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*Case Report*

# Osteogenesis Imperfecta Type IV in Siblings

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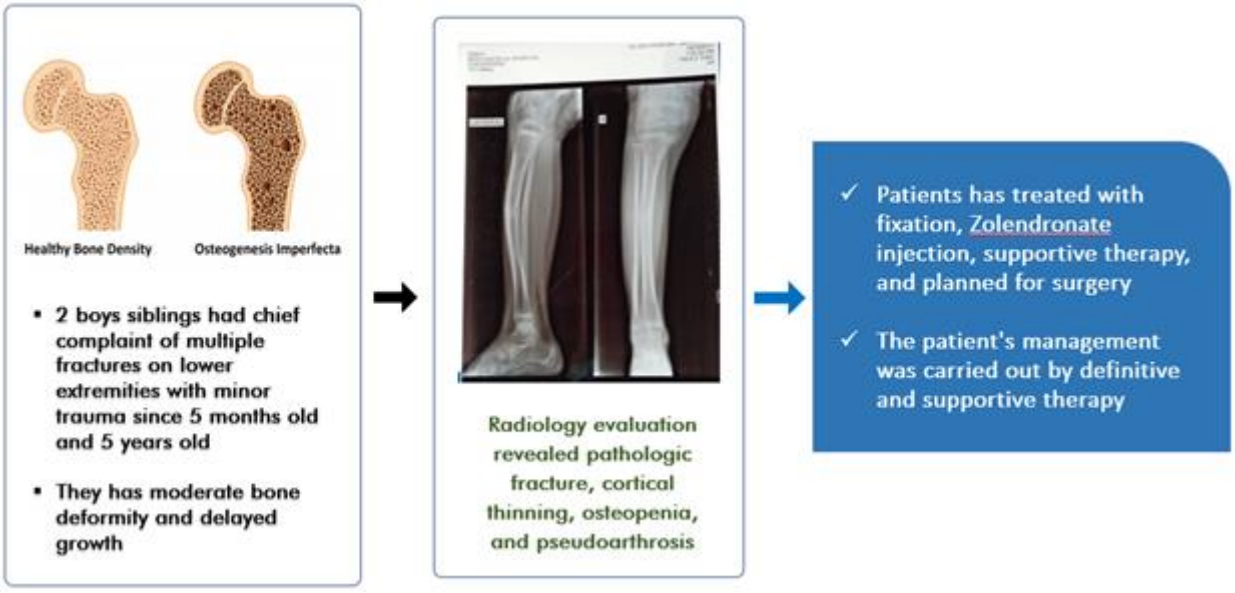
**ABSTRACT**

A rare bone condition known as osteogenesis imperfecta (OI) is brought on by an inherited connective tissue abnormality. Even within families who share a common mutation, symptoms might differ widely. H, a boy, aged 12, and F, a boy, aged 10, are siblings. Since they were 5 months old and 5 years old, their main complaint was repeated fractures in the lower extremities as a result of minor trauma. Only the mother's family had the same OI clinical manifestation characteristics. Physical examination revealed no signs of dentinogenesis imperfecta, blue sclera, hypermobility of the joints, or hearing problems. They have delayed growth and mild bone deformities. Pathologic fracture, cortical thinning, osteopenia, and pseudoarthrosis were all discovered during the radiology examination. The patient has received fixation, Biphosphonate injection, supportive care, and surgery. Therapy that was both definite and supportive was used to manage the patient. We monitored both patients physical and radiological examination, as well as the quality of life using PedsQL 4.0 Generic Core Scales aged 8-12 years for Child and Parent Report for Children before and after a year of monitoring, we observed that both the patient's symptoms and quality of life had improved.

