

0094 - BEYOND 21-HYDROXYLASE DEFICIENCY: RARE SALT-WASTING DISORDERS IN A HISTORICAL COHORT FROM A TERTIARY CENTER

Mode: Research paper

Thematic Unit: Rare Diseases

Thematic Unit 2: Adrenals

SOTOMAYOR, Ana L | OSIAK, Lucas | VIEL, Jacqueline M | FROES, Nathalia | SOARES, Gabriel J | MAUES DE OLIVEIRA, Ana Carolina | IE, Jéssica Me Lin | COSTA DE MIRANDA, Mirela | GALLIANO, Stefano | BATATINHA, Júlio | FRAGOSO, Maria Candida | LATRONICO, Ana Claudia | BILHARINHO DE MENDONCA, Berenice | DOMENICE, Sorahia | BACHEGA, Tania

HOSPITAL DAS CLÍNICAS DA FACULDADE DE MEDICINA DA UNIVERSIDADE DE SÃO PAULO (HC-FMUSP)

Background/Objectives: Salt-wasting congenital adrenal hyperplasia due to 21-hydroxylase deficiency (SW-CAH) is a life-threatening neonatal emergency, and delayed diagnosis contributes to significant morbidity and mortality. Despite newborn screening programs, diagnostic failures and delayed clinical recognition still occur, particularly in developing countries. Several rare conditions mimic SW-CAH clinically but require distinct management, making accurate differential diagnosis critical. This study aimed to characterize SW disorders in children up to 2 years of age from a single tertiary center, distinguishing SW-CAH from rare mimicking conditions.

Methods: We retrospectively reviewed 114 cases from a tertiary center (1999–2025) presenting with hyponatremic dehydration up to age 2. Hormonal workup included cortisol, 17-OHP, 17-hydroxypregnenolone, aldosterone, plasma

renin activity, ACTH, sodium, and potassium levels. Molecular diagnosis was performed by Sanger sequencing, MLPA or next generation sequencing.

Results: SW-CAH was the most frequent etiology (105 cases; F:M ratio=2.3:1); mean sodium levels at presentation were 118 mEq/L in males [$\pm$ 12.3] and 123 mEq/L [$\pm$ 15.1] in females; mean age at first SW crisis was 39 days [$\pm$ 39,5]. Severe intellectual impairment was observed in 8% of cases. All cases harbored CYP21A2 genotypes predicting the SW form. Another 5 rare SW etiologies were identified: 2 males with 3 β -HSD2 deficiency, both with atypical genitalia and recurrent severe adrenal crises before diagnosis. Two males with X-linked adrenal hypoplasia congenita (NR0B1), including one initially misdiagnosed as SW-CAH. One female with pseudo hypoaldosteronism, also misdiagnosed as SW-CAH, was reevaluated after persistently normal 17-OHP levels and CYP21A2 genotype. One male with Triple A syndrome (AAAS), whose diagnosis was delayed by achalasia-related vomiting.

Conclusion: This series characterizes the clinical and molecular spectrum of salt-wasting disorders in children up to 2 years, showing that recurrent adrenal crises and severe intellectual impairment reflect the consequences of significant diagnostic delay; whereas rare etiologies are frequently misdiagnosed. Improved newborn screening and greater physician awareness are essential to reduce preventable morbidity and mortality.

