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Three-dimensional ultrasound in the prenatal diagnosis of osteogenesis imperfecta

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Abstract

Objective: Fetal osteogenesis imperfecta (OI) is a heterogeneous group of collagen disorders characterized by bone fragility, blue sclerae, deafness, and dentinogenesis imperfecta. Ultrasonography is acknowledged as a reliable diagnostic modality for the prenatal diagnosis of OI, especially type II. In the past, two-dimensional (2D) ultrasound (US) has been applied as the mainstay of prenatal diagnosis of OI. In this series, we report our work of detecting OI using three-dimensional (3D) US.
Material and Methods: We reviewed our computer database of prenatal diagnosis of OI at the National Cheng Kung University Hospital from April 1996 to July 2010. All the cases were scanned by 2D and 3D US. In total, six cases of fetal OI were diagnosed.
Results: Compared with 2D US, 3D US can detect fetal OI precisely, and provide additional vivid illustration after various modes of reconstruction that 2D US cannot.
Conclusion: In conclusion, 3D US may contribute significantly to the detection of OI *in utero* and provide a novel visual depiction of this defect after reconstruction. The technique may thus substantially assist in prenatal diagnosis as well as consultations for fetal OI.
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Keywords: osteogenesis imperfecta; three-dimensional; ultrasound

Introduction

Osteogenesis imperfecta (OI) is characterized by brittle bone with an excessive tendency to antenatal and/or post-natal fractures, blue sclerae, deafness, and dentinogenesis imperfecta [1,2]. OI comprises a heterogeneous group of genetic disorders affecting connective tissue, particularly the skeletal system [3—5]. In pregnancy, the incidence of OI is estimated to be around 1 in 25,000 to 1 in 30,000 [6]. Ultrasonography is acknowledged as a reliable

diagnostic modality for the prenatal diagnosis of OI, especially type II disease [7—9]. At present, the prenatal diagnosis of OI is mainly obtained by prenatal two-dimensional (2D) ultrasound (US) and only case diag-nosed by three-dimensional (3D) US has previously been published [10—12].

Due to the complexity and large variety of these diseases, accurate prenatal diagnosis of skeletal dysplasias remains a challenge, with only approximately 65% of cases being accurately diagnosed by conventional 2D US [12—14]. Recent studies have suggested a potential advan-tage of 3D US in improving the accuracy of the prenatal diagnosis of skeletal dysplasia [15,16]. With the advent of 3D US, various rendering modes of imaging may help to depict congenital anomaly more clearly than conventional

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2D US [17]. Over the last decade, we have used 3D US in prenatal diagnosis and reported a clinical application of this technique in detecting congenital anomalies [17−20]. We have also previously reported a case of OI using 3D US [10]. In this series, we attempted to assess the efficacy of 3D US in detecting OI antenatally. We reviewed and analyzed our computer database of OI diagnosed using 3D US *in utero* retrospectively. To the best of our knowledge, our series is one of the largest series in Taiwan detecting OI using 3D US that has been described in the medical literature.

Materials and methods

From April 1996 to July 2010, we reviewed and analyzed our computer database of the prenatal diagnosis of fetal OI. All the US examinations were undertaken in the Antenatal Ultrasound Unit of the Department of Obstetrics and Gynecology, National Cheng Kung University Hospital, Tainan, Taiwan, a tertiary medical center in South Taiwan. Informed consent and permission to use the US images were also obtained before the US examinations.

All the cases of OI were scanned using 2D and 3D US. For 2D US examinations, we used conventional 2D US scanners (Aloka SSD680, Tokyo, Japan; Toshiba Nemio 20, Tokyo, Japan). For 3D US examinations, we used a 3.5−7.0 MHz Voluson US scanner (Kretz Voluson 530, 530D, Zipf, Austria) to obtain a tri-orthogonal multiplanar view and, further, to generate 3D reconstructive images of OI using a variety of rendering modes of 3D US, including surface-rendering mode, transparent mode, X-ray mode, gradient-light mode, and a mixture of the various modes. All the cases of OI were diagnosed prenatally. After routine genetic consultation, the parents chose to terminate the pregnancy or to continue the pregnancy to term. After termination or delivery, all the cases were confirmed by clinical, radiological, and/or histopathological examinations.

