Case Report

DOI: 10.7860/JCDR/2026/81702.22780

Paediatrics Section

Skeletal Dysplasia in a Neonate with Clinical Features of Edwards Syndrome: A Case Report

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ABSTRACT

Neonatal skeletal dysplasias present a unique diagnostic challenge due to their phenotypic overlap with various syndromic and metabolic conditions. Edward syndrome, also known as trisomy 18, is a genetic disorder caused by the presence of an extra copy of chromosome 18 in a cell. Skeletal dysplasias, a heterogeneous group of disorders affecting bone and cartilage development, are not commonly associated with trisomy 18 but can co-exist and complicate the clinical picture. In this case, a female neonate presented with the symptoms of skeletal dysplasia, such as a depressed nasal bridge, prominent frontal bossing, short, stubby fingers with apparent overcrowding, a short trunk, and bilateral rocker-bottom feet. Her X-ray demonstrated shortened metacarpals and phalanges with metaphyseal flaring. Routine laboratory investigations showed a normal alkaline phosphatase level (116 U/L) and serum calcium (8.2 mg/dL), but a significantly deficient vitamin D level (9.93 ng/mL); her mother's vitamin D level was also found to be deficient. In the present case, clinical findings of Edwards syndrome co-existed with skeletal dysplasia. This highlights the need to integrate clinical, biochemical and genetic insights for early diagnosis and holistic patient care. Additionally, comprehensive genetic and multi evaluations are essential to differentiate complex congenital anomalies and guide optimal neonatal management. Early identification is critical, not only for immediate clinical management but also for guiding long-term prognostic and genetic counselling strategies.

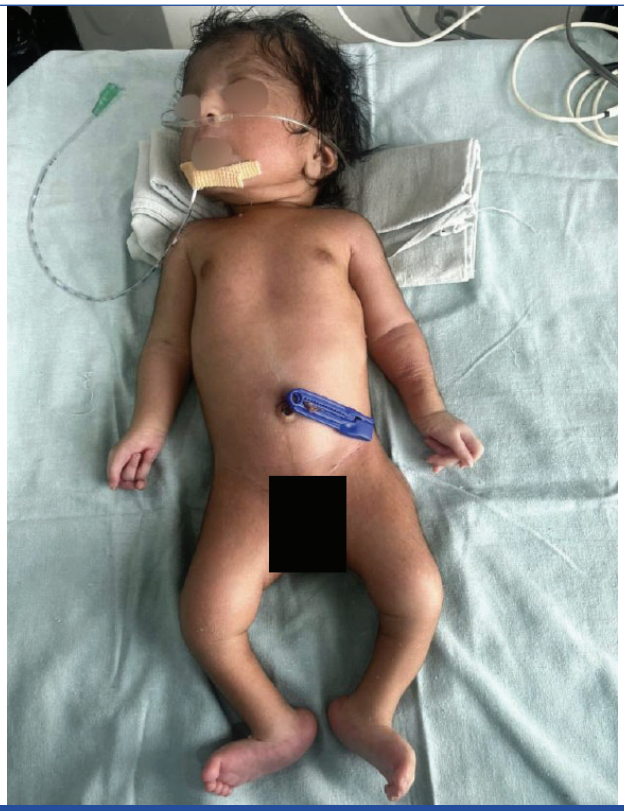
Keywords: Antenatal counselling, Antenatal screening, Chromosomal anomalies, Congenital anomalies, Genetic evaluation

