Quality of life (QoL) has been variously reported as normal or impaired in adults with congenital adrenal hyperplasia (CAH). To explore the reasons for this discrepancy we investigated the relationship between QoL and other health measures.

**METHODS**

**Patient recruitment**

The CaHASE cohort is a cross-sectional study of CAH adults recruited from 17 specialized British Endocrine centres. The study protocol was approved by West Midlands (MREC/03/7/086) and registered with ClinicalTrials.gov (NCT00749593). All centres contacted adult patients (18 years or older) with a confirmed diagnosis of CAH currently under their care. Recruitment started August 2004 and ended July 2007. All participants gave written informed consent.

**Outcome measures**

QoL: SF-36 questionnaires.

Androstenedione, 17-OHP, testosterone.

Waist circumference, triglycerides and HDL cholesterol, glucose and insulin (HOMA-IR).

Systolic and diastolic BP, gene mutations.

Type (hydrocortisone, prednisolone and dexamethasone) and dose of glucocorticoid expressed as prednisolone dose equivalent (PreDEq).

**Biochemistry measurements**

Performed at local laboratories (all participate in the UK NEQAS scheme for quality control of steroid immunoassays). Serum insulin was measured centrally using an ultrasensitive enzyme-linked immunosorbent assay (DRG instruments, Marburg, Germany).

**Mutation analysis, mutation groups and in vitro analysis of CYP21A2 mutations**

CYP21A2 gene deletion and chimeric genes were detected using a commercially available multiplex-ligation probe amplification (MLPA) strategy following the manufacturers protocol (mrc-Holland, Amsterdam, The Netherlands). Pseudogene-derived CYP21A2 point mutations were performed by targeted multiplex mini sequencing after allele specific PCR amplification of the CYP21A2 gene. If no common mutations were detected, direct DNA sequencing of the entire CYP21A2 gene was performed.

Patients were categorized into established CYP21A2 mutation groups according to their genotype with the less severe mutation determining the group: Null (mutations absent in vitro activity), A (introns 2 splice site mutation), B (mutations such as the H172N mutation and mutations with 1-10% in vitro residual enzyme activity), C (mutations such as P30L, V281L, and P453S or above 20-30% in vitro 21-hydroxylase activity).

**Data analysis**

Cross-sectional analysis of 151 adults with 21-hydroxylase deficiency (50M: 47 with classic and 3 with non-classic CAH; 101F: 75 with classic and 26 with non-classic CAH) aged 18-69 years in whom QoL (SF-36). Glucocorticoid regimen, anthropometric and metabolic measures were recorded. QoL was expressed as z-scores calculated from matched controls (14,430 subjects from UK population, courtesy of Professor John Brazier, Sheffield University). Relationships were examined between QoL and outcome measures. Principal Components Analysis (PCA) was undertaken to identify clusters of associated clinical and biochemical features and the principal component (PC) scores used in regression analysis as predictor of QoL.

**RESULTS**

QoL scores were associated with type of glucocorticoid treatment for vitality (P = 0.002) and mental health (P = 0.011), with higher z-scores indicating better QoL in patients on hydrocortisone than in patients receiving prednisolone or dexamethasone (P < 0.05). QoL did not relate to PreDEq or mutation severity. PCA identified three PCs (PC1, disease control; PC2, adiposity and insulin resistance; PC3, blood pressure and mutations) that explained 61% of the variance in observed variables. Stepwise multiple regression analysis demonstrated that PC2 (comprising waist circumference, serum triglycerides, HOMA-IR and HDL-cholesterol) was associated with QoL scores, specifically impaired physical functioning, body pain, general health, Physical Component Summary Score (P < 0.001) and vitality (P = 0.002).

**SUMMARY OF FINDINGS IN ADULT CAH PATIENTS**

- QoL was impaired in this cohort of patients.
- Increased adiposity and insulin resistance were associated with impaired QoL, predominantly in the physical health domains.

**CONCLUSIONS**

Increased adiposity and insulin resistance are associated with impaired QoL in adults with CAH. Further studies are justified to establish whether optimising the choice of glucocorticoid treatment and/or weight loss can improve QoL in this disadvantaged patient group.