

## Case Report

# Osteogenesis Imperfecta Type II in a 2-days-old Female Child from Tanzania: A Case Report and Review of Literature

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## Abstract

**Introduction:** Osteogenesis imperfecta (OI) is a spectrum of connective tissue disorders characterized by bones that break easily with little or no apparent cause. It is predominantly inherited in an autosomal dominant fashion and mutations affecting type I collagen, the main structural protein of the extracellular matrix of bone, skin, and other connective tissues are evident in over 90% of people with this disease. Owing to its 100% case fatality rate, OI type II which has an incidence of 1-2/100,000 live births is the most severe form inevitably resulting to intrauterine or perinatal deaths.

**Case presentation:** We report a case of a 2-days-old newborn female of African descent who presented with pathognomonic features of OI type II. She was born to a 28 years old primigravida by elective cesarean section at 36 weeks gestation due to breech presentation. She weighed 2,380 grams and had an Apgar score of 8/10 and 9/10 at one and five minutes respectively. Her mother had an uneventful pregnancy and she received all antenatal care as per protocol. Prenatal ultrasonography detected no abnormalities and the mother denied any history of babies born with fractures or an increased fracture tendency in the family. On examination, she had a blue-grey sclera, small thorax, relatively large cranium, and disproportionately short and curved limbs. Her thighs were held in a fixed abduction and external rotation posture. Subcutaneous crepitations of humerus, ulnar, femur and medial third of tibia and fibula was observed bilaterally. Total body skeletal survey revealed generalized osteopenia, decreased ossification of the skull and multiple fractures of humerus, ulnar, radius, femur, tibia and fibula. The child received enteral feeding with calcium, vitamin D and slow intravenous infusion of bisphosphonate. She died after eleven days of hospitalization due to respiratory failure.

**Conclusions:** OI is a complex genetic disease associated with impaired quality of life and potentially poor survival rates. Owing to the lethality of OI type II, early prenatal diagnosis and genetic counseling is crucial to assist parents in making informed decisions relative to pregnancy termination.

**Key Words:** Osteogenesis imperfect; brittle bone disease; type I collagen deficiency; Lobstein disease; blue sclera syndrome; fragile bone disease; case report.

## Introduction

Osteogenesis imperfecta (OI) refers to a group of connective tissue disorders exhibiting both clinical and genetic heterogeneity that is characterized by qualitative and/or quantitative anomalies of collagen metabolism and manifests with increased bone fragility [1-3]. OI is relatively rare (1:20,000-50,000 live births) and

mutations affecting type I collagen, the main structural protein of the extracellular matrix of bone, skin, and other connective tissues are evident in over 90% of people with the disease [2]. It is generally (95%) inherited in an autosomal dominant fashion, however autosomal recessive and sporadic mutation forms have been documented [3]. Severity of OI varies enormously from a normal life expectancy with slightly increased susceptibility to fractures to forms incompatible with life resulting to intrauterine or perinatal deaths [1].

Bone fragility with multiple fractures in the absence of an

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apparent trauma is the hallmark of OI. Additionally, OI patients may display a wide range of multi-systemic features including; constipation, dental problems, hearing loss, neurological disorders, ocular anomalies, respiratory and swallowing difficulties [1]. Radiologically, presence of generalized osteoporosis, thin cortices and bowing of the long bones, multiple cystic areas, codfish vertebra, and wormian bones are characteristic findings [1]. Although fibroblast cell culture can detect collagen abnormalities in about 85% of patients, the diagnosis of OI practically relies on the distinctive clinical and radiographic picture. We report a case of osteogenesis imperfecta type II in a 2-days-old newborn female of African descent.

### Case Presentation

A 2-days-old newborn female of African descent was referred to our institution from a private facility due to abnormal body posture and excessive crying. She was born to a 28 years old primigravida by elective cesarean section at 36 weeks gestation due to breech presentation. She weighed 2,380 grams and had an Apgar score of 8/10 and 9/10 at one and five minutes respectively. Her mother booked antenatal clinic at 20 weeks gestation, received routine antenatal care (antihelminthics, antimalarial, hematenics and tetanus toxoid) and tested negative for HIV, Hepatitis B and C, and syphilis. Prenatal ultrasonography detected no abnormalities and the mother denied any history of babies born with fractures or an increased fracture tendency in the family.

On examination, she had a blue-grey sclera, small thorax, relatively large cranium, and disproportionately short and curved limbs; Figure 1.

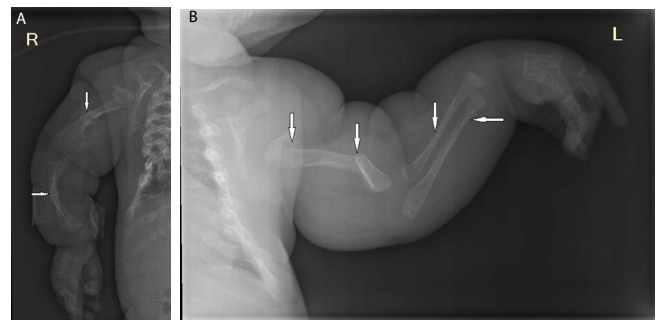


**Figure 1: (baby's photograph)** showing a small thorax, relatively large cranium, and disproportionately short and curved limbs i.e. frog-like position.

