Contents lists available at IOCS

Science Midwifery

journal homepage: www.midwifery.iocspublisher.org

Clinical features that need to be considered for crouzon syndrome in infancy: A rare case in Indonesia

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ARTICLE INFO

Article history:

Received Sep 18, 2025
Revised Sep 23, 2025
Accepted Sep 30, 2025

Keywords:

Congenital Disorder
Crouzon Syndrome
Craniosynostosis
Fibroblast Growth Factor
Receptor 2

ABSTRACT

Crouzon syndrome is a rare congenital disorder marked by premature cranial suture closure, leading to craniofacial deformities and potential neurological and respiratory complications. In Indonesia, reports are scarce, particularly in infants, and existing studies are largely limited to descriptive case reports. This study aims to describe the clinical features of Crouzon syndrome in Indonesian infants and examine the potential role of Fibroblast Growth Factor Receptor 2 (FGFR2) mutations in relation to local healthcare conditions. Using a retrospective observational case study design, data were obtained from medical records of infants with respiratory distress and swallowing difficulties since the neonatal period, complemented by radiological findings and clinical management notes. The results revealed characteristic signs such as craniosynostosis, maxillary hypoplasia, exophthalmos, and evidence of FGFR2 involvement in premature cranial bone fusion. In conclusion, early diagnosis and routine prenatal monitoring are essential to prevent severe complications, while this study contributes to the limited national literature and supports the development of more contextually appropriate diagnostic and therapeutic protocols.

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INTRODUCTION

Crouzon syndrome is a congenital disorder characterized by the premature closure of the coronal suture (synostosis), or, in rarer cases, involving the sagittal or lambdoid sutures (Sari et al., 2021; Singh et al., 2017). This condition results in deformities of the head and facial structure, such as a high forehead, a flattened occiput, and brachycephaly. In addition to craniosynostosis, patients often present with abnormal fusion of the cranial base and midfacial bones, leading to maxillary hypoplasia, a high and narrow palate, as well as shallow orbits that result in exophthalmos (Hughes et al., 2013; Kumar et al., 2017). The syndrome was first described by Louis Eduard Octave Crouzon, a French neurologist, through a case report of a child exhibiting a triad of calvarial deformities, facial anomalies, and exophthalmos (Bowling & Burstein, 2006; Derderian & Seaward,

2012; Kaushik et al., 2016). With such complex clinical manifestations, this syndrome has become one of the focal points in studies of neurology and pediatric medicine.

In the Indonesian context, Crouzon syndrome is considered a rare condition, particularly among infants. Available case reports remain highly limited and are generally descriptive in nature. One such case was reported in an infant in Indonesia with Crouzon syndrome linked to a mutation in the Fibroblast Growth Factor Receptor (FGFR) 2. FGFR2 belongs to the FGFR protein family, which plays a role in regulating cell growth and maturation, cell division, embryonic development, angiogenesis, and wound healing (Wilkinson et al., 2012). Moreover, FGFR2 is known to play an important role in intracellular signaling pathways that influence proliferation, differentiation, migration, apoptosis, and embryonic development (Itoh & Ornitz, 2004). This fact underscores the urgency of more comprehensive research to understand the relevance of FGFR2 mutations to the clinical variations of Crouzon syndrome in the Indonesian population.

The limitations of research on Crouzon syndrome in Indonesia are evident from the scarcity of studies focusing on infancy (Bangun et al., 2019; Talolena et al., 2021). Most global studies emphasize diagnostic and therapeutic aspects in children or young adults, whereas investigations specifically examining the clinical characteristics of infants in Indonesia are almost nonexistent (Ardani et al., 2021; Mapindra & Mahindra, 2021). Early diagnosis during infancy is crucial in determining appropriate interventions and preventing long-term complications. This situation highlights a significant information gap that urgently needs to be addressed through research more focused on the local context.

Preliminary literature indicates that research in Indonesia is largely limited to single case reports, which cannot provide a comprehensive picture of clinical variation or long-term prognosis (Kalanjiam & Manoharan, 2017; Widita et al., 2017) . For instance, there is a lack of data addressing growth patterns, neurological development, or outcomes following surgical intervention in infants with Crouzon syndrome. In addition, discussions on monitoring patients' cognitive and physical development are rare, despite their importance in improving quality of life from an early age (Aguado et al., 1999). This absence of data illustrates the limited understanding of the disease trajectory in Indonesia and the necessity for more in-depth investigation.

Another notable research gap is the lack of studies examining genetic and environmental factors among Indonesian patients with Crouzon syndrome. Global literature has identified several genetic mutations closely related to this condition, yet specific data regarding the Indonesian population remain virtually unavailable. Furthermore, social, economic, and healthcare system factors may significantly affect early detection and treatment outcomes, but these aspects have received little attention in current studies. This lack of focus on such variables indicates that research in Indonesia has yet to fully uncover the complex dynamics underlying the clinical course of this syndrome (Rosarina & Soebagdjo, 2011; Susantri et al., 2025).

