improving bone health typically requires the combined use of bisphosphonates with vitamin D and calcium supplements for most patients [33,34]. Denosumab, along with other novel treatments, can serve as alternatives for patients who do not respond to bisphosphonate therapy [33]. Additionally, antisclerostin antibodies may represent a potential new treatment option, as they promote bone formation [12].

Managing complications associated with OI often necessitates surgical intervention as an essential treatment for severe cases [1]. One common surgical procedure involves the insertion of metal rods inside long bones (intramedullary rodding) to provide stability, prevent deformities, and reduce the occurrence of fractures [35]. This surgical approach is particularly beneficial for young patients, as their developing bones are involved [35]. Patients requiring treatment for severe spinal curvature due to scoliosis can achieve better stability through spinal fusion procedures, both before and after surgical intervention [35].

The management of OI heavily relies on physical therapy to improve overall body functionality, alongside strength development and enhanced mobility [18]. A combination of fitness training tailoured specifically for patients with OI can build muscle strength and prevent fractures by incorporating non jarring exercises such as swimming [12]. Physical therapy enhances motor skills and physical coordination while also improving balance, as these abilities are often impaired in individuals with OI [1,2]. The use of assistive technology, such as wheelchairs, walkers and braces, should also be considered to help maintain independence and mobility [8,35]. Gene therapy represents a novel strategy aimed at restoring and correcting the genetic alterations associated with OI to address its root cause [36]. Stem cell therapy offers potential improvements in bone formation systems and repair techniques related to OI [36]. Treatment strategies for OI are detailed in [Table/Fig-5] [1,2,8,12,18,32-36].

Researchers have investigated Mesenchymal Stem Cells (MSCs) due to their promise in differentiating into osteoblasts and supporting bone tissue growth [37]. Medical research indicates

Treatment/Management	Description	References
Bisphosphonates	Improve bone density, reduce fractures and relieve bone pain. Typically used with vitamin D and calcium.	[2,32-34]
Denosumab	Alternative for patients unresponsive to bisphosphonates.	[33]
Antisclerostin antibodies	Encourages bone formation, a potential new treatment.	[12]
Surgical interventions	Metal rods in long bones to provide stability and prevent deformities. Spinal fusion for severe scoliosis.	[1,35]
Physical therapy	Enhances mobility, muscle strength and coordination through non jarring exercises (e.g., swimming).	[1,2,12,18]
Assistive technology	Use of wheelchairs, walkers and braces to maintain independence.	[8,35]
Gene therapy	Aims to correct genetic defects causing OI.	[36]
Stem cell therapy	Potential to improve bone formation and repair.	[36]

[Table/Fig-5]: Treatment strategies for Osteogenesis Imperfecta (OI) [1,2,8,12,18,32-36].
OI: Osteogenesis imperfecta

that MSC transplantation shows potential safety for patients while sometimes improving both bone density and growth rate, although these benefits may diminish over time [37]. A phase I clinical trial administering MSC infusions to paediatric patients over 2.5 years demonstrated better bone status and improved quality of life through the paracrine pro-osteogenic effects of MSCs [37]. Experimental gene therapy approaches have achieved significant success, with research utilising homologous recombination to modify COL1A1 genes in patient-derived induced pluripotent stem cells, achieving an 84% success rate [38].

Management approaches for OI show considerable variation between geographical areas, particularly affecting regions with limited resources [39]. Early diagnosis and targeted treatment methods are crucial, as countries like Uganda face numerous barriers due to a lack of medical knowledge, specialist training and limited resources [40]. The restricted availability of bisphosphonates, which are commonly used in the treatment of OI, forces patients to resort to alternative care options, including physical therapy and nutritional support [40]. Additionally, the limited availability of specialised surgical expertise and necessary equipment restricts the execution of bone-strengthening rodding procedures [40]. Improving health outcomes for OI patients in resource-limited regions requires the enhancement of healthcare facilities, development of medical practitioners and expanded access to essential treatments [40].

Emerging Treatment Techniques for Osteogenesis Imperfecta (OI)

New medical research has introduced multiple promising approaches to treating OI. CRISPR gene editing experimental methods demonstrate strong potential for establishing long-term curative options that can address the fundamental cause of the disease [41]. Researchers are applying MSCs in their investigations to enhance bone growth and strengthen skeletal structure [42]. The clinical use of anti-Transforming Growth Factor-beta (TGF-β) antibodies represents an emerging therapeutic method that shows promise in managing bone structure remodelling while decreasing bone brittleness [39].

These innovative therapies, highlighted in recent clinical experiments, suggest that such methods will enhance the effectiveness of OI treatment and provide longer-lasting benefits. Selective monoclonal antibodies target sclerostin proteins to promote bone formation. Setrusumab (BPS-804) is a monoclonal antibody with a specific application for treating OI [43]. The administration of setrusumab works through the suppression of sclerostin, leading to enhanced bone formation and increased bone density [43]. Medical researchers

have conducted structured tests to determine both the safety and effectiveness of setrusumab among individuals with OI [43].

