Comparing clinical practice with consensus guidelines for the investigation and management of British children with congenital adrenal hyperplasia.

RL Knowles[1], S Zheng[3], J Oerton[1], P Hindmarsh[1], C Kelnar[2], C Dezateux[1]
[1]University College London, UK; [2]University of Edinburgh, UK; [3]University of Oxford, UK

Background

- Congenital adrenal hyperplasia (CAH) is a group of recessively inherited disorders caused by a deficiency in one of the enzymes necessary for cortisol production in the adrenals.
- CAH affects approximately one in 18000 live births in Great Britain[1].
- The most common form is due to 21-hydroxylase (OH) deficiency, resulting in reduced mineralocorticoid and glucocorticoid production, and increased androgen production.
- Infants usually present with a life-threatening salt-losing adrenal crisis or female genital virilisation[1] whilst older children present with precocious puberty or growth disorders .[2]
- Management involves the replacement of deficient endogenous steroids, surgery to correct genital abnormalities and psychosocial support.

[1]Khalid JM, *et al.* Incidence and clinical features of congenital adrenal hyperplasia in Great Britain. *Arch Dis Child* 2012;95:101-06.
[2]Knowles RL, *et al.* Late clinical presentation of congenital adrenal hyperplasia in older children: findings from national paediatric surveillance. *Arch Dis Child* 2014;99:30-34.

Aim

- To review the assessment, management and follow-up of British children with CAH against consensus clinical guidelines (Box 1).
- To compare the management of children diagnosed under 12 months of age with those aged 12 months or more at diagnosis.

Box 1: Consensus guidelines

The **Endocrine Society (2010)**[3] and **European Society for Paediatric Endocrinology/Lawson Wilkins Pediatric Endocrine Society (2002)**[4] have published guidelines to help direct clinicians caring for children with CAH. Key points include:

1) Children should be evaluated by a paediatric endocrinologist and management should involve other specialists where appropriate, including geneticists, surgeons and psychosocial services.
2) Diagnostic investigation should include early morning serum 17-hydroxyprogesterone (17-OHP).
3) Additional investigations may include adrenocortical profile, imaging of internal genitalia and adrenals, karyotyping and genetic analysis.
4) Hydrocortisone is the preferred oral steroid replacement therapy in growing children.
5) Fludrocortisone should be given to infants with the classic salt-losing CAH. Salt (NaCl) supplementation may be required.

[3]Speiser PW, *et al.* Congenital adrenal hyperplasia due to steroid 21-hydroxylase deficiency: an Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab* 2010;95:4133-60.
[4]Clayton P, *et al.* Consensus statement on 21-hydroxylase deficiency from The European Society for Paediatric Endocrinology and The Lawson Wilkins Pediatric Endocrine Society. *Horm Res* 2002;58:188-95.

Methods

- Active surveillance was undertaken prospectively through the British Paediatric Surveillance Unit from Aug 2007 until Aug 2009.
- All new diagnoses of CAH in children under age 16 years and resident in Great Britain were identified.
- Questionnaires were sent to clinicians at the **time of diagnosis** and **12-months after diagnosis** to collect information on diagnosis, investigation, management and clinical outcome.

Results

- National surveillance identified 144 children newly diagnosed with CAH, of whom 137 were followed-up after 12 months. 82 children (60%) were diagnosed aged under 1 year.
- 108 (79%) children were referred to, or under the care of, a paediatrician with endocrinology as special interest (PESI) or endocrinologist
- 85 (62%) children were referred to other specialists within the first year after diagnosis , including to geneticists (n=75), psychological/counselling services (n=27), and surgeons (n=17).

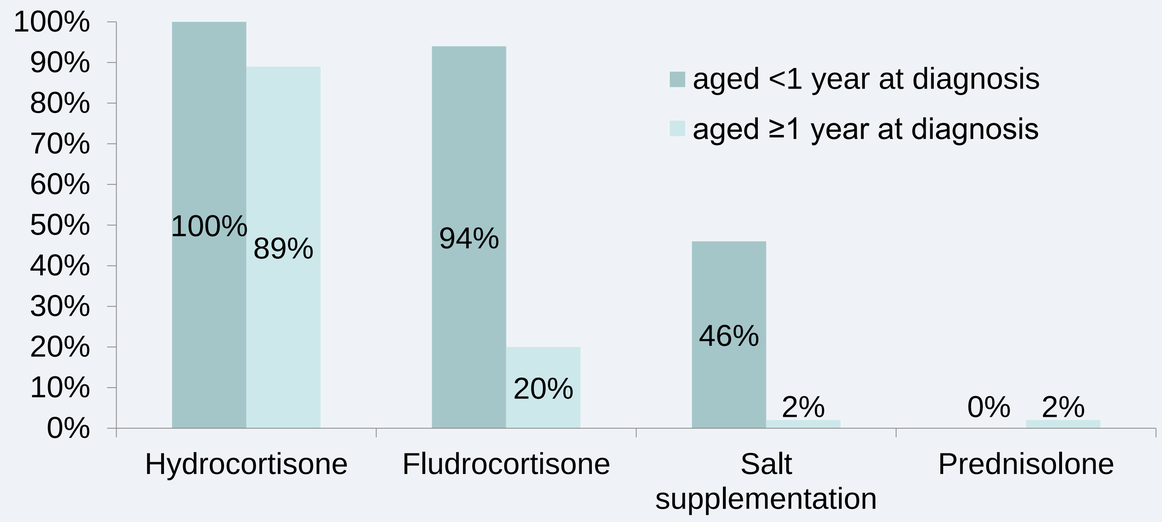
Specialist care	Diagnosed aged <1year	Diagnosed aged ≥1 year
Endocrinologist/PESI (n=108)	61 (74%)	47 (85%)
Geneticist (n=75)	49 (60%)	26 (47%)
Psychologist/counsellor (n=27)	16 (20%)	11 (20%)
Surgeons (n=17)	16 (20%)	1 (2%)

- 132 children (96%) received a serum 17-OHP test at diagnosis
- 94 (69%) children had urinary steroid analysis, 70 (51%) had DNA analysis and 52 (38%) a synacthen stimulation test

Investigations	Diagnosed aged <1year	Diagnosed aged ≥1 year
Serum 17-OHP (n=132)	81 (99%)	51 (93%)
Urinary steroid analysis (n=94)	49 (60%)	45 (82%)
DNA analysis (n=70)	40 (49%)	30 (55%)
Synacthen stimulation (n=52)	18 (22%)	34 (62%)

- At one year after diagnosis, 131 children were taking hydrocortisone and one was taking prednisolone, 88 children were taking fludrocortisone and 39 were taking sodium supplements.
- Seventeen children on steroid-replacement therapy experienced one or more adrenal crises in the first year after diagnosis.

Steroid replacement therapy



- Six of 30 severely virilised girls (Prader score ≥3) had genital surgery; eight less virilised girls also underwent surgery in the first year after diagnosis.

Discussion

- Our study confirms that international consensus clinical practice guidelines for assessing and managing children with CAH are generally being followed in Britain.
- Although current clinical guidelines recommend specialist care and multidisciplinary team approaches, by one year after diagnosis one-fifth of British children were not referred to or being managed by an endocrinologist or paediatrician with endocrinology as a special interest.

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