FREQUENCY OF ENZYME DEFICIENCIES IN A TURKISH COHORT OF CONGENITAL ADRENAL HYPERPLASIA: A SINGLE-CENTER EXPERIENCE WITH 145 PATIENTS

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Introduction and Objectives

Congenital adrenal hyperplasia (CAH) is an autosomal recessive disorder caused by a defect in any of the enzymatic steps of adrenal steroidogenesis. It occurs due to mutations in genes that encode enzymes involved in the synthesis of cortisol from cholesterol. The most common cause is 21-hydroxylase deficiency, with 11-beta hydroxylase, 3-beta hydroxysteroid dehydrogenase, 17-alpha hydroxylase and POR deficiency being among rarer causes.

The aim of this study was to characterize the clinical features and reveal frequency of enzyme deficiencies of Turkish patients with CAH in a single center.

Patients and Methods

One hundred and forty-five patients presenting with CAH to pediatric endocrinology clinic at Kanuni Sultan Suleyman Training and Research Hospital (Istanbul, Turkey) between January 1998 to January 2018 were recruited. Detailed clinical and biochemical data at the time of diagnosis and during follow-up were collected from the past records of the patients. Patients with non-CAH primary adrenal insufficiency and secondary adrenal insufficiency were excluded from the study.

Results

Clinical features of our patients with CAH are summarized in table 1. All patients were raised in accordance with their genetic sex.

Table 1. Clinical characteristics of patients with CAH

	n (%)
Number of all patients	145
Sex	
Female (46,XX)	82 (56.6)
Male (46,XY)	63 (43.4)
Consanguinity	107 (73.8)
Complaint	
46,XX	
Ambiguous genitalia	58 (70.7)
Cliteromegaly	8 (9.8)
Premature pubarche	7 (8.5)
Hirsutism and menstrual irregularity	7 (8.5)
Salt-wasting	2 (2.4)
46, XY	
Salt-wasting	46 (73.0)
Premature pubarche and macrogenitalia	15 (23.8)
Ambiguous genitalia	2 (3.2)
Central precocious puberty	15 (10.3)
Testicular adrenal rest tumor	9 (14.3)
PCOS	8 (9.8)

Table 2. Median age at diagnosis of 145 patients with CAH

	n	Median age at diagnosis	Range
46,XX			
21-OH deficiency	73		
Salt-wasting	45	newborn	1 day – 6 months
Simple-virilizing	14	newborn	1 day – 4 years
Late-onset	14	9.9 years	6.5 years – 16.3 years
11β-OH deficiency	6	newborn	1 day – 17 months
3β-HSD deficiency	2	newborn	
POR deficiency	1	newborn	
46,XY			
21-OH deficiency	54		
Salt-wasting	46	newborn	1 week – 9 months
Simple-virilizing	8	4.3 years	3 years – 7 years
11β-OH deficiency	7	2 years	18 months – 4 years
3β-HSD deficiency	2	newborn	

Median age of patients with CAH at the time of diagnosis are shown in Table 2.

While 88.2% of the patients were diagnosed with 21-hydroxylase deficiency (61.1% salt-wasting type, 17.4% simple virilizing type and 9.7% non-classical type), 9.0% had 11-beta hydroxylase deficiency, 2.1% had 3-beta hydroxysteroid dehydrogenase deficiency and 0.7% had POR deficiency. Consanguinity was present in 73.8% of cases.

70.7% of the female patients were diagnosed with ambiguous genitalia and 73.0% of the male patients were diagnosed with salt loss.

Fifteen patients were treated with GnRH analogues due to central precocious puberty. Testicular adrenal rest tumor (TART) was present in 14.3% of male cases and polycystic ovary syndrome was found in 9.8% of female cases. The youngest patient with TART was 5.5 years. The only patient with POR deficiency was diagnosed with Antley-Bixler Syndrome due to her syndromic features.

Conclusion

In this large Turkish cohort with CAH, frequency of enzyme deficiencies was consistent with the literature. The occurrence of hypertension during follow-up was an important clue for 11-beta hydroxylase deficiency.

Patients with clinical and hormonal features incompatible with 21-hydroxylase deficiency should be reevaluated for the rare forms of CAH.

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