RESEARCH PAPER

PSEUDO-BARTTER SYNDROME UNMASKING CYSTIC FIBROSIS IN A SEVEN-YEAR-OLD INDIAN GIRL CARRYING A SIX-YEAR CLINICAL LABEL OF BARTTER SYNDROME: A CASE REPORT

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ABSTRACT

Background: Bartter syndrome and the pseudo-Bartter syndrome of cystic fibrosis share the same biochemical picture of hypokalaemic, hypochloraemic alkalosis with normal blood pressure. Where genotyping is not routine, the first label applied tends to persist.

Case presentation: A seven-year-old girl from rural northern Karnataka was labelled with Bartter syndrome at one year of age, after presenting with fever and vomiting alongside sodium 116 mEq/L, potassium 2.3 mEq/L, chloride 76 mEq/L and a spot urinary calcium/creatinine ratio of 1345.45 mg/g. Over the following six years she was admitted five more times with fever, cough, vomiting and diarrhoea, and her growth never recovered despite electrolyte supplementation. At the index admission with acute gastroenteritis she weighed 15.5 kg, 60.8% of expected, measured 109 cm, and had grade III protein-energy malnutrition with power 3/5 in all four limbs. Sodium was 132 mEq/L, urea 42 mg/dL and uric acid 7.8 mg/dL, and stool culture grew an extended-spectrum beta-lactamase-producing *Escherichia coli* resistant to ceftriaxone, cefepime, gentamicin and ciprofloxacin.

Diagnosis: Whole exome sequencing on blood drawn during that admission reported two *CFTR* variants in likely compound heterozygous state, c.1521_1523del (p.Phe508del), pathogenic, and c.473G>A (p.Ser158Asn), likely pathogenic, with no variant in any Bartter syndrome gene. The working diagnosis was revised to pseudo-Bartter syndrome secondary to cystic fibrosis, pending sweat chloride confirmation and parental segregation studies.

Conclusion: Cystic fibrosis should be excluded in any child carrying a clinical label of Bartter syndrome who also has recurrent respiratory illness, chronic diarrhoea or growth failure resistant to electrolyte replacement.

Keywords: Cystic fibrosis; pseudo-Bartter syndrome; *CFTR*; p.Phe508del; whole exome sequencing; diagnostic delay; protein-energy malnutrition.

How to cite this article: 1Pradeep Parashuram Patroti 2Trupti Veerbhadrappa Baddi 3Bhumika Shivangouda Patil 4Raghavendra Shivaram Hegde*. PSEUDO-BARTTER SYNDROME UNMASKING CYSTIC FIBROSIS IN A SEVEN-YEAR-OLD INDIAN GIRL CARRYING A SIX-YEAR CLINICAL LABEL OF BARTTER SYNDROME: A CASE REPORT. Int J Drug Deliv Technol. 2026;16(87s):1174-1179. DOI: 10.25258/ijddt.16.87s.120.

INTRODUCTION

Bartter syndrome is an inherited salt-losing tubulopathy in which impaired sodium chloride reabsorption in the thick ascending limb of the loop of Henle produces chronic volume depletion, secondary hyperaldosteronism and a hypokalaemic, hypochloraemic metabolic alkalosis with blood pressure that stays low or normal.[1] Phenotypes overlap across the five causative genes, and clinical classification alone has been shown to misassign patients, which is why genetic confirmation is recommended wherever it can be obtained.[2]

That biochemical signature is not unique to the kidney. In cystic fibrosis, chloride and sodium are lost through sweat rather than urine, and in a hot climate the losses can reproduce the same picture in a child whose renal tubules are normal, an entity termed pseudo-Bartter syndrome. It affected 120 of 1,170 patients in the Turkish Cystic Fibrosis Registry, the commonest complication recorded there.[3] Among 33 children in whom cystic fibrosis first declared itself this way, recurrent respiratory infection was present in 88%, malnutrition in 79% and pancreatic insufficiency in 55%.[4] Diagnostic

delay is the recurring problem and it is wide in India, where one series reported a median age at diagnosis of 10.5 years against symptom onset at about 12 months.[5] We report a seven-year-old girl who carried a clinical diagnosis of Bartter syndrome for six years before whole exome sequencing identified cystic fibrosis.

