

# Bartter Syndrome Presenting with Metabolic Alkalosis: A Case Series

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## ABSTRACT

Bartter Syndrome (BS) is a rare, inherited renal tubulopathy characterised by hypokalaemic, hypochloaemic metabolic alkalosis. Children present with the complaint of polyuria, dehydration, failure to thrive and normal blood pressure despite hyperreninemia and hyperaldosteronism. This is a series of eight children (2 months -1 years of age, 5 males and 3 females children) diagnosed with BS. Mean age of onset was five months with male predominance. Most common presentation was failure to thrive and polyuria. All children showed metabolic alkalosis with hyponatraemia, hypokalaemia and hypochloaemia. Urinary losses of sodium, potassium and chloride were noted in all the eight children. Diagnosis was based on clinical manifestation and electrolyte abnormalities. All children were started on indomethacin and positive response was noted. On follow-up correction of electrolyte abnormalities along with adequate weight gain was seen. Although, it is a rare disease requiring high index of suspicion, but with prompt clinical diagnosis and early treatment, morbidity and mortality can be significantly reduced.

**Keywords:** Electrolyte imbalance, Hypokalaemia, Polyuria, Tubulopathy

## INTRODUCTION

The BS was described in the 1962 by Bartter FC et al., [1]. BS is a genetically heterogenous group of disorders with autosomal recessive inheritance. The exact incidence of BS is unknown, but it is estimated in 1.2/1,000,000 birth [2]. It is characterised by hyponatraemia, hypokalaemia, hypochloaemic metabolic alkalosis [2,3]. The primary defect involves the transporter of sodium and chloride in the thick ascending limb of loop of Henley viz., Na-k-2Cl Co-Transporter (NKCC2), apical K channel (ROMK) or baso-lateral Calcium Channel Kb (ClCNKB). This results in urinary losses of sodium, potassium, chloride and calcium resulting in hypovolemia and dehydration. There is also, consequent hyperreninemia with normotension [2,3].

The present case series aimed to assess clinical presentation and investigations required to make clinical diagnosis of BS and follow-up to assess effectiveness of treatment.

## CASE SERIES

### Case 1

A five-month-old, male child presented with the chief complaint of increased frequency of urination and not gaining weight for past two months. There was no history of fever or feeding difficulty. There was no significant antenatal or family history. At presentation, child was haemodynamically stable. Physical examination showed no dysmorphic features and weight of the child was 5.8 kg (below -2SD for age and sex). Child was evaluated with provisional diagnosis of failure to thrive. The laboratory investigations revealed- metabolic alkalosis (ph-7.49), hyponatraemia (136 mEq/L), hypokalaemia (3.2 mEq/L), chloride (97 mEq/L). Urine analysis showed losses of sodium (35 mEq/L), potassium (16 mEq/L) and chloride (35 mEq/L) in urine [Table/Fig-1]. The abdominal ultrasound showed no nephrocalcinosis or any other abnormality.

A final diagnosis of BS was confirmed. With clinical diagnosis of Bartter syndrome child was started on indomethacin (3 mg/kg/day) and potassium chloride supplementation. Follow-up after one month of therapy showed correction of electrolyte disturbances and a weight of 6.1 kg was noted with a gain of 300 gm. In view of which potassium supplementation was stopped.