**GRAPHICAL ABSTRACT**

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## Introduction

A rare bone condition known as osteogenesis imperfecta (OI) is brought on by an inherited connective tissue abnormality. Even within families who share a common mutation, the severity of clinical characteristics and symptoms might vary substantially. Patients OI type IV have mild to severe bone fragility. In addition to minor to moderate bone abnormalities and varied short stature, children with this type of OI have a higher incidence of fractures and decreased quality of life [1]. A multidisciplinary approach is crucial for diagnosis and treatment, as well as communication with the patient and their parents, based on the patient's age and the disease severity [2]. This report aims to look at both patients' symptoms and quality of life a year after they had supportive, surgical, and pharmaceutical treatment. This case was designed to help people become more proficient at comprehending how this condition is inherited from family members and how to diagnose and treat it.

*Case Reports*

*Case report I*

H, a boy aged 12 years and 10 months who weighs 27 kg, has a primary complaint of many fractures as a result of mild trauma like tripping or slipping at home since he was 5 months old. Twelve recorded traumas that caused lower extremity fractures were the outcome of the patient's anamnesis. Since birth, there had been no history of illness, congenital abnormalities, or physical dysmorphia. The patient had reached a normal developmental milestone. His grandmother had a similar issue of recurring fractures to her lower extremities, but none of his parents had a history of frequent fractures or any other sickness.

He was admitted to the hospital on May 4, 2019, with a broken femur after falling at school two weeks prior. No hearing problems, dentinogenesis imperfecta, or blue sclera were found after a physical examination (Table 1). Despite having numerous lengthy bone abnormalities, there was no bone discomfort, limb or joint pain, or muscle weakness. The patient was using crutches to walk.

**Table 1:** Profile characteristic of 2 cases with osteogenesis imperfecta

| Subject | Case I | Case II |
|---|---|---|
| Gender | M | M |
| Family history | Yes | Yes |
| Weight at birth (grams) | 2,500 | 1,900 |
| Gestation | Term | Preterm |
| Labor | Spontaneous | Spontaneous |
| Consanguineous Parents | No | No |
| OI on Family | Yes | Yes |
| Onset of symptoms (of life) | 5 months | 5 years |
| Several Fracture | Yes | Yes |
| Blue Sclera | No | No |
| CDC Stature for Age | <P3 | <P3 |
| CDC Weight for Age | P10-3 | <P3 |
| Hearing Impairment | No | No |
| Beaded Ribs | No | No |
| Walking Difficulties | Yes | Yes |
| Dismorphic | No | Yes |
| Perinatal asphyxia | No | Yes |
| Radiologic | OI Suspected | OI Suspected |
| Treatment | Biphosphonate injection<br>Calcium supplement<br>Rodding Surgery<br>External Fixation | Biphosphonate injection<br>Calcium supplement<br>Rodding Surgery<br>External Fixation |
| Frequency of medical treatement | 3 | 2 |