CASE PRESENTATION

Patient description. The patient is a seven-year-old girl from a rural taluk of Bagalkot district, Karnataka. She was born at term weighing 3.5 kg, cried immediately and required no neonatal intensive care. She is immunised to date and developmentally normal, with a developmental quotient of 100 and good scholastic performance. Her parents are non-consanguineous, her younger sister is well, and there is no family history of similar illness. A household contact with pulmonary tuberculosis was recorded. The family belongs to class II of the modified B.G. Prasad scale.

Case history. The six admissions are summarised in Table 1. The first, at one year of age in May 2020, established the label she would carry: fever and vomiting for two days with sodium 116 mEq/L, potassium 2.3 mEq/L and chloride 76 mEq/L, and a spot urinary calcium/creatinine ratio of 1345.45 mg/g, equivalent to 1.35 mg/mg. The electrolytes corrected within 48 hours and Bartter syndrome was diagnosed after an endocrinology opinion, with serial review advised. Five further admissions followed over six years, two of them for fever with cough, one for a week of fever and vomiting during which blood culture grew *Enterobacter aerogenes*, and one in April 2026 whose admission form carried a provisional label of Gitelman syndrome and prompted a nephrology opinion. She presented at the index admission in July 2026 with periumbilical abdominal pain of three days, vomiting and watery diarrhoea of two days and refusal of both solid and liquid feeds, having been febrile the previous day.

Table 1: Chronology of hospital admissions, May 2020 to July 2026

Admission (age)	Presentation	Key findings and management
May 2020 (1 year)	Fever and vomiting, 2 days	Sodium 116, potassium 2.3, chloride 76 mEq/L; urinary calcium/creatinine 1345.45 mg/g. Corrected over 48 hours; Bartter syndrome diagnosed after endocrinology opinion
September 2021 (2 years)	Fever and cough	Symptomatic treatment
May 2022 (3 years)	Fever, cough, coryza, reduced urine and stool output	Symptomatic treatment
June 2023 (4 years)	Fever and vomiting, 1 week	Blood culture grew *Enterobacter aerogenes*; intravenous amikacin for 3 days
April 2026 (6 years)	Vomiting and abdominal pain	Sodium 133, potassium 3.6, chloride 98 mEq/L. Admission form carried a provisional label of Gitelman syndrome; nephrology opinion sought; discharged on potassium chloride
July 2026 (7 years),	Abdominal pain,	Acute gastroenteritis (Tables 2 and 3); blood

index	vomiting and watery diarrhoea	sent for whole exome sequencing

Physical examination. She looked unwell. The pulse was 102 per minute, blood pressure 100/70 mmHg between the 50th and 75th centile for age, sex and height, respiratory rate 27 per minute, temperature 98.7 °F and oxygen saturation 98% in room air, with a capillary refill time of three seconds. There was no pallor, icterus, cyanosis, clubbing, lymphadenopathy or oedema. The abdomen was soft with tenderness confined to the periumbilical region, no organomegaly and normal bowel sounds; cardiovascular and respiratory examination were unremarkable. Cranial nerves were intact and tone and reflexes were normal, but power was recorded as 3 out of 5 in all four limbs.

Investigations. Findings are given in Table 2. Sodium 132 mEq/L, urea 42 mg/dL and uric acid 7.8 mg/dL together indicated volume contraction, while potassium and chloride were within range on oral potassium chloride. The blood gas showed no alkalosis, although the sample was venous. Stool culture grew an extended-spectrum beta-lactamase-producing *Escherichia coli*, susceptible to amoxicillin-clavulanic acid, piperacillin-tazobactam, amikacin, the carbapenems and trimethoprim-sulfamethoxazole, and resistant to ceftriaxone, cefuroxime, cefepime, gentamicin and ciprofloxacin. The report was authorised on the morning of discharge.