These conditions create a significant opportunity for new research that not only describes cases but also emphasizes more comprehensive analyses, both from clinical and healthcare system perspectives. By integrating medical and social viewpoints, research could provide a more contextual understanding of Crouzon syndrome in Indonesia. The novelty of such a study lies in the effort to link molecular aspects, particularly FGFR2 mutations, with clinical variations in infants, while simultaneously situating these findings within the framework of the national healthcare system.

Furthermore, this study seeks to introduce an interdisciplinary approach that integrates clinical, genetic, and social analyses. Such an approach is expected to address the limitations of previous studies that often focused solely on medical diagnosis without considering systemic factors that influence therapeutic outcomes. Consequently, this research aims not only to generate new academic knowledge but also to provide practical implications for designing more relevant treatment strategies within the Indonesian context.

Based on this background, the objective of this study is to identify and describe Crouzon syndrome in Indonesian infants by emphasizing clinical features, the potential role of FGFR2 mutations, and the relevance of these aspects to local healthcare conditions. Through this research, it is expected that significant contributions will be made to enrich the still-limited literature, while simultaneously strengthening the scientific foundation for developing more accurate diagnostic and therapeutic protocols. Ultimately, this study aspires to provide tangible benefits for improving patient quality of life and to open new directions for broader future research.

RESEARCH METHOD

The research method employed in this study is a retrospective observational design with a case study approach. Retrospective observational studies examine secondary data or pre-existing medical records of patients who experienced certain conditions during a previous time period, without direct intervention from the researcher (Kim et al., 2021). This approach is appropriate for describing and documenting clinical characteristics of patients, particularly in rare cases such as Crouzon syndrome, which is a congenital disorder with a low incidence (Neto et al., 2008). The data analyzed include clinical records of diagnosed patients, CT scan results, and clinical signs that appeared since the neonatal period (Kearney et al., 2014). This retrospective study enables researchers to identify key clinical features that should be considered in diagnosing Crouzon syndrome during infancy, based on actual cases that have occurred, thereby providing a detailed overview of the presentation and potential complications.

In this study, data were collected through the review of patient medical records over one month of individuals presenting with symptoms of respiratory distress and difficulty swallowing, who were subsequently diagnosed with craniosynostosis, a hallmark feature of Crouzon syndrome. Data analysis was conducted descriptively, focusing on the presentation of clinical features, radiological findings, and management that had been performed (Porto Junior et al., 2024). As this was an observational study, no interventions were provided by the researcher during data collection, and thus internal validity depended on the completeness and accuracy of the available medical records (Kim et al., 2021). The study also emphasizes the importance of early pregnancy monitoring and regular prenatal examinations to detect congenital disorders such as this syndrome at an earlier stage, thereby enabling timely diagnostic and therapeutic measures to prevent serious complications such as neonatal respiratory failure (Helman et al., 2014). Accordingly, this research not only describes a rare case but also contributes clinical knowledge by strengthening the understanding of the distinctive features of Crouzon syndrome in infancy through a retrospective observational approach.

RESULTS AND DISCUSSIONS

Results

A one-month-old boy presented to the emergency room (ER) came with shortness of breath since the morning, which worsened in the afternoon, and difficulty to swallow. The patient appeared cyanotic upon arrival and was admitted to the Neonatal Intensive Care Unit (NICU) for respiratory failure due to aspiration, with a blood saturation of 80 percent. Rhonchi were heard on lung auscultation.

The patient was born by cesarean section at Mardi Rahayu Hospital, Kudus, with a maternal history of preeclampsia. His birth weight was 3,860 grams, his length was 52 cm, and his Apgar score was 9 at the first minute and 10 at the fifth minute. At birth, he was diagnosed with an abnormal head shape, craniosynostosis, and a high palate. There was no family history of congenital abnormalities. The patient was born to a 28-year-old mother and a 36-year-old father. He did not undergo routine medical examinations during the pregnancy, so the fetal condition was unknown. The patient was then referred to a type A hospital for further care. According to his

mother, the patient is scheduled for surgery at a type A hospital if his weight increases further. He is currently undergoing observation and regular check-ups. However, the patient developed shortness of breath and worsened, leading to his admission to the emergency room at Mardi Rahayu Hospital. While at the Type A hospital, the patient was diagnosed with Crouzon syndrome and scaphocephalia.

From the physical examination, exophthalmos, craniosynostosis, palatoschisis, and beak-like nose were found. Then, the patient underwent an CT-Scan examination and the results showed craniosynostosis. From the chest X-ray, bronchopneumonia was found. Laboratory examination revealed leukocytosis (19.500). The patient was treated in the ICU and improved, then weaning was performed on a ventilator. However, the patient's condition was unstable so he had to be reattached to the ventilator for a long period of time. After being treated for 1 month in the ICU, the patient was referred to a type A hospital for further treatment.

