Serum cortisol and cortisone ratio as sensitive tool to identify subjects with severe or partial 11β-hydroxysteroid dehydrogenase type 2 deficiency

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Fig 1. MR activation by cortisol observed in AME.

**Background**
Severe deficiency of 11β-hydroxysteroid dehydrogenase type 2 (11BHS2) triggers activation of mineralocorticoid receptor (MR) by cortisol and causing apparent mineralocorticoid excess (AME) syndrome characterized mostly by low-renin arterial hypertension and hypokalemic. AME subjects and first degree relatives could give us clues about the biochemical presentation of partial deficiencies of 11BHS2. In Chile, we have found two pediatric patients with AME, associating the D223N (rs121917833) and R213C mutations.

**Aim**
To study the current clinical and biochemical status of 2 patient with AME including their first degree relatives, and to evaluate serum cortisol/cortisone as a biomarker of partial 11BHS2 deficiency.

**Subjects and Methods**
We have recently evaluated 2 AME patients and their families. In all of them, we measured serum potassium, aldosterone and plasma renin activity (PRA). Serum cortisol (F) and cortisone (E) were measured by LC-MS/MS, and F/E ratio was calculated. Genetic analyses of HSD11B2 gene were performed by PCR-HRM and DNA-sequencing.

**Results**

**Case (1):** Male patient with the D223N mutation in HSD11B2, 17 y-old, HT (165/110mmHg), BMI 22.6 Kg/m2 (p69), K+ (2.1 mEq/L), aldosterone (1ng/dl), PRA (<0.2ng/ml*h) and a high F/E ratio (28.8 [RV: 1.63-5.15]). His sister and mother are heterozygous for D223N. They are normotensive and do not show biochemical abnormalities, but a high F/E ratio (Both in percentile p97).

**Case (2):** Female Patient with the R213C mutation in HSD11B2, 2 y-old, HT (197/133mmHg), K+ (2.9mEq/L), aldosterone (1ng/dl), PRA (<0.2 ng/ml*h) and a high F/E ratio (175 [RV: 1.63-5.15]). Her father, mother and sister are heterozygous for R213C. Their clinical and biochemical parameters are mostly normal, but with a high F/E ratio E (percentile p92, p93 and p85,

**Discussion**
Clinical and biochemical findings in AME patients and their families support that high serum cortisol/cortisone ratio (>p90), in general associated to serum cortisone levels (<p30), could be a sensitive tool to identify biochemically subjects with severe or partial 11BHS2 deficiency, independent to a low-renin hypertension, low aldosterone or hypokalemic condition. Other complementary biomarkers are necessary to evaluate the progression of this condition.

**Supported by FONDECYT 1150437, 1130427, Becado UC PB-01/15, IMII P09/016-F (ICM) and Corfo 13CTI-21526-P1.