Subjective health status in men and women with congenital adrenal hyperplasia: a population-based survey in Norway

Ingrid Nermoen1,2, Eystein S Husebye3,4, Johan Svartberg5,6 and Kristian Lovás1,4

1Faculty Division, Akershus University Hospital, University of Oslo, 1478 Lørenskog, Norway, 2Division of Medicine, Akershus University Hospital, 1478 Lørenskog, Norway, 3Department of Medicine, Haukeland University Hospital, 5021 Bergen, Norway, 4Institute of Medicine, University of Bergen, 5021 Bergen, Norway, 5Division of Medicine, University Hospital of North Norway, 9038 Tromsø, Norway and 6Institute of Clinical Medicine, University of Tromsø, 9037 Tromsø, Norway

(Correspondence should be addressed to I Nermoen; Email: ingrid.nermoen@ahus.no)

Abstract

Background: Patients with classical congenital adrenal hyperplasia (CAH) require life-long corticosteroid therapy, with uncertain health outcome. Investigations of subjective health status in unselected populations of adult patients are needed.

Objective: To identify all adult Norwegian patients with CAH and obtain population-based data on subjective and psychological health status, working ability and fertility.

Patients, methods and design: Classical CAH patients were identified through search in electronic diagnosis registries at all the university hospitals in Norway. The diagnosis was verified by scrutiny of medical records. The patients were invited to a questionnaire survey including medical history, and the Short Form-36 (SF-36) and Quality of Life Scale questionnaires. The questionnaire responses and fertility data were compared with normative data.

Results: We identified 104 adult patients (101 alive) with classical CAH (63% female), yielding overall incidence at 1/20 000 live births (1/16 000 in females). Seventy-two (72%) responded; median age 38 years (range 18–72). All the SF-36 scales were significantly impaired, most pronounced for general health and vitality perception. Working disability was reported by 19% of the patients, compared with 10% in the general population. The female patients were often single, and the CAH women had only 21% of the expected number of children compared with the general population.

Conclusion: In this population-based survey of patients with classical CAH, we found that subjective health status and working ability were impaired, and that fertility was reduced in females. There is a need for improvement of the medical treatment and the general care of this patient group.

European Journal of Endocrinology 163 453–459

Introduction

Congenital adrenal hyperplasia (CAH) is an autosomal recessive disorder with impaired biosynthesis of adrenal corticosteroids. Reduced cortisol biosynthesis leads to reduced feedback inhibition of ACTH secretion from the pituitary, and alteration of mineralocorticoid and adrenal androgen secretion (1). In Caucasian populations, typically more than 95% of the CAH cases are due to defective cytochrome P450 enzyme CYP21A2, called 21-hydroxylase (21-OH) deficiency.

21-OH deficiency is divided into classical CAH, which includes the salt-wasting (SW) and simple virilising (SV) forms, and non-classical or ‘late-onset’ form. SW is the most severe phenotype, characterised by deficiency of both cortisol and aldosterone. One study found that about 70% of those with classical CAH had the SW form (2). Female newborns with the SW and SV forms may have severe virilisation of external genitalia, usually less pronounced in SV than in SW. The non-classical form is caused by less severe CYP21A2 mutations, with sufficient cortisol and aldosterone production, but increased ACTH driven production of adrenal androgens. The world-wide incidence of the classic form of CAH based on neonatal screening programs has been estimated at 1/15 000 (2), but there is wide ethnic and geographical variation.

CAH is treated with the replacement of glucocorticoids and mineralocorticoids. Furthermore, the glucocorticoid doses aim to suppress the elevated ACTH secretion, and hence attenuate the increase in androgen levels. There is no consensus as to which type of glucocorticoid and which dose should be used for adult CAH patients (3). The conventional glucocorticoid therapy does not completely restore the normal circadian cortisol profile, and new modes of glucocorticoid delivery have been proposed. Modified-release hydrocortisone tablets have been produced, which
better mimic the normal rhythm and hence might yield suppression of adrenal androgen production with lower glucocorticoid doses (4). Recently, Bryan et al. (5) reported a boy with poorly treated CAH, who had been successfully controlled with continuous s.c. hydrocortisone infusion (CSHI) for 4 years, similar to our experience with CSHI in Addison’s disease (6).