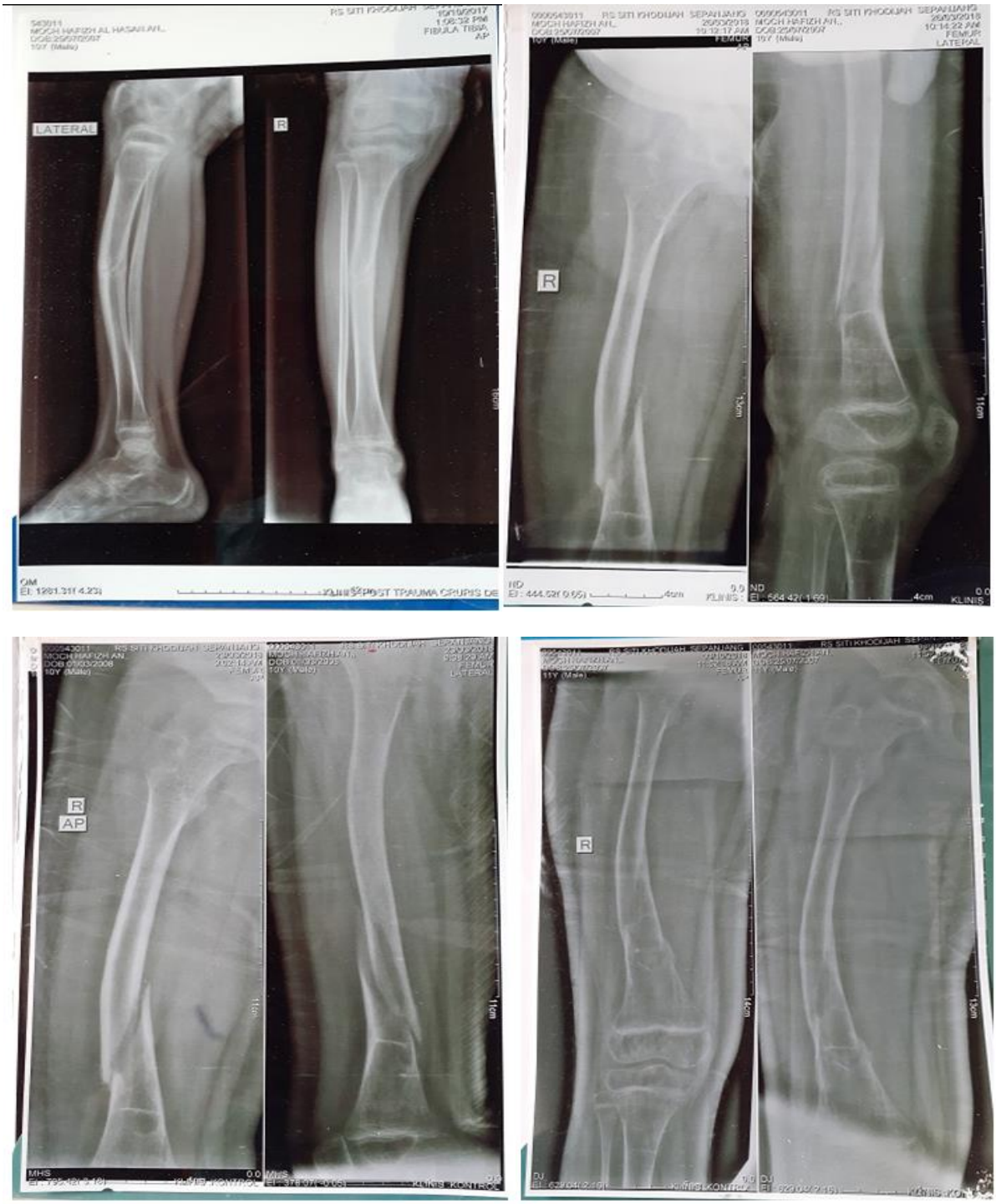


**Figure 1:** The 1st patient radiologic evaluation

Examination of the fractures revealed that external fixations did not cause any delayed healing. His growth in height and weight was delayed according to the anthropometry evaluation. Pathologic fracture, cortical thinning, osteopenia, and pseudoarthrosis suggested by radiologic examination were all seen (Figure 1). We diagnosed this patient with osteogenesis imperfecta and suggested bone density, family screening, and bone survey.

He received biphosphonate injection, calcium supplement, rodding surgery, and external fixation. In addition, the patient saw a physiotherapist, and as of right now, the patient could walk with crutches. After receiving treatment for OI for a year, the patient's symptoms and life quality improved, patient attend school regularly. The patient kept taking biphosphonate injection and calcium supplement.

*Case report II*

The first patient's younger brother, F, is a boy aged 10 years and 2 months. Since he was five years old, his main complaint has been recurring below-knee fractures.It was his third fracture in terms of minor injuries. At the age of five, he suffered his first fracture when he fell off a chair in kindergarten. He had no physical dysmorphia or congenital defects from birth. The patient's developmental milestone was delayed; he had head control at six months, stand at age 2 years old, and walk unassisted in his age of 2.5 years old. His grandmother had a similar issue of recurring fractures to her lower extremities, but neither of his parents had a history of frequent fractures or any other sickness.