Table 2: Findings at the index admission

Investigation	Result
Haemoglobin / leucocytes / platelets	12.1 g/dL / 8,400/mm³ (8% band forms) / 2.90 lakh/mm³
Sodium / potassium / chloride	132 / 4.5 / 99 mEq/L (on oral potassium chloride)
Urea / creatinine / uric acid	42.0 / 0.7 / 7.8 mg/dL
Blood gas (venous)	pH 7.39; bicarbonate 22.7 mmol/L; base excess −3.3
Urine routine	Protein 1+; leucocytes 1+; ketones 1+; pus cells 2–5/hpf
Stool microscopy	Mucus present; many pus cells/hpf; no ova, cysts or trophozoites
Stool culture	ESBL-producing *Escherichia coli*
Anthropometry	Weight 15.5 kg (60.8% of expected); height 109 cm (88.6%); grade III protein-energy malnutrition
Dietary recall	1000 kcal and 19 g protein daily against 1700 kcal and 30 g

Serum magnesium was requested, struck out and replaced by phosphorus, and was never measured. Electrolytes were estimated once only, on the day of admission.

Treatment plan and expected outcome. She was rehydrated with intravenous 5% dextrose in 0.9% sodium chloride and given ondansetron, ranitidine, a dicyclomine and simethicone syrup, zinc 20 mg daily, oral rehydration salts, a probiotic and oral potassium chloride. Intravenous ceftriaxone was added on the second day, after stool microscopy showed many pus cells. On this plan, resolution of vomiting and diarrhoea with restoration of volume and electrolytes was expected within 48 to 72 hours.

Actual outcome. Vomiting and diarrhoea settled within 48 hours and she remained afebrile. She was discharged on the fourth day on oral cefixime for five days and lansoprazole, with advice to take coconut water or fruit juice. Blood for whole exome sequencing had been drawn on the third day.

Genetic analysis and revised diagnosis. The report, issued a month later, identified two *CFTR* variants in likely compound heterozygous state (Table 3), classified according to American College of Medical Genetics and Genomics criteria.[6] No variant was reported in any Bartter or Gitelman syndrome gene. The laboratory recorded three caveats: zygosity was inferred rather than proven, so parental sequencing is

required; *CFTR* has a pseudogene, so orthogonal validation is advised; and the variants were not confirmed by Sanger sequencing. Read together with six years of recurrent respiratory and gastrointestinal illness and unremitting growth failure (Table 4), the working diagnosis was revised to pseudo-Bartter syndrome secondary to cystic fibrosis. Sweat chloride testing, parental studies, faecal elastase, sputum culture and chest imaging had not been performed at the time of writing.

Table 3: Whole exome sequencing findings

Feature	Variant 1	Variant 2
Gene (transcript)	*CFTR* (NM_000492.4)	*CFTR* (NM_000492.4)
Exon; nucleotide change	11; c.1521_1523del	4; c.473G>A
Protein change	p.Phe508del	p.Ser158Asn
ACMG classification	Pathogenic	Likely pathogenic
ClinVar accession	VCV000007105.209	VCV000618959.32
Zygosity	Likely compound heterozygous	Likely compound heterozygous

Associated disorder: cystic fibrosis (OMIM #219700), autosomal recessive. No clinically significant copy number variants were detected, and no variant was reported in any gene associated with primary Bartter or Gitelman syndrome. Average sequencing depth 215×, with 99.65% of target bases at ≥ 20×.

Table 4: Clinical features reconciled against the two diagnoses

Feature	Expected in Bartter syndrome	Observed in this child
Hypokalaemic hypochloraemic alkalosis	Present and persistent	Present at 1 year; no alkalosis on the only blood gas obtained
Blood pressure	Low to normal	Low to normal throughout
Polyuria and salt craving	Characteristic	Not documented at any admission
Growth failure	Common; improves with electrolyte replacement	Severe and unremitting; 150 g gained in 3 months
Recurrent respiratory illness	Not a feature	Fever with cough in 2021 and 2022
Chronic loose stools and feed refusal	Not a feature	Recurrent
Recurrent Gram-negative infection	Not a feature	*Enterobacter aerogenes* in 2023; ESBL *Escherichia coli* in 2026
Causative genotype	Variant in *SLC12A1*,	Two *CFTR* variants; no

	KCNJ1, *CLCNKB*, *BSND* or *CASR*	tubulopathy gene variant

DISCUSSION

The diagnosis made in May 2020 was not careless. A one-year-old with vomiting, profound salt loss, normal blood pressure and prompt correction on replacement fits Bartter syndrome, and the urinary calcium/creatinine ratio of 1.35 mg/mg, more than double the 95th centile for that age,[7] appeared to settle it, since hypercalciuria distinguishes Bartter from Gitelman syndrome. What followed is the instructive part. That ratio was never repeated, the diagnosis was never revisited, and the features that did not fit accumulated quietly over six years. In an Indian series of seven children with Bartter syndrome the mean ratio was 0.30 mg/mg, with only one child frankly hypercalciuric,[8] so this value was unusual even for the diagnosis it was taken to support. Hypercalciuria is not a feature of pseudo-Bartter syndrome, and without a repeat measurement we cannot reconcile it.