CASE REPORT

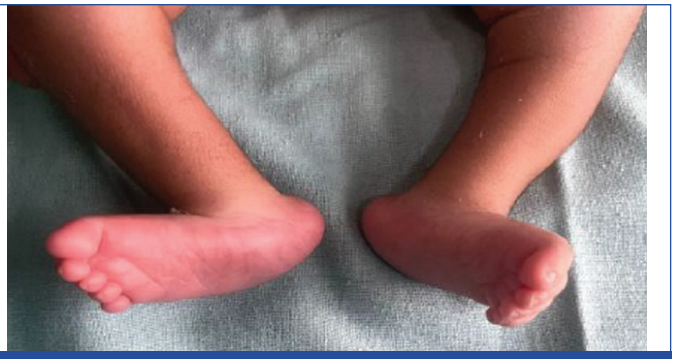
A female neonate, weighing 3.03 kg, was born to a multi-gravida mother (G5P0A4) at 39+1 weeks of gestation. The child was delivered by caesarean section, as the mother was an elderly gravida with a bad obstetric history (previous 4 abortions). Antenatal imaging at 21 weeks of gestation had raised concerns of skeletal dysplasia and antenatal counselling was provided to the parents regarding the outcome of the baby. Immediately post-delivery, the infant exhibited a cry but developed mild respiratory distress with a score of 3 on the Downes scale [1]. Consequently, the neonate was admitted to the Neonatal Intensive Care Unit (NICU) for close observation and management. Respiratory support was initiated with High-Flow Nasal Cannula (HFNC) oxygen therapy, and the support was given for five days. The distress subsequently resolved, allowing for the successful weaning and discontinuation of oxygen. With good cry, tone, and activity, the infant progressed to Orogastric (OG) feeding.

On examination, her heart rate was 136 bpm, Respiratory Rate (RR)-46/minutes, Spo2-98%, and Capillary Refill Time (CRT) was less than three seconds. Physical examination revealed a depressed nasal bridge, prominent frontal bossing, short, stubby fingers with apparent overcrowding, a short trunk, and bilateral rocker-bottom feet [Table/Fig-1,2]. Her X-ray demonstrated shortened metacarpals and phalanges with metaphyseal flaring [Table/Fig-3]. Routine laboratory investigations showed a normal alkaline phosphatase level (116 U/L) and serum calcium (8.2 mg/dL), but a significantly deficient vitamin D level (9.93 ng/mL). Correspondingly, with the routine antenatal investigations, the mother's vitamin D level was also found to be deficient at 8.23 ng/mL, while her alkaline phosphatase and serum calcium levels were within normal limits.

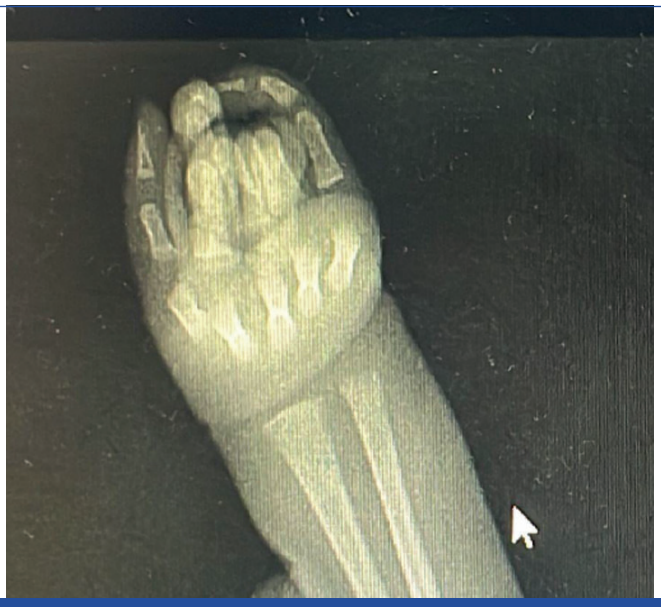
A 2D echocardiogram of the infant revealed a 1.2 mm Patent Ductus Arteriosus (PDA) [Table/Fig-4] and a ventricular septal defect [Table/Fig-5]. Further genetic evaluation via whole-genome exon sequencing demonstrated heterozygosity at exon 9 of the FGFR3 gene. Following stabilisation and initial management, after maintaining airway, breathing, and circulation, a close watch was kept on respiratory distress, and the need for oxygen was adjusted accordingly.



