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A CYP21A2 gene mutation in patients with congenital adrenal hyperplasia: Molecular genetics report from Saudi Arabia

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Background: Congenital adrenal hyperplasia (CAH) is an autosomal recessive condition caused by a deficiency of one of 5 enzymes involved in the steroidogenesis pathway. Although the clinical presentations of congenital adrenal hyperplasia (CAH) have been studied in Saudi children, the literature review revealed no molecular report of 21-hydroxylase was published.

Objective and hypotheses: The aim of this study was to determine the pattern of CYP21A2 gene-mutations of CAH in Saudi children.

Method: Between January 2011 and March 2014 at King Fahad Military Complex, Dhahran, Saudi Arabia, we thoroughly examined 11 patients with CAH and 2 asymptomatic individuals with a history of affected siblings. Additionally, we sequenced the full coding regions of the CYP21A2 gene and screened the gene for deletion(s)/duplication(s) using the multiplex ligation-dependent probe amplification (MLPA) technique.

Results: Nine patients had classic CAH and presented with ambiguous genitalia and/or salt-losing crisis. Two patients had the non-classic form of CAH and presented with precocious puberty. The remaining 2 subjects were asymptomatic. Screening the CYP21A2 gene, we detected p.Gln318X mutation in 4 patients, c.290 -13 C>G (IVS2-13C>G) in another 4, and a common deletion, involving exons 6 and 8 in 3 patients.

Conclusion: Our strategy of Sanger sequencing followed by MLPA was very successful in detecting CYP21A2 mutations in all patients with CAH.

Table 1 Clinical characteristics of patient with congenital adrenal hyperplasia.

Patient I.D	Sex	Age at presentation	Consanguinity	Family history	Clinical phenotype
CAH-01	M	3 weeks	Yes	Yes	Salt losing
CAH-02	M	30 months	Yes	No	Precocious puberty/ non-classic
CAH-03	F	At birth	Yes	Yes	Salt losing /ambiguous genitalia
CAH-04	F	At birth	Yes	Yes	Salt losing /ambiguous genitalia
CAH-05	F	At birth	Yes	Yes	Salt losing /ambiguous genitalia
CAH-06	M	3 weeks	Yes	Yes	Salt losing
CAH-07	F	At birth	Yes	Yes	Salt losing /ambiguous genitalia
CAH-08	F	At birth	No	No	Salt losing /ambiguous genitalia
CAH-09	M	4 weeks	Yes	Yes	Salt losing
CAH-10	M	4 years	No	No	Precocious puberty/non- classic
CAH-11	F	At birth	No	No	Salt losing/ambiguous genitalia
CAH-12	F	1 year	Yes	Yes	Asymptomatic/sibling of patient with CAH
CAH-13	M	6 years	Yes	Yes	Asymptomatic/sibling of patient with CAH

Table 2 Mutations detected in the CYP21A2 gene.

Patient I.D	Sequencing Results	HOMO/ HETERO	MLPA	HOMO/ HETERO	Comments
CAH-01	c.952 C>T (p.Gln318X)	Homozygous	None	N/A	Involving exon 8 / reported mutation
CAH-02	c.290 -13 C>G (IVS2-13C>G)	Homozygous	None	N/A	Intron 2 / reported mutation
CAH-03	c.952 C>T (p.Gln318X)	Homozygous	None	N/A	Involving exon 8 / reported mutation
CAH-04	c.952 C>T (p.Gln318X)	Homozygous	None	N/A	Involving exon 8 / reported mutation
CAH-05	None	N/A	Deletion	Homozygous	Involving exons 6 and 8 / Reported mutation
CAH-06	None	N/A	Deletion	Homozygous	Involving exons 6 and 8 / Reported mutation
CAH-07	None	N/A	Deletion	Homozygous	Involving exons 6 and 8 / Reported mutation
CAH-08	c.290 -13 C>G (IVS2-13C>G)	Homozygous	None	N/A	Intron 2 / reported mutation
CAH-09	c.952 C>T (p.Gln318X)	Homozygous	None	N/A	Involving exon 8 / reported mutation
CAH-10	c.290 -13 C>G (IVS2-13C>G)	Homozygous	None	N/A	Intron 2 / reported mutation
CAH-11	c.290 -13 C>G (IVS2-13C>G)	Homozygous	None	N/A	Intron 2 / reported mutation
CAH-12	None	N/A	Deletion	Heterozygous	Involving exons 6 and 8 / reported mutation
CAH-13	c.1436 G>T (p.Arg479Leu)	Heterozygous	None	N/A	Involving exon 10 / reported mutation

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