Figure 1. Dysmorphic appearance of the skull and face

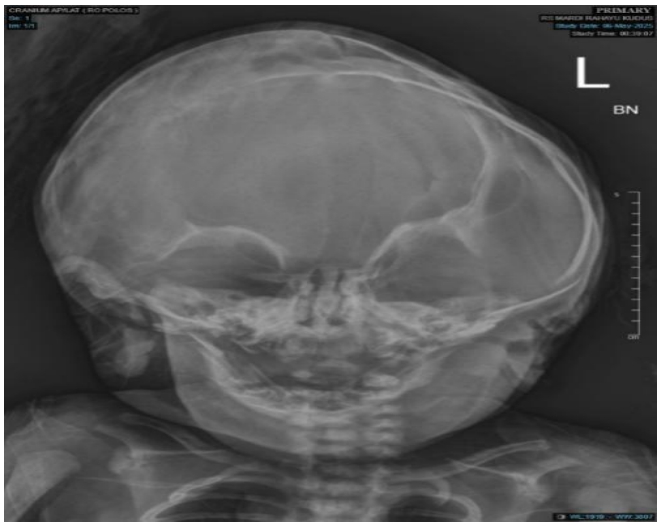

Figure 2. CT-Scan result

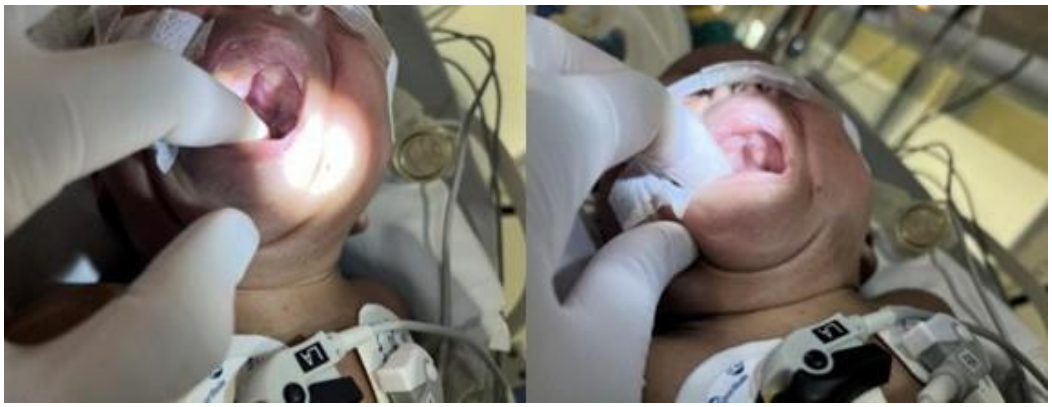

Figure 3. Palatoschisis

Discussions

Crouzon syndrome occurs in approximately 1 in 25,000 births and is caused by a mutation in the fibroblast growth factor receptor (FGFR) 2 gene on chromosome 10. The syndrome affects males more than females in a 3:1 ratio (Hughes et al., 2013; Kumar et al., 2017). The diagnostic categories for Crouzon syndrome include craniosynostosis (brachycephaly, oxycephaly), exophthalmos, nasal deformity (beak-like nose), external strabismus, hearing loss, maxillary and mandibular hypoplasia, prognathism, and brain gray matter abnormalities (Fauzi, 2022). Additionally, approximately 30% of patients develop progressive hydrocephalus, often accompanied by tonsillar herniation. Although nearly all patients with Crouzon's syndrome exhibit normal brain development, 13% exhibit mental retardation, 11.5% have a history of epilepsy, and 30%–50% develop severe recurrent headaches (Cohen, 2009). Differential diagnosis of Crouzon's syndrome is Apert, Pfeiffer. Appert syndrome is a congenital disorder characterized by craniosynostosis, prominent forehead, hypertelorism, proptosis, strabismus, midface hypoplasia, cleft palate, syndactyly of fingers and toes. Pffeifer syndrome have major diagnostic clues craniosynostosis, short broad thumbs and big toes (Wilkie et al., 2001).

CONCLUSION

This case report has shown the clinical findings that can occur in Crouzon Syndrome, a rare congenital abnormality. The differential diagnosis of this syndrome includes Apert and Pfeiffer syndromes. Mutations in the FGFR2 gene on the chromosome have been implicated in the etiology of Crouzon syndrome. FGFR2 signaling induces immature cells to become bone cells during embryonic development. Overexpression of FGFR2 can cause the skull bones to fuse prematurely, resulting in abnormal bone growth and facial deformities. Pregnant women need regular checkups to monitor the condition of the fetus. If any abnormalities are found, the patient can undergo immediate examination and treatment early.

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