The long-term outcome of the disease and its various treatment strategies have been addressed in a few studies, mostly in females (3, 7, 8). Gender atypical behaviour has been described in young girls as well as in women with CAH due to a CYP21A2 deficiency (7, 9). The consequences for psychological functioning and well-being in adult life are not well known (8, 10–13). To our knowledge, only two previous studies addressed subjective health status in men with CAH. One study showed favourable subjective health status in 16 Finnish men aged 16 years or more (11), and the other showed unfavourable emotionality scores in adolescent and adult males with CAH (8).

The aims of this study were to identify an unselected Norwegian population of adult patients with CAH, to describe the treatments that are used, and to investigate subjective and psychological health status, and working ability. Previous studies have shown that women with CAH have reduced pregnancy and delivery rates, the women with SW being most severely affected (14). We therefore also undertook to investigate fertility rates in men and women with CAH.

Patients and methods

Patients and design

We aimed to identify all patients in Norway ≥ 18 years with classical CAH, identified through search in electronic diagnosis registries at the six university hospitals in Norway that have adult endocrine units. The diagnosis registries had start dates ranging from 1972 to 1999. The search criteria were the International Classification of Diseases (ICD) codes 255 (ICD 8 and 9) and codes E25 and E27.9 (ICD 10), i.e. adrenogenital syndromes and unspecific adrenal diseases. Furthermore, endocrinologists at all the regional hospitals were contacted and requested to record CAH patients. All practitioners in the country were approached in an advertisement in The Journal of the Norwegian Medical Association, on the web pages of the Norwegian Society for Endocrinology, and in the Journal of the Norwegian Addison’s Association, which organises patients with CAH.

The CAH diagnosis was verified by endocrinologists by scrutiny of original medical records in all the patients, including data on genital examination, symptoms at presentation (hypotension, nausea and electrolyte abnormalities), levels of adrenal steroids, and, if investigated, genetic analyses. Norway has not established a newborn screening program for CAH; therefore, all the diagnoses had been made clinically. The patients were classified with the SW form if they had signs of severe mineralocorticoid deficiency during the first 3 years of life (hypovolemic shock, vomiting, low serum sodium or high serum potassium), and if the term salt-loser was used, in girls with the presence of virilisation of external genitalia. The SV form was diagnosed in females with virilisation of external genitalia, and in men with signs of peripheral precocious puberty before 6 years of age, and no signs of mineralocorticoid deficiency.

All the registered patients were invited to participate in a questionnaire survey. Each participant completed a registration form covering medical history, diagnosis, treatment and working ability. The form also included questions about marital status, number of children, and symptoms and interventions related to sex hormone disturbances. Further, they completed the Short Form-36 (SF-36) and Quality of Life Scale (QOLS) questionnaires (see below). Non-responders were reminded with a second letter. The Regional Ethics Committee of Western Norway and the Data Inspectorate of Norway approved the study. The study was performed according to the Helsinki Declaration.

Measurement

Subjective health status was assessed with the SF-36 form (15), with normative data available from the general Norwegian population (16). The SF-36 questionnaire comprises 36 items; the responses are transformed into eight subscales, namely, perception of physical functioning, role limitations due to physical problems, bodily pain, general health (GH), vitality (VT), social functioning, role limitations due to emotional problems and mental health (17). Higher scores are favourable.

No disease-specific questionnaire for CAH is available. We chose to include the QOLS (18) in the survey; this questionnaire is a 16-item, domain-specific instrument, which measures an individual’s overall satisfaction with life in different areas not usually included in health-related QOL instruments, such as independence, material comfort, work satisfaction, recreation, etc. (Supplementary Table 1, see section on supplementary data given at the end of this article). The QOLS has been used in both cross-sectional and randomised controlled studies of different patient groups with chronic diseases (18), tested for validity and reliability (19), and normative reference ranges for the general Norwegian population exist (20). The scale is scored by adding up the items to obtain a total score (min 16–max 112); higher scores are favourable.
Statistical analysis

The patient scores (SF-36) were compared with the normative data by two sample T-test and multiple linear regression analysis, with age and gender as independent variables. As the SF-36 results were consistent across the scales, the data are presented without Bonferroni correction. QOLS data were compared with published confidence intervals in the general population (20) and considered statistically significant if the confidence intervals (CI) did not overlap. Two sample T-test was run to look for differences between gender and SW versus SV forms. The data are also presented as median and total range.