S. No.	Age/ Gender	Presenting clinical features	Biochemical findings	Treatment provided
1	5 m/Male	Polyuria, Failure to thrive	Metabolic alkalosis (ph-7.49), potassium (3.2 mEq/L)	Oral potassium supplementation, indomethacin
2	7 m/Male	Failure to thrive, Some dehydration	Metabolic alkalosis (ph-7.54), potassium (2.8 mEq/L)	i.v. dehydration correction, oral potassium supplementation, indomethacin
3	2 m/Female	Polyuria, Failure to thrive Some dehydration	Metabolic alkalosis (ph-7.3), potassium (2.9 mEq/L), Urine calcium:creatinine ratio- 0.2	i.v. dehydration correction, oral sodium and potassium supplementation, indomethacin
4	12 m/Male	Failure to thrive	Metabolic alkalosis (ph-7.51), potassium (3.2 mEq/L)	Oral potassium supplementation and indomethacin
5	5 m/Female	Polyuria, Failure to thrive	Metabolic alkalosis (ph-7.49), potassium (3.1 mEq/L)	Oral potassium supplementation and indomethacin
6	8 m/Male	Failure to thrive	Metabolic alkalosis (ph-7.9), potassium (2.5 mEq/L), Urine calcium:creatinine ratio- 0.4	Oral potassium supplementation and indomethacin
7	4 m/Female	Failure to thrive	Metabolic alkalosis (ph-7.58), potassium (2.2 mEq/L), Urine calcium:creatinine ratio- 0.4	i.v. potassium supplementation. Oral sodium and potassium supplementation, indomethacin
8	6 m/Male	Failure to thrive, some dehydration	Metabolic alkalosis (ph-7.48), potassium (3 mEq/L)	i.v. dehydration correction, oral potassium supplementation, indomethacin

**[Table/Fig-1]:** Summary of clinical, biochemical findings and management of all the cases.  
m: Months

### Case 2

A seven-month-old male child presented with the complaint of diarrhoea and not gaining weight for the past one month. There was no significant antenatal and family history.

Physical examination showed sign of dehydration such as delayed skin turgor and dry mucous membranes which were corrected with 75 mL/kg ringer lactate over four hours. Child was treated for diarrhoea and worked up for failure to thrive. The weight of the child at admission was 6.4 kg (below -2SD for age and sex). The laboratory investigations revealed- persistent metabolic alkalosis (ph-7.54) and hypokalaemia (2.8 mEq/L) despite subsidence of diarrhoea [Table/Fig-1]. Stool examination was normal. Urine analysis showed losses of sodium (55 mEq/L), potassium (25 mEq/L) and chloride (40 mEq/L) in urine. There was no loss of calcium in urine and ultrasound abdomen was normal. Hence, a diagnosis of BS was made.

With clinical diagnosis of BS, the child was started on indomethacin (3 mg/kg/day) along with potassium chloride supplementation. Sodium supplementation was given till correction. On follow-up after two months electrolyte disturbances were corrected and weight gain of 600 gm (7 kg) was noted. Potassium supplementation was stopped on follow-up.

### Case 3

A two-month-old female child presented with excessive urination and thirst since birth. Antenatal history of polyhydramnios was present. There was no significant family history.

On physical examination dysmorphic triangular face was noted. Sign of dehydration such as delayed skin turgor and dry mucous membrane were present. Weight at presentation was 3.7 kg (below -3SD for age and sex). Initial work-up showed metabolic alkalosis (ph-7.3), hyponatraemia (126 mEq/L), hypokalaemia (2.9 mEq/L) and hypochloreaemia (90 mEq/L). Urine analysis showed losses of sodium (59 mEq/L), potassium (32 mEq/L) and chloride (38 mEq/L) [Table/Fig-1]. Urinary calcium losses were also noted with calcium:creatinine ratio of 0.2. Abdominal ultrasound showed renal parenchymal changes without nephrocalcinosis.

With clinical diagnosis of BS, indomethacin (3 mg/kg/day) was started sodium and potassium supplementation was given. Child required regular titration of sodium and potassium supplementation based on serum levels. Sodium supplementation was given for 10 days and stopped before discharge. At follow-up after two months electrolyte abnormalities were corrected and adequate weight gain of 1.3 kg with a total weight of 5 kg (below- 2SD for age and sex) was noted. Potassium supplementation was stopped on follow-up and indomethacin was continued. Electrolyte monitoring was continued on follow-up.

### Case 4

A one-year-old male child presented with the complaint of not gaining weight since third month of life. There was no significant antenatal or family history.