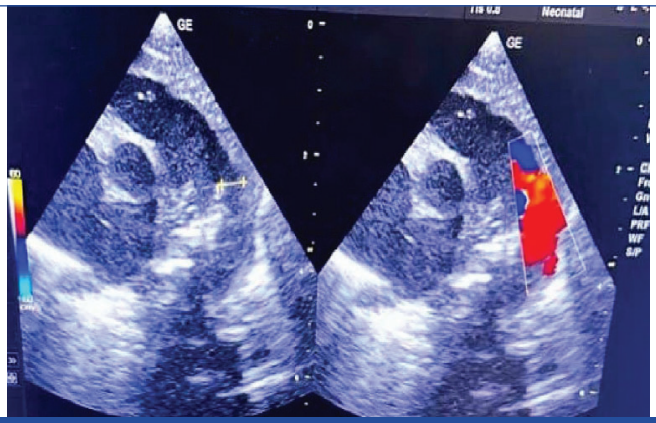
[Table/Fig-1]: Neonate showing frontal bossing, depressed nasal bridge, short trunk, and limb abnormalities, representative of a syndromic skeletal dysplasia phenotype.



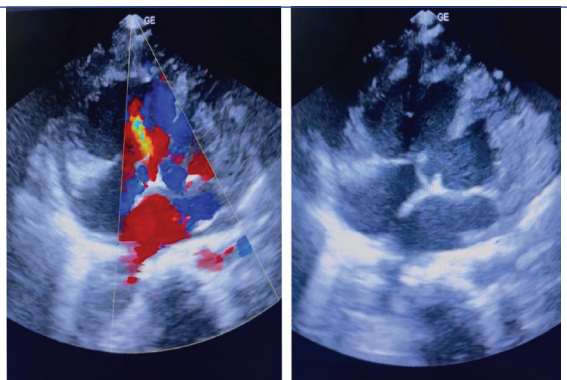
[Table/Fig-2]: Bilateral rocker-bottom deformity.



[Table/Fig-3]: Shortened metacarpals and phalanges with metaphyseal flaring, consistent with features of a Fibroblast Growth Factor Receptor 3 (FGFR3)-related skeletal dysplasia.



[Table/Fig-4]: In ductal view/short axis parasternal view colour alliance is visibly seen from pulmonary artery to aorta.



[Table/Fig-5]: Ventricular septal defect is visible in 4 chamber 2D echo, approximately measuring 4.5 mm with colour alliance, which is suggestive of blood flow across the defect from the left side of the heart to the right side.

The infant was discharged after seven days of NICU stay, with the final diagnosis of skeletal dysplasia with clinical features suggestive of Edwards syndrome, like microcephaly, overlapping of fingers, decreased muscle tone, and rocker bottom feet. Parents received counselling regarding the findings and were advised to arrange follow-up screening for trisomy 18. The testing for the presence of trisomy 18 was not done as the parents were not willing. A detailed discussion was held with the parents to review their child's diagnosis and the possible effects on multiple body systems, including skeletal development, hearing, vision, cardiac function, and respiratory health. This counselling was informed by a comprehensive assessment of the child's prenatal, perinatal, and postnatal history, together with clinical findings and relevant genetic and laboratory results. The condition's inheritance pattern and the associated recurrence risks for future pregnancies were also addressed. The value of coordinated, multidisciplinary care was highlighted to ensure ongoing monitoring and timely intervention across the child's various medical needs. In terms of future family planning, we reviewed available options for early prenatal or pre-implantation diagnosis, including chorionic villus sampling, amniocentesis, and pre-implantation genetic testing in conjunction with In-vitro Fertilisation (IVF).

The parents were asked to follow up with the child after one week of discharge, but no follow-up visit was made by the parents.

DISCUSSION

Skeletal dysplasias are a heterogeneous group of disorders that consist of over 250 disorders that are characterised by abnormal bone and cartilage growth, resulting in disproportionate short stature or dwarfism. Approximately 70% of these conditions can be lethal during the perinatal period [2]. Skeletal dysplasias can be inherited through various patterns: autosomal recessive, autosomal dominant, X-linked recessive, X-linked dominant, and Y-linked inheritance [3].