Results

Incidence of CAH in Norway

We identified 104 adult patients (101 alive and 3 deceased) with classical CAH in Norway, of whom 65 (63%) were females. Age, gender and disease categories are shown in Table 1. The majority of the patients were found in diagnosis registries at the university hospitals; endocrine consultants at local hospitals reported six additional patients. There was no response to the advertisement in The Journal of the Norwegian Medical Association, but four patients responded to the advertisement in the Journal of the Norwegian Addison’s Association. The deceased patients died at ages 59, 63 and 73 years; one died from pulmonary cancer, and two of the causes of death remain unknown.

During the period of 1970–1990, Norway had 1 113 130 live births. In the same period, 35 girls and 21 boys with CAH were born, yielding an overall incidence of classical CAH in Norway at 1/20 000 live births, and an estimated incidence for girls at 1/16 000.

Table 1  Patient characteristics and medical treatment.

<table>
<thead>
<tr>
<th></th>
<th>SW</th>
<th>SV</th>
<th>21-OH deficiency total</th>
</tr>
</thead>
<tbody>
<tr>
<td>All subjects identified through diagnosis search</td>
<td>54 (52)</td>
<td>50 (48)</td>
<td>104 (100)</td>
</tr>
<tr>
<td>Female sex, n (%)</td>
<td>31 (57)</td>
<td>34 (68)</td>
<td>65 (63)</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>23 (43)</td>
<td>16 (32)</td>
<td>39 (37)</td>
</tr>
<tr>
<td>Age (years), median (range)</td>
<td>33 (19-55)</td>
<td>42 (18-80)</td>
<td>35 (18-80)</td>
</tr>
<tr>
<td>Women</td>
<td>30 (19-55)</td>
<td>42 (21-80)</td>
<td>35 (19-80)</td>
</tr>
<tr>
<td>Men</td>
<td>38 (19-54)</td>
<td>44 (18-73)</td>
<td>38 (18-73)</td>
</tr>
<tr>
<td>Participants in survey</td>
<td>32 (44)</td>
<td>40 (56)</td>
<td>72 (100)</td>
</tr>
<tr>
<td>Female sex, n (%)</td>
<td>20 (61)</td>
<td>27 (69)</td>
<td>47 (65)</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>12 (36)</td>
<td>13 (33)</td>
<td>25 (35)</td>
</tr>
<tr>
<td>Age (years), median (range)</td>
<td>35 (19-51)</td>
<td>43 (18-72)</td>
<td>38 (18-72)</td>
</tr>
<tr>
<td>Women</td>
<td>33 (19-51)</td>
<td>44 (21-72)</td>
<td>39 (19-72)</td>
</tr>
<tr>
<td>Men</td>
<td>38 (19-50)</td>
<td>41 (18-58)</td>
<td>38 (18-58)</td>
</tr>
<tr>
<td>Glucocorticoid type, n (%)</td>
<td>4 (13)</td>
<td>0 (0)</td>
<td>4 (6)</td>
</tr>
<tr>
<td>Hydrocortisone</td>
<td>4 (13)</td>
<td>0 (0)</td>
<td>4 (6)</td>
</tr>
<tr>
<td>Cortisone acetate</td>
<td>8 (25)</td>
<td>8 (23)</td>
<td>16 (22)</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>11 (34)</td>
<td>16 (43)</td>
<td>27 (38)</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>4 (13)</td>
<td>9 (23)</td>
<td>13 (18)</td>
</tr>
<tr>
<td>Mix of two</td>
<td>4 (13)</td>
<td>4 (8)</td>
<td>8 (11)</td>
</tr>
<tr>
<td>Glucocorticoid doses, mg, median (range)</td>
<td>27.5 (15-35)</td>
<td>28.2 (25-37.5)</td>
<td>34.5 (25-100)</td>
</tr>
<tr>
<td>Hydrocortisone</td>
<td>27.5 (15-35)</td>
<td>28.2 (25-37.5)</td>
<td>34.5 (25-100)</td>
</tr>
<tr>
<td>Cortisone acetate</td>
<td>37.5 (25-100)</td>
<td>28.2 (25-37.5)</td>
<td>34.5 (25-100)</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>7.5 (2.5-15)</td>
<td>7.5 (2.5-15)</td>
<td>7.5 (2.5-15)</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>0.5 (0.25-0.5)</td>
<td>0.5 (0.25-1.5)</td>
<td>0.5 (0.25-1.5)</td>
</tr>
<tr>
<td>Fluocortisone use, n (%)</td>
<td>29 (91)</td>
<td>3 (8)</td>
<td>32 (44)</td>
</tr>
<tr>
<td>Fluocortisone dose</td>
<td>0.1 (0.025-0.2)</td>
<td>0.1 (0.1-0.2)</td>
<td>0.1 (0.025-0.2)</td>
</tr>
<tr>
<td>Salt tablets</td>
<td>3 (9)</td>
<td>2 (5)</td>
<td>5 (7)</td>
</tr>
</tbody>
</table>