Results

In total, six cases were diagnosed *in utero* as fetal OI by 3D US. The results of this series are summarized in Table 1. The mean gestational age at prenatal diagnosis by US was 21
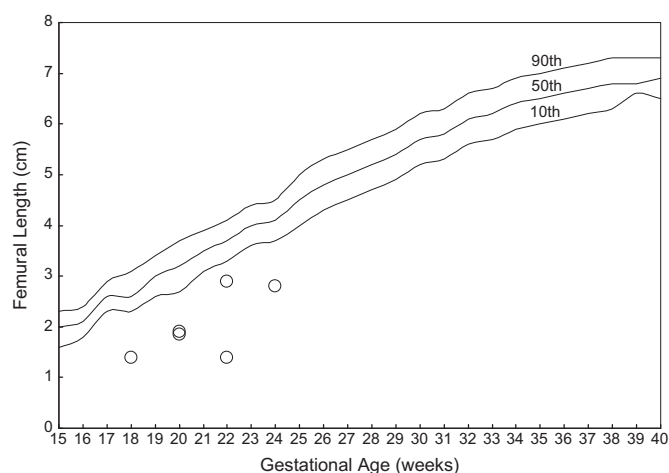

Fig. 1. Biometric trends of femur length in fetal osteogenesis imperfecta (OI). The three curves are normal ranges of fetal femur length in Taiwanese fetuses (10th, 50th, and 90th percentiles as indicated). All the data for femur length in OI are depicted in terms of gestational age at diagnosis (○).

weeks (range 18−22 weeks). Maternal age ranged from 22 to 43 years, with a mean age of 26.8 years. One case had karyotyping after termination of pregnancy, the result showing a normal female karyotype of 46,XX (case 1).

Fig. 1 illustrates the biometric trends of femur length in fetal OI. The US images revealed short extremities with fragmented femurs and humeruses, and beaded ribs in all cases. The mean ratio of femur length to abdominal circumference was 0.14 (range 0.105−0.192).

When comparing 2D and 3D US in terms of imaging efficacy, 3D US imaging can provide more complete, thorough, and comprehensive illustrations after various modes of reconstruction that 2D US cannot. For instance, in a case at 20 weeks of gestation (case 5), 3D US was able to depict the severely shortened limbs with bone fracturing (Fig. 2). The surface mode of 3D ultrasonography, especially the lateral view, showed a normal contour of the face and characteristic very clearly visible intracranial structures (Fig. 3). Moreover, in a case at gestational age 22 weeks, the significantly short lower extremity was demonstrated by 3D US (Figs. 4−6). Similarly, in another case at 22 weeks, 3D US illustrated very small extremities (Figs. 7−9).

Table 1
Prenatal diagnosis of fetal osteogenesis imperfecta (OI) by three-dimensional ultrasound.

Case no.	Maternal age (y)	Obstetric history	Gestational age (weeks)	Ultrasound findings	Ratio of femur length to abdominal circumference	Outcome	Associated conditions
1	31	G3P0A2	22	SE, BF, DM	0.105	TOP	OI type2, 46 XX
2	25	G3P2	24	Twin with one SE, BF, DM	0.167	C/S at 35 weeks	OI type 3
3	22	G3P1A1	18	SE, BF, DM	0.122	TOP	OI type 2
4	26	G3P2	20	SE, BF, DM	0.144	TOP	OI type 2
5	31	G3P1A1	20	SE, BF, DM	0.142	TOP	OI type 2
6	26	G2P1	22	SE, BF, DM	0.192	C/S at 38 weeks	