He was using crutches when he was admitted, and he showed no signs of pain. His prior fractures had completely healed. He has trouble bearing weight, but no blue sclera. He has slowed growth in both height and weight, according to anthropometry examination (Table 1). Pathologic fracture, cortical thinning, osteopenia, and pseudoarthrosis suggested by radiologic examination were all seen (Figure 2). He claimed that while he could hear normally, received biphosphonate injection, calcium supplement, rodding surgery, and external fixation. Furthermore, the patient saw a physiotherapist, and as of right now, the patient could walk with crutches. After receiving treatment for OI for a year, the patient's symptoms and life quality improved, thereby the patient attend school regularly. The patient kept taking biphosphonate injection and calcium supplement.

Osteogenesis imperfecta (OI) is a genetic bone fragility illness that is mostly brought on by dominant mutations that disrupt the synthesis of type 1 collagen, but several other genes have recently been linked to OI [1, 3].

There is a wide range in the degree of bone fragility in OI, from asymptomatic people with the modest expression to fractures and even perinatal fatal [2].

The synthesis and structure of type I procollagen alpha 1 or alpha 2 chains are affected by dominant mutations in either COL1A1 or COL1A2, which are the main causes of OI. In the event of a person who has an autosomal dominant disorder, there is a one in two or 50% probability of passing on the defective gene copy and therefore having an affected child during each pregnancy [3, 4].

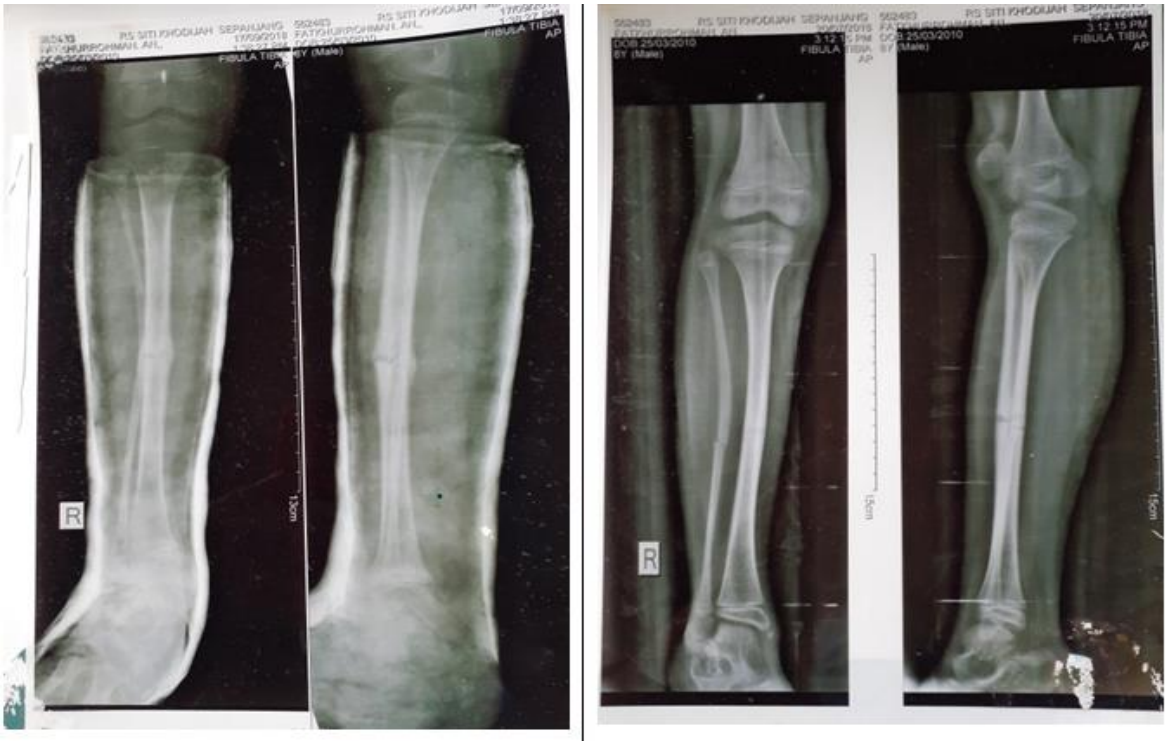


**Figure 2:** The second patient radiologic evaluation

An earlier case report study on OI Type IV in siblings had not only similarities to this case report study in that both siblings similarly showed growth retardation and pathologic fractures, but this case also included dental findings and a consanguineous parent. However, in this trial, logistical challenges prevented the two patients from completing their treatment [5]. Significant intra- and interfamilial variation characterizes OI type IV, a hereditary illness. It has a mild to moderately severe form type and is distinguished by normal or greyish sclerae, mild to moderate bone malformation, and varied short stature [6].