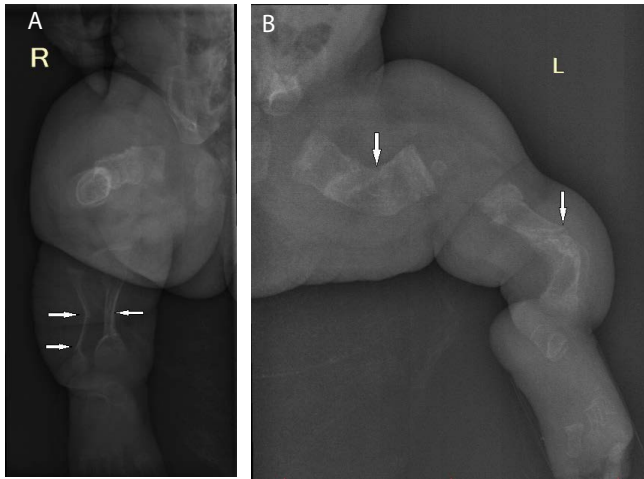
Her thighs were held in a fixed abduction and external rotation posture. She was afebrile (36.2°C), with a pulse rate of 140 beats/minute, respiratory rate of 41 breaths/minute and saturated at 96% oxygen on room air. Subcutaneous crepitations of humerus, ulnar, femur and medial third of tibia and fibula was observed bilaterally. The provisional diagnosis of OI was conceived and the child underwent a number of investigations. Full blood count, renal and liver function tests were normal. Total body skeletal survey revealed generalized osteopenia, decreased ossification of the skull and multiple fractures of humerus, ulnar, radius, femur, tibia and fibula; Figure 2-4.



**Figure 2: (total body skeletal survey)** showing generalized osteopenia, decreased ossification of the skull, bowing and multiple fractures in all four limbs



**Figure 3 a, b: (plain x-ray)** showing multiple fractures involving the humerus, ulna and radius on both right and left upper limbs.



**Figure 4 a, b: (plain x-ray)** showing bowing of the femur together with fractures of tibia and fibula on both right and left lower limbs

Cranial ultrasonography and echocardiography revealed normal findings. Calcium and phosphorus levels were low at 1.54 mg/dl and 1.98 mg/dl respectively. The child received enteral feeding with calcium and vitamin D together with a slow intravenous infusion of bisphosphonate (pamidronate 2mg/day in 50mls of 0.9% sodium chloride for 2 consecutive days). Genetic counseling was also offered to the parents. Despite all efforts, the child progressively deteriorated and died of respiratory failure on the 11<sup>th</sup> day of hospitalization.

## Discussion

Osteogenesis imperfecta represents a spectrum of genetic disorders characterized by bones that fracture easily with little or no obvious cause. Owing to the advancements in genomics, Glorieux and Rauch (2004) [4] expanded the classification of OI to 8 types; however, in practice the 4 classical types proposed by Sillence (1984) [5] are still used in phenotypic description. With a 100% case fatality rate, OI type II which has an incidence of 1-2/100,000 live births is the most severe form [1-6]. Clinically, OI type II is associated with intrauterine fractures, low birth weight, short limbs, small chests, soft skulls, blue sclera and macrocephaly as it was observed in the case presented [1]. Respiratory failure is the predominant cause of death either in utero or during early neonatal period as it was witnessed in this case [1].

Depending on the presenting features and associated complications various methods including; cast immobilization, dietary supplements (vitamin D and calcium), medications (bisphosphonates, growth hormone and analgesics), surgical stabilization (intramedullar rods, osteotomies), orthoses and mobility aids (wheelchairs, ankle/foot orthoses, spinal braces) are employed in the management of OI [1]. Results from newer treatment options like fetal mesenchymal stem-cell graft in bone

after in utero transplantation is promising, however its availability and cost implications especially in resource limited settings remains a challenge [7]. Fractures in most OI patients heal at a relatively normal rate; nevertheless complications including nonunion, fixation device migration, fracture at the rod tip and joint penetration are frequently observed [8].

## Conclusions

In conclusion, OI is a complex genetic disease associated with impaired quality of life and potentially poor survival rates. Owing to the lethality of OI type II, early prenatal diagnosis is crucial to assist parents in making informed decisions relative to pregnancy termination. Furthermore, genetic counseling and family screening are of paramount importance and should be an integral component in management of OI.

## Consent

Written informed consent was obtained from the patient's legal guardians for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

## Abbreviations

**HIV:** Human immunodeficiency virus

**OI:** Osteogenesis imperfecta.

## Declarations

## Ethics approval

Ethical clearance was sought from the Directorate of Research of the Jakaya Kikwete Cardiac Institute

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## Authors' contributions

PP, PN and IM took the history and performed physical examination. FL interpreted the radiographs. PP wrote the initial draft of the manuscript. All authors reviewed and contributed to the final version of this case report.

## Competing interests

The authors declare that they have no competing interests

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