On physical examination, no dysmorphic features were noted and child was haemodynamically stable at presentation. Weight at presentation was 7 kg (below-3SD for age and sex). On initial work-up metabolic alkalosis (ph-7.510), hyponatraemia (128 mEq/L), hypokalaemia (3.2 mEq/L) and hypochloreaemia (92 mEq/L) were noted [Table/Fig-1]. Urine analysis showed losses of sodium (60 mEq/L), potassium (26 mEq/L) and chloride (36 mEq/L) in urine. There was no loss of calcium in urine and ultrasound abdomen was normal.

With clinical diagnosis of BS, child was started on indomethacin (3 mg/kg/day) and potassium chloride supplementation was given. Follow-up after one month showed correction of electrolyte disturbances and good weight gain. (Precise weight record was lost after follow-up).

### Case 5

A five-month-old female child presented with the complaint of excessive urination and thirst since first month of life. There was no significant antenatal or family history.

On physical examination no dysmorphic features were seen and child was haemodynamically stable at presentation. Weight at admission was 6 kg (below -2SD for age and sex). On initial work-up, metabolic alkalosis (ph-7.49), hyponatraemia (133 mEq/L), hypokalaemia (3.1 mEq/L) and chloride (96 mEq/L) was noted [Table/Fig-1]. Urine analysis showed losses of sodium (42 mEq/L), potassium (26 mEq/L) and chloride (36 mEq/L) in urine. There were no calcium losses in urine and ultrasound abdomen was normal.

With clinical diagnosis of BS, child was started on indomethacin (3 mg/kg/day) and potassium chloride supplementation was given. Follow-up showed correction of electrolyte disturbances and good weight gain. (Precise weight record was lost after follow-up).

### Case 6

An eight-month-old male child presented with the chief complaint of not gaining weight since fourth month of life. There was no significant antenatal or family history.

On physical examination no anomalies are seen. Weight at admission was 6.5 kg (below -3SD for age and sex). Initial work-up showed metabolic alkalosis (ph-7.9), sodium (136 mEq/L), hypokalaemia (2.5 mEq/L) and hypochloreaemia (93 mEq/L). Urine analysis showed losses of sodium (27 mEq/L), potassium (61 mEq/L) and chloride (20 mEq/L) in urine [Table/Fig-1]. Urinary losses of calcium was noted with a calcium:creatinine ratio of 0.4 (normal <0.2). Ultrasound abdomen showed no abnormalities.

With clinical diagnosis of BS child was started on indomethacin (3 mg/kg/day) and potassium chloride supplementation was given. Follow-up after 1 month showed correction of electrolyte disturbances and good weight gain of 500 gm was noted. (Total weight of 7 kg, below- 2SD for age and sex).

### Case 7

A four-month-old female child presented with the chief complaint of not gaining weight since birth. Child was exclusively breastfed. History of polyhydramnios was present antenatally. There was no significant family history.

On physical examination no anomalies are seen. Weight at admission was 4.2 kg (below -3SD for age and sex). Initial work-up showed metabolic alkalosis (ph-7.58), hyponatraemia (120 mEq/L), hypokalaemia (2.2 mEq/L) and hypochloreaemia (57 mEq/L). Stool examination was normal. Urine analysis showed losses of sodium (95 mEq/L), potassium (80 mEq/L) and chloride (73 mEq/L) [Table/Fig-1]. Urinary calcium losses was noted with calcium:creatinine ratio of 0.4. Abdominal ultrasound showed renal parenchymal changes in the form of Grade-2 hyperechogenicity (hyperechoic compared to liver) was noted without nephrocalcinosis.

In view of severe hypokalaemia, i.v. potassium was given at a dose of 2 meq/kg/day for 24 hours. With clinical diagnosis of BS, indomethacin (3 mg/kg/day) was started along with oral sodium and potassium supplementation. Child required regular titration of sodium and potassium supplementation based on serum levels. At two month follow-up sodium levels were maintained within normal limits in view of which sodium supplementation was stopped. As hypokalaemia was still present, potassium supplementation was continued. Weight on follow-up was 5 kg (below -3SD for age and sex). Adequate weight gain was not noted.