Additionally, scientific investigations have explored allele-specific silencing as a potential treatment method for OI [44]. This method silences the defective allele associated with OI, reducing the production of defective collagen while stimulating the synthesis of normal collagen [44]. The experimental phase of allele-specific silencing demonstrates potential as a treatment for the genetic basis of OI [44]. Emerging treatment techniques for OI are described in [Table/Fig-6] [39,41-44].

Therapeutic approach	Description	Potential benefits	Reference
CRISPR gene editing	Experimental method for precise genetic modification	Potential for a long-term cure	[41]
Mesenchymal Stem Cells (MSC)	Applied in research to strengthen bones	Supports skeletal structure enhancement	[42]
Anti-TGF-β antibodies	Targets bone remodeling and reduces brittleness	Helps manage bone structure effectively	[39]
Setrusumab (BPS-804)	Monoclonal antibody that suppresses sclerostin	Enhances bone formation and increases density	[43]
Allele-specific silencing	Silences defective allele to reduce abnormal collagen	Promotes normal collagen synthesis	[44]

[Table/Fig-6]: Emerging treatment techniques for Osteogenesis Imperfecta (OI) [39,41-44].

Psychological and quality of life challenges in Osteogenesis Imperfecta (OI): OI causes significant deterioration in the quality of life for patients as they transition from early childhood into adulthood, affecting their physical dimensions, emotional stability and social interactions [45]. Children diagnosed with OI report markedly lower quality of life ratings across physical, emotional, social and school-functioning dimensions compared to children without the disorder [45]. The level of impairment associated with this condition tends to increase with the advancing severity of the disease [45].

Adults with OI exhibit diminished quality of life as assessed through their physical health status and various aspects of mental health, with their physical health scores reflecting the extent of their condition [45]. The presence of respiratory issues has detrimental effects on psychosocial health and restricts daily activities among patients with OI, regardless of age or OI subtype [35].

The stress levels and quality of life among caregivers of children with OI significantly worsen when caring for patients who experience more intense pain and impaired physical abilities [18,35,45]. Comprehensive support programmes must focus on addressing both healthcare challenges and psychiatric issues for OI patients and their families [35,45]. OI patients often experience increased emotional distress due to the unpredictability of bone injuries, which leads to heightened anxiety levels [46]. This constant fear can result in poor self-perceptions and amplify disease-related stress, particularly during recovery [46]. The ongoing pain and fatigue associated with OI create substantial challenges that impact routine activities and strain family relationships, as parents with OI may need to limit their activities with their children, ultimately affecting family dynamics [46].

Age-specific management and transitional care in Osteogenesis Imperfecta (OI): The successful treatment of OI requires the continuous development of specific strategies that adapt to patients as they age [47]. Developmental support and fracture avoidance are prioritised in infancy through appropriate handholding techniques, therapy adjustments and the potential use of bisphosphonates for enhancing bone density [47]. The care plan for children and adolescents includes ongoing bisphosphonate therapy combined with orthopaedic intramedullary rodding procedures and supportive measures to encourage safe physical activities that enhance muscle strength [47].

Adults need to monitor and manage hearing loss, alongside cardiovascular health issues, while maintaining bone health as they transition from childhood into adulthood [48]. The change in healthcare providers necessitates collaboration between paediatric and adult medical professionals for continuous care management [48].

Care for adult patients with OI focuses on maintaining bone density, implementing lifestyle changes to reduce the risk of fractures and addressing ongoing pain and mobility issues [48]. Optimal care for OI patients requires a multidisciplinary team that includes physicians, orthopaedic surgeons, physiotherapists and other specialists at each life stage to improve medical outcomes and enhance the quality of life for patients [46,48]. Age-specific management strategies for OI are detailed in [Table/Fig-7] [46-48].

Age group	Management focus	References
Infancy	Fracture avoidance, proper handling, therapy adjustments, possible bisphosphonate use.	[46,47]
Childhood	Bisphosphonate therapy, orthopaedic rodding, safe physical activities for muscle strength.	[47]
Adolescence	Continuation of bisphosphonate therapy, orthopaedic support, monitored physical engagement.	[47]
Adulthood	Bone density maintenance, hearing loss and cardiovascular monitoring, pain and mobility management.	[48]
Transition phase	Coordination between paediatric and adult healthcare providers for seamless care.	[46-48]

[Table/Fig-7]: Age-specific management in Osteogenesis Imperfecta (OI) [46-48].

CONCLUSION(S)

The OI is an inherited condition that affects bone health by causing weak bones, as well as skeletal irregularities and tissue defects stemming from mutations in the type I collagen gene. The disorder presents in various forms, ranging from moderate to severe, leading to bone fractures, height limitations, blue-tinted sclera and dental health problems. The treatment and diagnostic approach for managing OI encompasses bisphosphonates, surgery, physical therapy, assistive devices, genetic testing, clinical evaluation and imaging. Newly discovered methods of gene and stem cell therapy show promise in addressing the underlying causes of the condition. As a global health problem, OI requires a multidisciplinary approach to achieve better treatment outcomes for patients.

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