While some instances have mild femoral bending, others have birth fractures and abnormalities. It is defined by normal body weight and length at birth, but by the time it is 2 to 3 years old, the stature is typically below the 3rd centile [7].

Reduced final standing height, particularly for truncal height, is the outcome of stature, which continues parallel with the usual curve for final height, but it rests two or more standard deviations below it. Although osteogenesis imperfecta is characterized by growth insufficiency, neither the etiology nor the specific kind of low stature are known [8].

Similar to the other types of OI, the fractures prevalence rises in the older age group, notably in postmenopausal women, after puberty, but it is low throughout adulthood. Clinically substantial basilar invagination and increasing scoliosis are also typical in type IV patients, frequently impairing respiratory function [9].

The major goal of OI treatment is to increase mobility and allow for normal daily activities while reducing bone pain and bone fragility [10].

Accordingly, medical care should always be viewed as a component of a well-coordinated multidisciplinary strategy for treating kids with OI, which further includes timely corrective surgery, physical therapy, and occupational therapy. The severity of clinical phenotype determines the required intervention level [11].

The objectives of pharmacologic therapy include reducing the risk of fractures, accelerating growth, reducing pain, improving bone metabolic indicators, bone histomorphometry, and bone mineral density, as well as enhancing mobility and independence [12].

Instead of bone mineral density or collagen mutation status, the choice of pharmacotherapy is determined by the severity of the child's condition (presence of long bone abnormalities, bone pain, and frequent fractures) [13, 14]. Bisphosphonate therapy should be used in conjunction with OI surgery [15].

Surgical intervention in children older than 2 years old comprises numerous osteotomies and the use of intramedullary telescopic roding until considerable linear growth continues. Properly timed surgeries for the insertion of intramedullary rods, besides supportive splints and braces, may be undertaken for a more functional architecture of the limbs, correcting long-bone abnormalities, and reducing fracture frequency [1].

Improvements in the patients' mobility and life quality are the result of this. Combining orthopedic surgery and bisphosphonate treatment necessitates multiple scheduling coordinations to reduce the danger of postponed osteotomy healing [16].

Moreover, the psycho-social implications of this diagnosis on various developmental stages of childhood and adolescence should be taken into account. A thorough transition plan to adult services is another crucial component of management. Community-based organizations and societies are frequently beneficial add-ons to medical care and can offer patients and their families extra support [16, 17].

## Conclusion

To improve the life quality for patients and their families, management of many different fields, including pediatrics, orthopedics, medical rehabilitation, radiology, OI Community, and psychiatry is required. It is important to periodically provide education, self-monitoring, and motivation for progress and achievement for children who are still developing. The macro- and micro-communities support managerial success in addition to healthcare. It is important to provide information on diseases and the

possibility of passing down traits to future generations.

This longitudinal case study demonstrates that growth and developmental outcomes will improve for children with moderate osteogenesis imperfecta if they receive adequate evaluation and education. Periodic therapy and evaluation, supported by various sectors, is a cutting-edge strategy for improving patients' quality of life. Double-blind controlled trials may be required for additional confirmation to see favorable treatment on the OI morbidity.

