Congenital Adrenal Hyperplasia (CAH)

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Congenital adrenal hyperplasia (CAH) refers to several autosomal recessive diseases resulting from mutations of genes for enzymes involved in the production of cortisol from cholesterol by the adrenal glands (steroidogenesis).

Classical congenital adrenal hyperplasia is rare, affecting only one in 14,000 patients, but mild forms of the disease may occur in one of every 100 to 1,000 persons. (Deaton et al., 1999)

Late-Onset CAH
Non-classic or late-onset congenital adrenal hyperplasia (NCAH) due to 21-hydroxylase deficiency is one of the most common autosomal recessive disorders. Reported prevalence is approximately 1 in 1000. (Witchel, 2013)

Metabolic Abnormalities
Metabolic abnormalities are common in adults with CAH, including obesity (41%), hypercholesterolemia (46%), insulin resistance (29%), osteopenia (40%), and osteoporosis (7%). (Arlt et al., 2010)

PCOS and Hirsutism
A study included 107 women with hirsutism and PCOS. After ACTH stimulation test, 10 women were diagnosed as having NC-CAH because of high 17-OHP60 values. The prevalence of NC-CAH among women with hirsutism and PCOS was relatively high (10%). (Trakakis et al., 2008)

Genetics
CAH enzymes include:
- 21-hydroxylase
- 11beta-hydroxylase
- 3beta-HSD
- 17alpha-hydroxylase
- 20,22-desmolase
21-hydroxylase deficiency accounts for about 95% of diagnosed cases of CAH. The 12-hydroxylase is involved in the conversion of progesterone into cortisol.

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17OH\text{-progesterone} \rightarrow \text{Deoxycorticosterone}
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17\text{alpha-hydroxy-progesterone} \rightarrow 11\text{-Deoxycorticosterone}
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**Conventional Lab Tests**

Conventional lab tests include hormones (Cortisol, progesterone), serum electrolytes, aldosterone and renin. Genetic tests can help diagnose or confirm the disorder, but are rarely needed.

**Cortisol**

Decreased cortisol production is a hallmark of most forms of CAH. Decreased cortisol results in rising levels of ACTH, which stimulates adrenal cortex overgrowth (hyperplasia).

**Progesterone**

Classic 21-hydroxylase deficiency shows very high concentrations of 17-hydroxyprogesterone (greater than 242 nmol/L in random blood sample; with the normal being less than 3 nmol/L at 3 days age in a full-term infant). due to 21-hydroxylase deficiency accounts for about 95% of diagnosed cases of CAH.

**Aldosterone-To-Renin Ratio**

A study found that the aldosterone-to-renin ratio provides a simple index for disease severity in 21-hydroxylase deficiency congenital adrenal hyperplasia. (Nimkarn et al., 2007)

**Liver Function Tests**

The aims were assessing liver function tests (LFT) in women with congenital adrenal hyperplasia (CAH) on glucocorticoids. Sixty-one women with genetically verified CAH due to 21-hydroxylase deficiency, aged 18-63 years were compared to 61 controls. ALT and GGT were higher in the entire patient group (p=0.01 and 0.002); AST, GGT and ALP in patients > or =30 years (p=0.007-0.045); all LFT in salt-wasting (p<0.001-0.042); GGT in simple virilizing (p=0.008); ALT, GGT and ALP in Null/Null genotype (p=0.018-0.040); ALT and GGT in 12splice genotype (p<0.001 and 0.011). Using a recently proposed cut-off level for ALT (>0.317 microkat/L), 54% of patients vs 23% of controls had elevated levels (p=0.028). In patients, GGT and ALP correlated with waist circumference and with total body and trunk fat (r=0.274-0.406, p=0.001-0.043). However, ALT, GGT and ALP were increased even in non-obese patients (waist circumference < or =88 cm and body mass index <30 kg/m(2)) (p=0.012-0.045) mainly attributed to the
patients > or =30 years who also demonstrated elevated insulin levels and HOMA-indices. In conclusion, compared with controls, women with CAH have higher LFT, in particular patients > or =30 years and those with severe forms, probably reflecting a higher lifetime glucocorticoid exposure. (Falhammar et al., 2009)

**Conventional Treatments**

Glucocorticoid and mineralocorticoid replacement therapies are the mainstays of treatment of CAH. Glucocorticoids include hydrocortisone (26%), prednisolone (43%), and dexamethasone. (Kamoun et al., 2013)

Current glucocorticoid therapy is suboptimal because it is often difficult to reduce excess androgen without giving excess glucocorticoid, and patients may experience hypercortisolism, androgen excess, or a combination of these states. (Merke, 2008)

**Natural Therapies**

**Vitamin D**

Several studies found that decreased bone mineral density (BMD) and vitamin D deficiency were common in children with CAH. (Demirel et al., 2014) (Okten et al., 2012)

A cross-sectional study included 244 CAH patients (183 classic, 61 non-classic; NC). The majority had elevated or suppressed androgens, with varied treatment regimens. Mean adult height SD score was -1.0 +/- 1.1 for classic vs. -0.4 +/- 0.9 for NC patients (P = 0.015). Obesity was present in approximately one third of patients, across phenotypes. Elevated BP was more common in classic than NC patients (P <= 0.01); pediatric hypertensive BP was associated with suppressed plasma renin activity (P = 0.001). Insulin resistance was common in classic children (27%) and adults (38% classic, 20% NC); 18% of adults had metabolic syndrome. The majority (61%) had low vitamin D; 37% of adults had low bone mineral density. Hirsutism was common (32% classic; 59% NC women). TART was found in classic males (33% boys; 44% men). (Finkielstain et al., 2012)
References


