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Case Report

# Antenatally diagnosed congenital chloride diarrhea with a de novo mutation: The first reported case from Azerbaijan

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## ABSTRACT

A case study reveals a prenatal diagnosis of congenital chloride diarrhea (CCD) in a consanguineous couple's fetus. Despite successful amnioreduction, persistent polyhydramnios led to genetic testing. A multidisciplinary approach involved obstetricians, geneticists, and neonatologists. Whole-exon sequencing identified a homozygous de novo SLC26A3 gene mutation. Treatment included oral electrolyte supplementation and lansoprazole, resulting in improvement. The case underscores the importance of early detection and intervention in managing CCD.

Healthcare providers should consider early prenatal screening, including advanced genetic testing such as whole-exon sequencing, for couples with consanguineous relationships due to the association of congenital chloride diarrhea with such unions. A multidisciplinary approach involving obstetricians, geneticists, and neonatologists is crucial for comprehensive management, emphasizing the need for close collaboration among healthcare professionals.

**Keywords:** chloride diarrhea, congenital, SLC26A3 gene

## INTRODUCTION

Congenital Chloride Diarrhea (CCD) is a rare condition when an autosomal recessive abnormality is detected before birth. It is characterized by severe and long-lasting diarrhea. An inquiry into the complex aspects of prenatal diagnosis, emphasizing the challenges, results, and approaches used in controlling the condition.[1] When intestinal electrolyte transport does not work right, it can cause low sodium, potassium, and chloride levels, as well as metabolic alkalosis, which is similar to Bartter syndrome.[2] Occasionally, instances of CCD have been documented as being identified prenatally, providing valuable information on the maternal symptoms and the manifestation of this hereditary condition in the newborn.[3,4] This case report specifically examines the identification of a fetus with CCD during the prenatal stage and discusses topics such as the diagnosis process, the genetic implications of de novo mutation, and the comprehensive management of the disorder, including multiple disciplines.

## PRESENTATION OF THE CASE

Prenatal ultrasound demonstrated markedly dilated fetal bowel loops with a honeycomb appearance (Figure 1) and polyhydramnios in the fetus of a consanguineous couple in the second trimester. After successful amnioreduction in the second trimester of gestation, polyhydramnios persisted, and additional tests like genetics indicated that CCD should be diagnosed as hereditary. A multidisciplinary approach was implemented to address the challenges associated with the perinatal

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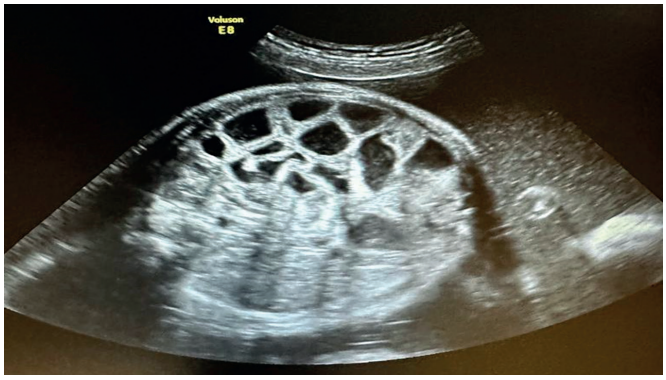


**Figure 1.** The honeycomb appearance of the bowel loops

management of CCD. This approach involved the collaboration of obstetricians, geneticists, and neonatologists. A whole-exon sequencing study using amniocentesis found a homozygous de novo *c.239 G>T/p.Gly80Val* mutation in exon 3 of the *SLC26A3* gene. There was no similar history in the family or relatives, and a male sibling aged five years has not had any illness or neurodevelopmental failure.