*For patients using one type of glucocorticoid only.
All except four patients (two females and one male with SV; one female with SW) received glucocorticoid therapy at the time of the survey. These four patients had previously used glucocorticoids, but stopped the treatment due to side effects. Prednisolone was the most used glucocorticoid, whereas about one-third of the Norwegian adult patients used hydrocortisone or cortisol acetate. Forty-four per cent of the patients used fludrocortisone (Table 1).

Subjective health status

Age- and gender-adjusted analysis showed that all the SF-36 scales were significantly impaired compared with the general population, most pronounced for GH and VT perception (Table 2). The subgroups of patients < 30 and > 30 years of age showed similar trends, however, not significantly in the younger age group, possibly due to low number of patients. Subgroup analysis did not reveal any differences between the sexes, or between the SW and SV forms (Table 2), and the scores did not correlate with glucocorticoid doses. The patients who received disability benefit had significantly impaired SF-36 scales compared with the working patients (data not shown). The QOLS scores with normative values are given in Supplementary Table 1. The QOLS total scores for the patients were not significantly lower than normal, and among the individual items in the questionnaire, only item no. 2 (health: being physically fit and vigorous) was significantly lower than the normal. Item no. 1 (material comforts: home, food, modern conveniences and financial security) and item no. 5 (close relationship with spouse or significant other) differed between disease category, with better scores in the SV group. Nineteen per cent of the patients aged 18–27 received full time (13%) or part time (6%) disability benefit, which is a high number compared with 10% (8% full time and 2% part time) in the general population (data from Statistics Norway: http://www.ssb.no). Twenty per cent of the women and 18% of the men received disability benefit. The frequency of

Table 2 Subjective health status Short Form-36 (SF-36); mean (s.d.) scores in patients with congenital adrenal hyperplasia compared with normative data.

<table>
<thead>
<tr>
<th>SF-36</th>
<th>n</th>
<th>PF</th>
<th>RP</th>
<th>BP</th>
<th>GH</th>
<th>VT</th>
<th>SF</th>
<th>RE</th>
<th>MH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients, all</td>
<td>72</td>
<td>82.7 (23.5)</td>
<td>70.4 (39.0)</td>
<td>70.0 (28.8)</td>
<td>62.7 (29.7)</td>
<td>50.0 (25.4)</td>
<td>77.4 (26.5)</td>
<td>70.4 (39.7)</td>
<td>74.0 (19.2)</td>
</tr>
<tr>
<td>SW</td>
<td>32</td>
<td>83.0 (21.1)</td>
<td>69.4 (38.0)</td>
<td>69.6 (31.9)</td>
<td>60.8 (30.4)</td>
<td>49.1 (26.8)</td>
<td>74.8 (28.4)</td>
<td>66.7 (43.0)</td>
<td>71.6 (21.5)</td>
</tr>
<tr>
<td>SV</td>
<td>40</td>
<td>82.5 (25.5)</td>
<td>71.3 (40.3)</td>
<td>70.4 (26.4)</td>
<td>64.2 (29.4)</td>
<td>50.9 (24.5)</td>
<td>79.5 (25.1)</td>
<td>73.3 (37.2)</td>
<td>75.8 (17.3)</td>
</tr>
<tr>
<td>P value&lt;sup&gt;a&lt;/sup&gt;</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Normative</td>
<td>2311</td>
<td>87.2 (18.7)</td>
<td>77.9 (35.8)</td>
<td>75.1 (28.0)</td>
<td>76.8 (22.0)</td>
<td>60.0 (20.8)</td>
<td>85.5 (22.2)</td>
<td>81.6 (32.4)</td>
<td>78.8 (16.5)</td>
</tr>
<tr>
<td>P value&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.047</td>
<td>NS</td>
<td>0.04</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>0.002</td>
<td>0.005</td>
<td>0.017</td>
<td>0.036</td>
</tr>
<tr>
<td>P value&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.002</td>
<td>0.012</td>
<td>0.012</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>0.002</td>
<td>0.004</td>
<td>0.004</td>
<td>0.006</td>
</tr>
</tbody>
</table>

PF, physical functioning; RP, role limitations due to physical problems; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role limitations due to emotional problems; MH, mental health.