The case demonstrates the typical diagnostic and clinical challenges seen in neonates suspected of skeletal dysplasia. Key features like craniofacial anomalies, shortened limbs, and rocker-bottom feet required comprehensive clinical and genetic evaluation to differentiate among syndromes. Identification of a heterozygous FGFR3 gene mutation supports diagnosis within the Achondroplasia (ACH) spectrum. Concurrent vitamin D deficiency in both mother and child may have influenced skeletal features and complicated radiologic interpretation. The incidental detection of a small, currently insignificant PDA highlights the importance of cardiovascular screening in syndromic cases. Early neonatal intensive care, genetic counselling, and multidisciplinary follow-up are crucial to optimising long-term outcomes, considering the implications for growth, development, and family planning.

Certain patterns of inheritance in skeletal dysplasias are rarely observed. One such pattern is somatic mosaicism, where one parent may be mildly affected by the condition, while their offspring exhibit more severe symptoms [3]. The most common clinical features observed in over 75% of cases of Trisomy 18 (T18) include developmental delays and failure to thrive, poor sucking ability, hypotonia followed by hypertonia, limited adduction, flexion deformities, overlapping fingers, hypoplastic nails, a short sternum, and various other congenital anomalies [4]. The combination of skeletal dysplasia and Edwards syndrome is quite rare and presents a complex clinical picture due to overlapping features such as rocker-bottom feet and short limbs. These signs, common in skeletal dysplasias, can also be observed in Edwards syndrome, making accurate diagnosis challenging. This underscores the importance of thorough clinical and genetic evaluations in newborns with multiple congenital anomalies. Typically, infants with trisomy 18 show features like intrauterine growth restriction, craniofacial abnormalities, heart defects, and limb malformations. Outcomes tend to be poorer in males, with higher survival rates noted in those with mosaic trisomy.

The main causes of mortality are cardiac failure and respiratory complications. Recognising these overlapping features is crucial in guiding prognosis and management, highlighting the need for comprehensive testing and multidisciplinary care for affected neonates [4].

Advancements in medical care, driven by increased hospitalisations, surgeries, and technological interventions like cardiac surgery, highlight the need to update outdated terminology [5]. However, these characteristics are not specific to ACH. It is the most common genetic form of dwarfism [6].

One illustrative case described a neonate with ACH who unusually presented with an extra finger (postaxial polydactyly). Diagnosis was established through detailed radiological imaging and genetic testing, which revealed a mutation in the FGFR3 gene. This example reflects how skeletal malformations beyond typical features can complicate early diagnosis, highlighting the need for comprehensive physical and molecular assessments soon after birth [7].

Another significant report involved homozygous ACH, a rare and severe form of the disorder with markedly worse skeletal deformities and poor survival. In this case, a prenatal ultrasound raised concerns, confirmed later by genetic analysis. The infant experienced respiratory distress after birth, underscoring the crucial role of antenatal screening, multidisciplinary care planning, and thorough parental counselling for high-risk pregnancies [8].

Additionally, a neonate with Edwards syndrome presented an atypical clinical picture. Although features like finger deformities and rocker-bottom feet were present, the characteristic facial traits were absent, delaying diagnosis until chromosomal analysis was performed. This case stresses the importance of detailed genetic testing when physical signs are unclear or incomplete [9].

A recent genetic study also emphasised the variability in skeletal disorders caused by mosaic mutations, particularly in the COL2A1 gene. This mutation led to severe fetal skeletal dysplasia and recurrent pregnancy losses in one family, with mild or unnoticed symptoms in the mother detected only after genetic sequencing. This reveals the need for detailed family history and phenotypic examination to guide accurate diagnosis and genetic counselling in suspected inherited skeletal conditions [10].

CONCLUSION(S)

This case emphasises the challenges of diagnosing and managing newborns with multiple congenital anomalies. A multidisciplinary approach that includes paediatricians, geneticists, cardiologists, and orthopaedic specialists is crucial for providing the best care for these patients. Early detection and supportive management can enhance the quality of life and offer valuable insights for genetic counselling.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jul 07, 2025
- Manual Googling: Dec 13, 2025
- iThenticate Software: Dec 16, 2025 (3%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Jul 01, 2025**
Date of Peer Review: **Oct 03, 2025**
Date of Acceptance: **Dec 18, 2025**
Date of Publishing: **Apr 01, 2026**