A cesarean section was performed for labor at 37 weeks of gestation, and a 3450-gram female was delivered. At 1 and 5 minutes, the Apgar scores were 8 and 9, respectively. The neonate's abdomen was considerably distended, and he had regular, unrelenting, watery diarrhea. Fecal chloride content was 141 mmol/L (normal <90 mmol/L), supporting CCD. On the third day of life, natrium, chloride, and potassium levels began to drop. Oral NaCl (1.5 mmol/kg/day divided into four doses), KCl (1.0 mmol/kg/day divided into two doses), and lansoprazole (1.0 mg/kg/day) were administered for better-tolerated treatment. On the seventh day of life, the infant was discharged from the hospital, and a strict follow-up program was planned for her. We referred our patient to an advanced center after she failed the hearing screening test (ABR). In the second month of her life, the number of daily stools and electrolyte needs continued to decrease.

## DISCUSSION

The benign clinic of our patient may be explained by the genetic origin (de novo mutation) of the illness, particularly when it comes to antenatal diagnosis and early evaluation of the disease using a multidisciplinary approach (Table 1). Congenital chloride diarrhea is a chronic disease where one has watery diarrhea with elevated chloride.[5] Insufficient chloride absorption in the intestines is the cause of this uncommon and fatal disease, which is an autosomal recessive disorder. CCD is related to various mutations in the *SLC26A3* gene, which encodes an ion transporter in epithelial cells.[6-9] We were able to confirm a homozygous de novo *c.239 G>T/p.Gly80Val* mutation on the *SLC26A3* gene, which was never reported before.

Congenital chloride diarrhea was first reported in 1945 and involved infants who were severely ill from diarrhea, alkalosis, and electrolyte abnormalities.[10] It is more prevalent in nations with a high occurrence of consanguineous marriage.[11] Due to comparable antenatal ultrasonographic findings, CCD is frequently misdiagnosed as a surgically treatable condition, such as bowel obstruction, despite being a medically treatable condition.[12] Hence, obtaining an accurate diagnosis prior to commencing treatment is critical. Despite the publication of some methodologies for antenatal differential diagnosis, antenatal CCD diagnosis remains challenging.[13] The report helped in understanding the CCD prenatal diagnostic tools. In these, chorionic villus sampling and amniocentesis are used to find *SLC26A3* mutations during pregnancy.[12]

After that, the usual way of treating chronic diarrhea is by treating the symptoms, preventing dehydration, and preserving the balance of the electrolytes.[1,9] Symptomatic treatments like medications (captopril[14], cholestyramine[15] and butyrate[16]) and specialized regimens may also be used.[1] Proton pump inhibitors have been demonstrated to help reduce diarrhea in some circumstances.[17] It is, however, a chronic condition, and people with CCD can lead a relatively normal life with appropriate

**Table 1. Similarities and differencies among the cases**

| Patients | GW, weeks | BW, grams | Antenatal Diagnosis | Antenatal amnioreduction | Electrolytes abnormalities | GI surgery | Hospital stay, days |
|---|---|---|---|---|---|---|---|
| Gils C. et al. | 36 | 2915 | - | - | + | + | >7 |
| Hui P. et al. | 36 | 2400 | - | - | + | - | >7 |
| Lee H.D. et al. | 34 | 2780 | - | - | + | - | 21 |
| Dogan E. et al. | 36 | 3200 | - | - | + | - | >7 |
| Elbayiyev S. et al. | 37 | 3450 | + | + | + | - | 7 |

management. Long-term clinical outcomes include enuresis, hospitalizations for gastroenteritis and intestinal inflammation, end-stage renal disease, hyperuricemia, male subfertility, spermatoceles, and inguinal hernias.[18] Sensorineural hearing loss should be evaluated in patients with *SLC26* gene mutations.[19] Antenatal detection is also significant because early detection and intervention are essential for better outcomes.

## CONCLUSION

In conclusion, prenatal genetic testing and ultrasound findings are essential for detecting and diagnosing congenital chloride diarrhea. In order to make proper decisions and come up with a controlled management plan, an early diagnosis is crucial.

### Ethical approval

Written informed consent was obtained from the participants.

### Author contribution

Surgical and Medical Practices: TJ; Concept: SM; Design: NR; Data Collection or Processing: NR; Analysis or Interpretation: SM; Literature Search: SE; Writing: SE. All authors reviewed the results and approved the final version of the article.

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### Conflict of interest

The authors declare that there is no conflict of interest.

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