Child was kept under regular follow-up for six months with routine serum electrolyte monitoring and urine output monitoring. After six months of management, adequate weight gain was noted with a weight of 7.5 kg (between 3<sup>rd</sup> and 50<sup>th</sup> centile for age and sex).

### Case 8

A six-month-old male child presented with the complaint of not gaining weight since fourth month of life. There was no significant antenatal or family history.

On physical examination no anomalies were seen. Weight at admission was 5.1 kg (below -3SD for age and sex). Child presented with the sign of dehydration such as delayed skin turgor and dry mucous membranes. On initial work-up metabolic alkalosis (pH-7.48), hyponatraemia (130 mEq/L), hypokalaemia (3 mEq/L) and chloride (95 mEq/L) [Table/Fig-1]. Urine analysis showed losses of sodium (44 mEq/L), potassium (20 mEq/L) and chloride (44 mEq/L). There was no calcium loss in urine and ultrasound abdomen was normal.

With clinical diagnosis of BS child was started on indomethacin (3 mg/kg/day) and potassium chloride supplementation was given. Follow-up after two months showed correction of electrolyte disturbances and good weight gain. (Precise weight recording was lost after follow-up).

## DISCUSSION

The BS has two forms of presentation, a severe one of antenatal onset (neonatal Bartter) and one of later onset, during the early years of life (classic Bartter). Although seven genetic variants have been described, only two clinical forms of the disease are distinguished. A form of prenatal onset characterised by polyhydramnios and premature birth, with the neonate presenting severe dehydration due to polyuria in the first days of life, evolving early with nephrocalcinosis, and characteristic biochemical alterations (neonatal BS), and a less severe form called classical BS of later onset, usually in the first two years of life, with growth deficit and recurrent episodes of dehydration [4,5].

Abdelgadir IS et al., have reported antenatal BS in a 20-day-old neonatal girl presenting with failure to thrive, hypokalemic hypochloremic metabolic alkalosis. Diagnosis was confirmed by Chloride Channel KB (CLCNKB) gene mutation [6]. This present study showed two children with early onset severe BS, both affected infants were girls. Genetic testing was not done in both the cases. However, there is no clinical evidence that female child has higher risk of developing neonatal BS. The remaining six cases in present study were diagnosed as classic BS.

Sampathkumar K et al., did a similar study in India with seven cases of BS. The mean age of onset was 6.5 months compared to the present series which has a mean age of onset of three months. The present study has male:female ratio of 6:1 compared to the present series which shows 4:1. All cases were diagnosed clinically and started on potassium supplementation and Non Steroidal Anti-inflammatory Drugs (NSAIDs). Genetic testing was not done in these cases [7].

Two children in the present series showed renal parenchymal changes. Nephrocalcinosis was not seen in any of the cases

discussed here. Sampathkumar K et al., detected nephrocalcinosis in one out of seven cases and increased echogenicity in three cases [7].

All the above cases were treated with indomethacin and sodium, potassium supplementation after diagnosis based on clinical manifestations and laboratory values. Improvement in urine output and electrolyte disturbances was noted before discharge. Follow-up was done for weight gain.

Long-term follow-up of 20 BS cases was done by Nascimento CL et al., [8]. All the cases were diagnosed on clinical and laboratory basis. A total of 17 out of 20 cases showed good weight and height gain with indomethacin [8]. In the present series, six out of eight cases showed effective response to treatment. The remaining two cases with severe form of barter syndrome showed partial response. Duration of indomethacin is recommended to be continued till school age or lifelong maintenance [9].

## CONCLUSION(S)

Bartter Syndrome which is a rare tubulopathy can be diagnosed based on clinical manifestations and cost-effective investigations. Any child within two years presenting with polyuria and failure to thrive should be suspected of having renal tubulopathy. Investigations in the form of serum and urinary electrolytes along with acid-base level are sufficient to make clinical diagnosis of BS.

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