A = abortion; BF = bone fractures; C/S = Cesarean section; DM = decreased mineralization; G = gravida; P = para; SE = short extremities; TOP = termination of pregnancy.
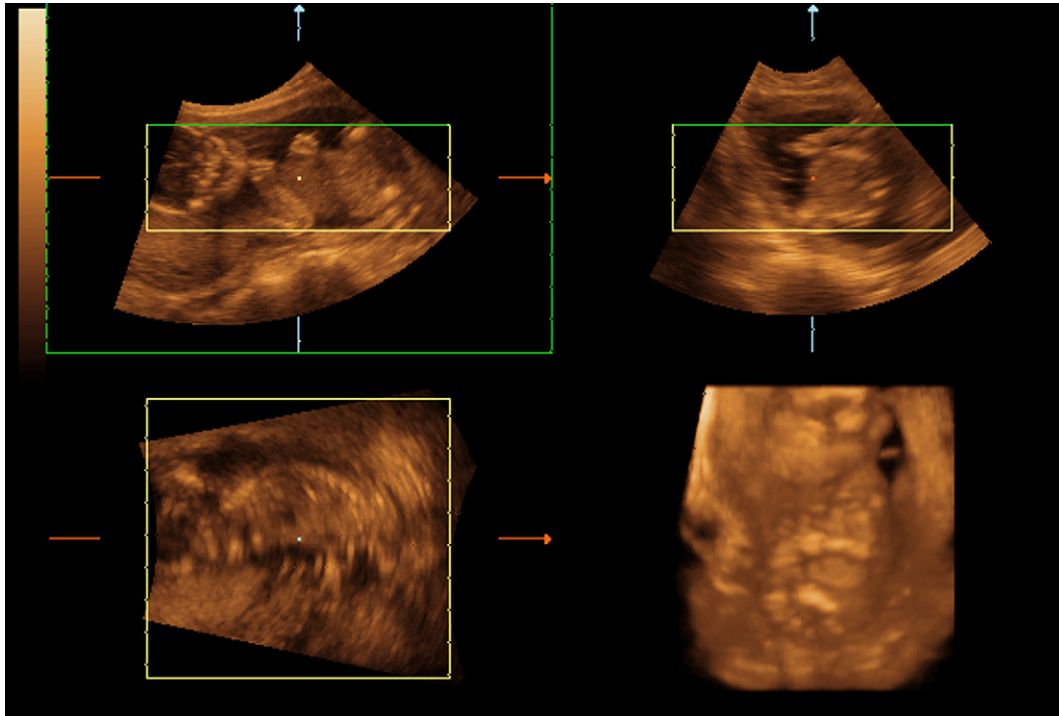
Fig. 2. Multiplanar three-dimensional ultrasound (3D US) image of fetal osteogenesis imperfecta at 20 weeks' gestation. The image shows significantly short extremities with bone fracture graphically observed by 3D US.

Discussion

Most varieties of OI are due to type I collagen abnormalities and exhibit a highly variable phenotype [2]. The most widely accepted classification was proposed by Sillence et al [21], based on phenotype. OI types I and IV are relatively mild forms with few bone fractures and variable degrees of hearing loss or abnormal dentinogenesis. Type II is the lethal form of OI. Type III is progressive with short stature, dentinogenesis imperfecta, and hearing loss.

To date, ultrasonography has been considered to be a reliable diagnostic modality for the prenatal diagnosis of type II and deforming type III OI [7–9]. In general, type II OI is usually lethal *in utero* or in the early neonatal period. In this
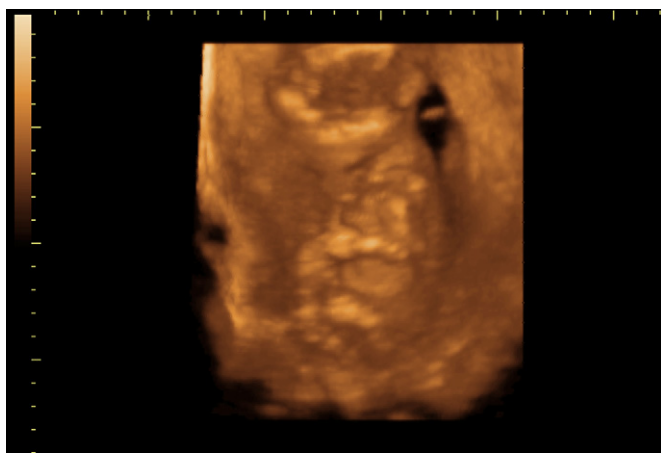