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## Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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## References

[1]. Antoniazzi F., Mottes M., Fraschini P., Brunelli P.C., Tatò L., Biologia-genetica D.M., Practical treatment guidelines, *Paediatric drugs*, 2000, **2**:465 [Crossref], [Google Scholar], [Publisher]

[2]. Rauch F., Glorieux F.H., Osteogenesis imperfecta, *The Lancet*, 2004, **363**:1377 [Crossref], [Google Scholar], [Publisher]

[3]. Ben Amor I.M., Roughley P., Glorieux F.H., Rauch F., Skeletal clinical characteristics of osteogenesis imperfecta caused by haploinsufficiency mutations in COL1A1, *Journal of Bone and Mineral Research*, 2013, **28**:2001 [Crossref], [Google Scholar], [Publisher]

[4]. Beary J.F., Chines A.A., Osteogenesis imperfecta : Clinical features and diagnosis, *Waltham, MA: UpToDate*, 2020, 1 [Publisher]

[5]. Shetty S.R., Dsouza D., Babu S., Balan P., Osteogenesis imperfecta (Type IV) with dental findings in siblings, *Case reports in dentistry*, 2011, **2011**:970904 [Crossref], [Google Scholar], [Publisher]

[6]. Harrington J., Sochett E., Howart A., Update on the evaluation and treatment of osteogenesis imperfecta, *Pediatric Clinics*, 2014, **61**:1243 [Crossref], [Google Scholar], [Publisher]

[7]. Graff K., Syczewska M., Developmental charts for children with osteogenesis imperfecta, type I (body height, body weight and BMI), *European Journal of Pediatrics*, 2017, **176**:311 [Crossref], [Google Scholar], [Publisher]

[8]. Lund A.M., Müller J., Skovby F., Anthropometry of patients with osteogenesis imperfecta, *Archives of Disease in Childhood*, 1999, **80**:524 [Crossref], [Google Scholar], [Publisher]

[9]. Beary J.F., Chines A.A., Osteogenesis imperfecta: Management and prognosis, UpToDate, 2020, 1 [Publisher]

[10]. Biggin A., Munns C.F., Osteogenesis imperfecta: diagnosis and treatment, *Current osteoporosis reports*, 2014, **12**:1 [Crossref], [Google Scholar], [Publisher]

[11]. Lund A.M., Nicholls A.C., Schwartz M., Skovby F., 1997. Parental mosaicism and autosomal dominant mutations causing structural abnormalities of collagen I are frequent in families with osteogenesis imperfecta type III/IV, *Acta Paediatrica*, **86**:711 [Crossref], [Google Scholar], [Publisher]

[12]. Marr C., Seasman A., Bishop N., Managing the patient with osteogenesis imperfecta : a multidisciplinary approach, *Journal of multidisciplinary healthcare*, 2017, 145 [Google Scholar], [Publisher]

[13]. Rauch F., Glorieux F.H., Treatment of children with osteogenesis imperfecta, *Current*

*Osteoporosis Reports*, 2006, **4**:159 [Crossref], [Google Scholar], [Publisher]

[14]. Horwitz E.M., Prockop D.J., Fitzpatrick L.A., Koo W.W., Gordon P.L., Neel M., Sussman M., Orchard P., Marx J.C., Pyeritz R.E., Brenner M.K., Transplantability and therapeutic effects of bone marrow-derived mesenchymal cells in children with osteogenesis imperfecta, *Nature medicine*, 1999, **5**:309 [Crossref], [Google Scholar], [Publisher]

[15]. Shaker J.L., Albert C., Fritz J.M., Harris G., Shaker JL, Albert C. Recent Developments in Osteogenesis Imperfecta referees : 3 approved ] Referee Status , *F1000Research*, 2015, **681**:1 [Crossref], [Google Scholar], [Publisher]

[16]. Shapiro J., Byers P, Glorieux F, Sponseller P., Osteogenesis imperfecta: a translational approach to bittle bone disease, *Academic Press*, 2014, 476 [Google Scholar], [Publisher]

[17]. Valadares E.R., Carneiro T.B., Santos P.M., Cristina A., Zabel B., What is new in genetics and osteogenesis imperfecta classification, *Jornal de pediatria*, 2014, **90**:536 [Crossref], [Google Scholar], [Publisher]

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