Two *CFTR* variants, one of them the commonest cystic fibrosis-causing variant worldwide, point to a different disease, and the history supports it in retrospect. Recurrent chest infection, chronic diarrhoea, feed refusal and malnutrition that worsened despite supplementation are precisely the pattern described in children whose cystic fibrosis presents as pseudo-Bartter syndrome,[4] and salt loss through sweat is amplified by heat, as the Turkish registry authors observed of their own climate.[3] Her two Gram-negative infections also read differently once cystic fibrosis is considered.

The case is not closed, and three limits deserve emphasis. Cystic fibrosis is diagnosed by demonstrating abnormal CFTR function, and a genotype does not substitute for a sweat chloride measurement; even two disease-causing variants require confirmation by sweat testing.[9] Until the parents are sequenced, both variants could lie on the same allele, which would leave the child a carrier rather than affected. The second variant carries a likely pathogenic classification resting partly on supporting rather than strong functional evidence.[6] Serum magnesium, urinary electrolytes, renin and aldosterone were never measured, so a primary tubulopathy has not been formally excluded, and the urinary calcium/creatinine ratio central to the original diagnosis could not be verified against its source report. This is also a single retrospective case, and its conclusions are illustrative rather than generalisable.

If the diagnosis is confirmed, management changes substantially, and this is where the case carries value for practice. Potassium chloride treats a consequence rather than the cause, since the primary deficit is sodium and chloride lost through sweat; sustained sodium chloride supplementation, pancreatic enzyme replacement, fat-soluble vitamins and a high-energy diet become central, and CFTR modulator therapy is effective in patients carrying a single p.Phe508del allele,[10] although cost places it beyond most Indian families. Antimicrobial choices acquire long-term weight for a child facing repeated exposure. Ceftriaxone was defensible empirically, but she was discharged on cefixime on the morning the susceptibility report was issued, against an organism resistant to third-generation cephalosporins, when two oral agents had tested susceptible; most paediatric gastroenteritis needs no antibiotic at all.[11] Among diarrhoeagenic *Escherichia coli* from hospitalised Indian children, 37.6% are extended-spectrum beta-lactamase producers, of which 98.1% resist ceftriaxone.[12] One further observation applies whichever diagnosis proves correct: electrolytes were measured once, on the day of admission, and not again before discharge four days later, in a child whose entire illness is defined by an inability to conserve them.

CONCLUSION

A girl carried a clinical diagnosis of Bartter syndrome for six years, through six admissions and a nutritional state that deteriorated throughout, until whole exome sequencing reported two *CFTR* variants and none in any Bartter syndrome gene. The biochemistry of hypokalaemic hypochloraemic alkalosis with normal blood pressure is shared by a renal disease and a sweat gland disease; when the clinical course includes recurrent respiratory illness, chronic diarrhoea or growth failure that resists electrolyte replacement, the second deserves exclusion before the first is accepted. A diagnosis made in infancy on a single set of values should be re-examined whenever the illness stops behaving as that diagnosis predicts. For this child the immediate priorities are a sweat chloride test, sequencing of both parents, faecal elastase estimation and chest imaging, and referral to a specialist centre if cystic fibrosis is confirmed.

PATIENT CONSENT

Written informed consent for publication of this case report was obtained from the child's mother, who is her legal guardian, and verbal assent was obtained from the child. Institutional permission was obtained for the retrospective review of the record, and all identifying particulars have been removed. The report follows the CARE guideline for case reports.[13]

ACKNOWLEDGEMENTS

The authors thank the Departments of Paediatrics, Microbiology, Pathology and Biochemistry of S. Nijalingappa Medical College and Hanagal Shri Kumareshwar Hospital and Research Centre, Bagalkot, for access to the clinical record and for help in verifying the laboratory data, and the Principal and Head of the Department of Pharmacy Practice for institutional support.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

SOURCE OF FUNDING

This work received no specific grant from any funding agency.

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