Fig. 3. The reconstructed multiplanar three-dimensional ultrasound (3D US) image of fetal osteogenesis imperfecta at 20 weeks' gestation. Short extremities with clearly visible intracranial structures can be clearly noted. 3D US showed a normal contour of the face, especially on the lateral view.
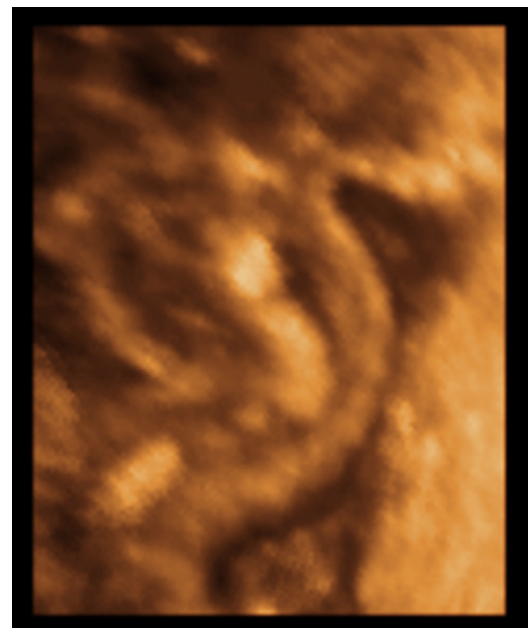

Fig. 4. Reconstructed multiplanar three-dimensional ultrasound (3D US) image of the thigh in a case of fetal osteogenesis imperfecta at gestational age 22 weeks. The image revealed noteworthy short extremities with bone fracture depicted by 3D US.
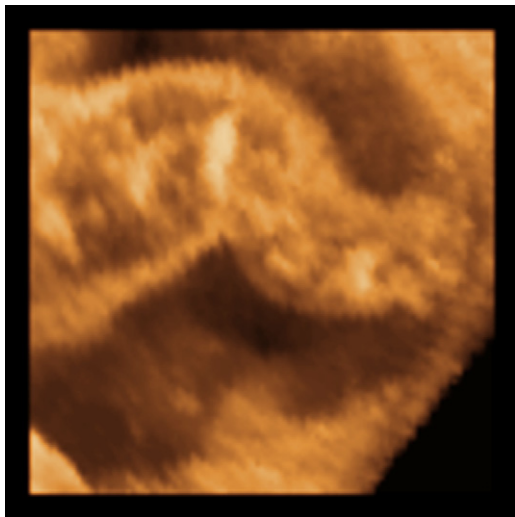
Fig. 5. Reconstructed multiplanar three-dimensional ultrasound (3D US) image of the leg in a case of fetal osteogenesis imperfecta of gestational age 22 weeks.

series, all the cases showed the characteristic findings of OI, including short extremities, bone fractures, and decreased mineralization (Table 1). Notably, 3D US may provide more comprehensive 3D images after a variety of 3D rendering modes that 2D US cannot (see Figs. 2 and 3).

In our series, the earliest gestational age for the diagnosis of OI was 18 weeks. Because our institute is the tertiary medical center in Southern Taiwan, almost all cases of suspected fetal anomalies were referred to our unit for further US confirmation and management. The fact that all our cases were referred from local clinics after the first trimester may explain why all the diagnoses were made in the second trimester.

In previous reports, OI has been demonstrated to be associated with certain additional abnormalities, including microcephaly [22,23], congenital heart defects [22], anencephaly [24], and encephalocele [25]. However, no associated anomalies were noted in our series (Table 1).

Fig. 7. Reconstructed multiplanar three-dimensional ultrasound (3D US) image of a case of fetal osteogenesis imperfecta at gestational age 22 weeks.

In addition to femoral shortness, the ratio of femur length to abdominal circumference can be used in predicting lethal skeletal dysplasia. Rahemtullah and co-workers [26] reported a cut-off value of less than 0.16 for the femur length-to-abdominal circumference ratio in order to diagnose a lethal skeletal dysplasia. In our series, the mean ratio of femur length to abdominal circumference was 0.14 (range 0.105–0.192). Among our cases, the ratio of femur length to abdominal circumference was higher than 0.16 for two fetuses. Both were delivered by Cesarean section, one at
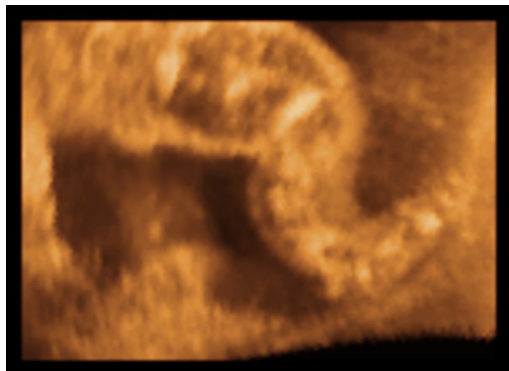

