Classic Bartter Syndrome
Clinical Profile And Short-term Outcome
Experience From A Tertiary Care Centre In South India

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Background :

Bartter syndrome is a monogenic salt wasting tubulopathy, characterized by hyponatremia, hypokalaemia, hypochloremic metabolic alkalosis, elevated renin-aldosterone levels with normal-to-low blood pressure, hypercalciuria and normal serum magnesium levels. It occurs due to affliction of specific channels in the thick ascending loop of Henle. Classical Bartter syndrome or type 3 Bartter Syndrome is due to *CLCNKB* mutation. Here, we describe single Centre experience of genetically proven classical BS.

Methodology :

A retrospective observational study was done to analyse the clinical profile and genetic spectrum of classical Bartter syndrome followed up at SAT Hospital, Govt. Medical College, Thiruvananthapuram ,Kerala, India. After retrospective chart review of all children with clinical Bartter syndrome, we enrolled all children with pathogenic/likely pathogenic variants in *CLCNKB gene* expressed in homozygous or compound heterozygous state . Children with incomplete details were excluded. The clinical, biochemical parameters and genetic profile at presentation and follow-up were analysed.

Results :

9 children with genetic diagnosis of classical BS were enrolled after the screening of 14 patients with clinical suspicion of Bartter syndrome. Male to female ratio- 0.5:1. Median age of presentation was 5 months with infantile BS in 88%. 55% had polyhydramnios in utero. All babies had failure to thrive and the triad of polyuria, hypokalaemia, hypochloremic metabolic alkalosis. 57% had AKI at initial presentation. 42% had seizures at onset and 28% had nephrocalcinosis(Figure1). Homozygous pathogenic large deletion of CLCNKB gene involving regions of Exon 1-22 was reported in all children with the clinical phenotype. All were treated with Potassium supplements and prostaglandin inhibitor Indomethacin. 57% needed aldosterone antagonist Spironolactone. Follow-up period ranged form 1.5 years to 7 years. 66% had hypercalcemia and hypercalciuria on follow-up. Two children had hypomagnesemia requiring supplements. SNHL and Growth hormone deficiency was detected in one. 4 (44%) children had CKD stage 2 and one child had CKD stage 3 on follow up. Though there was improvement in hydration status, electrolyte balance and weight on follow up, height remained below the 3rd centile in all children.

Figure 1 : Initial Clinical Presentation

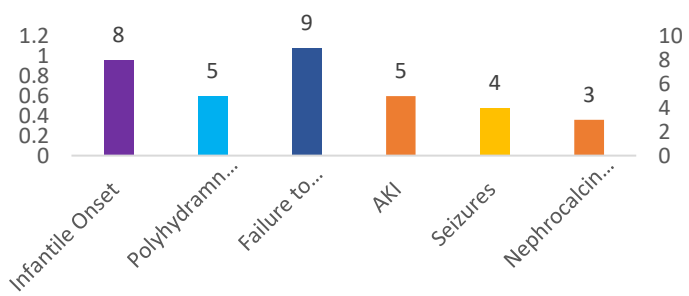
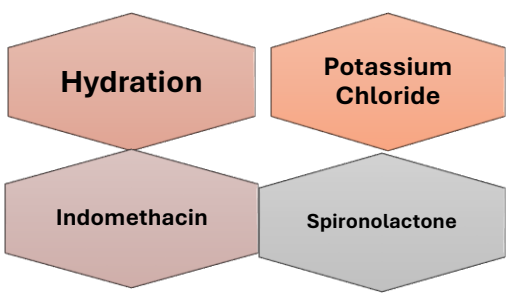


Figure 2 : Treatment in BS



Conclusion:

Bartter syndrome type 3 (BS3) is a monogenic tubulopathy caused by deleterious variants in the chloride channel gene *CLCNKB*, a high proportion of these being large gene deletions. Majority of children with Bartter syndrome type 3 (OMIM#607364) from our centre presented in infancy with failure to thrive, polyuria, hyponatremia, hypochloraemia, hypokalaemia, and growth retardation. Genetic analysis revealed homozygous deletions involving regions of Exon 1-22 in the CLCNKB gene. 57% had antenatal presentation with polyhydramnios and 71% with hypercalcemia on follow-up.

References:

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2. Cunha TDS, Heilberg IP. Bartter syndrome: causes, diagnosis, and treatment. Int J Nephrol Reno-vasc. Dis. 2018 Nov 9;11:291-301