Fig. 6. Reconstructed multiplanar three-dimensional ultrasound (3D US) image of short leg with special posture in a case of fetal osteogenesis imperfecta of gestational age 22 weeks.
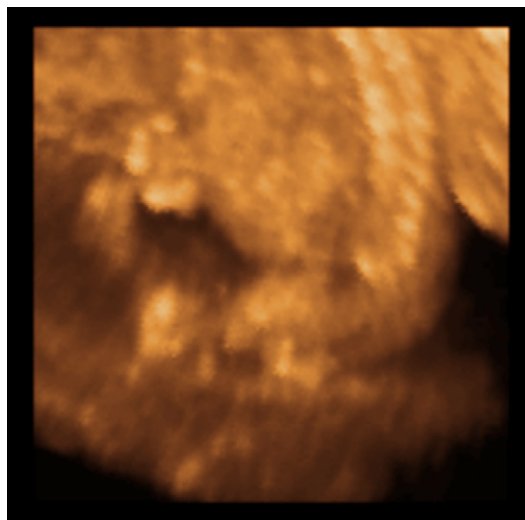

Fig. 8. Reconstructed multiplanar three-dimensional ultrasound (3D US) image of the lower extremities and body in a case of fetal osteogenesis imperfecta at gestational age 22 weeks.
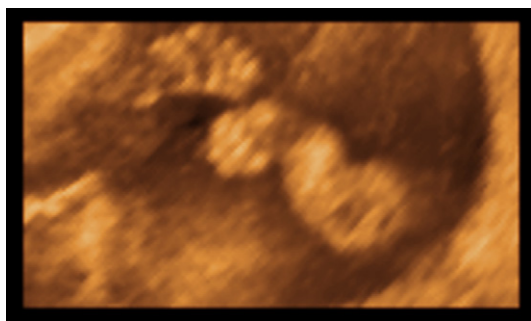
Fig. 9. Reconstructed multiplanar three-dimensional ultrasound (3D US) image of the upper extremity in a case of fetal osteogenesis imperfecta at gestational age 22 weeks. The image revealed a significantly short upper extremity graphically observed by 3D US.

gestational age 35 weeks, the other at 38 weeks. Given these results, our series further proved that the ratio of femur length to abdominal circumference is clinically useful in the prenatal diagnosis of OI.

3D US has recently been used to screen normal fetal structure and detect various kinds of fetal anomalies. Previous reports have indicated the superiority of 3D US scanning over traditional 2D US in the prenatal diagnosis of fetal anomaly [17,27,28]. Additional advantages of the 3D technique include more accurate biometric measurement and a reduction in scanning time and exposure [11]. Three-dimensional imaging also aids in counseling patients because the images are more easily interpreted by an inexperienced observer.

Benoit et al [29] and Garjian et al [15] reported a superior diagnostic ability when 3D sonography was used as an adjunct to the 2D technique in evaluating the fetal neural axis and skeletal system, respectively. In our series, we detected six cases over a 10-year period, and all proved that a better visualization of fetal OI can be achieved using various 3D modes of reconstruction, irrespective of the presentation or position of the fetus. We also confirmed that 3D ultrasound was able to enhance visualization of the short limbs and bones fractures associated with OI, as claimed in a previous report [12]. The recorded data can also be reviewed by consulting physicians after the examination and may be used for teaching purposes [25]. A vivid picture of reconstructed 3D US can give the parents a better understanding of this lethal defect, thus helping them to decide whether or not to terminate the pregnancy.

In conclusion, our study showed the efficacy of 3D US in the prenatal diagnosis of OI. Also taking into account our previous studies using 3D US to detect other fetal anomalies [18—20], we believe that 3D US may be an important diagnostic tool in clinical fetal medicine.

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