<sup>a</sup>Comparison between SW and SV in women.

<sup>b</sup>Comparison between patients and normative data, two sample T-test.

<sup>c</sup>Comparison between patients and normative data, multiple linear regression with correction for age and gender.

Table 3 Fertility-related conditions in men and women with congenital adrenal hyperplasia.

<table>
<thead>
<tr>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>SW (n=20)</td>
<td>SV (n=27)</td>
</tr>
<tr>
<td>Single status (no stable relationship), n (%)</td>
<td>18 (90)</td>
</tr>
<tr>
<td>Own children, n (%)</td>
<td>2 (10)</td>
</tr>
<tr>
<td>Number of children (group total)</td>
<td>2</td>
</tr>
<tr>
<td>Infertility investigation, n (%)</td>
<td>2 (10)</td>
</tr>
<tr>
<td>Genital surgery, n (%)</td>
<td>20 (100)</td>
</tr>
<tr>
<td>Never been to gynaecological investigation as adult, n (%)</td>
<td>9 (45)</td>
</tr>
<tr>
<td>Irregular menstruation, women ≤ 50 years, n (%)</td>
<td>9 (45)</td>
</tr>
<tr>
<td>Amenorrhoea last 3 months, women ≤ 50 years, n (%)</td>
<td>6 (30)</td>
</tr>
<tr>
<td>Hirsutism, n (%)</td>
<td>3 (15)</td>
</tr>
</tbody>
</table>

NS, not significant; ND, not done; NA, not applicable.

<sup>a</sup>Comparison between SW and SV in women.

<sup>b</sup>Comparison between SW and SV in men.

<sup>c</sup>Comparison between women and men; two sample T-test.
disability was similar in the younger and the older age group; in the normal population, disability increases with age.

**Fertility**

Issues related to reproductive health are shown in Table 3. Among the women, 53% were single as compared with 38% in the general female population in the age group 18–80 years (Statistics Norway: http://www.ssb.no); the increased frequency of single status was confined to the SW females. The proportion of women who were childless was significantly higher in the SW than in the SV group. The female patients with CAH had given birth to 15 children, while the expected number of children was 70.4, as estimated from the birth rates of the population cohorts of each of the patients (Statistics Norway: http://www.ssb.no). This yields a standardised incidence ratio (SIR) for child birth in CAH females at 0.21 (CI 0.11–0.31), significantly lower in SW than SV (SIR 0.08 vs 0.29, \( P = 0.048 \)). Irregular menses were common in females with CAH; amenorrhoea was more frequent in SW than in SV. Interestingly, 40% of the females had never been to gynaecological examination in adult age. The CAH males had significantly more children than the females, with no difference between the SW and the SV groups. The exact SIR for child birth of the CAH males could not be estimated as age-matched control data for men are not available. In our study, ten men were older than 45 years, and two of them (20%) had no children, which is similar to data from Statistics Norway indicating that a maximum of 20% of Norwegian men older than 45 years are childless.

**Discussion**

The CAH patients in this population-based survey had significantly impaired subjective health status as measured by the SF-36 questionnaire, and a higher proportion of the patients than the general population received working disability benefit. The females with CAH had significantly reduced fertility, most pronounced for those with the SW form.

The particular strength of the current study is that it does not represent data from one single centre. Our study population was also older than that of all the previous studies on CAH patients. The case identification was approached from several angles, and the diagnosis was verified by scrutiny of medical records. The epidemiological data are reliable, since the Norwegian population has little migration. Every citizen has a unique identification number, and can be traced in several registries. This approach yielded an estimated incidence 1/16 000 for females with classical CAH in Norway, which is comparable with that of neighbouring countries and other Caucasian populations (2).

However, a recent incidence estimate at 1/9800 based on new-born screening programs in Sweden (21) indicates that the incidence may be underestimated, or that some die undiagnosed. Notably, we identified fewer adult men than women with classical CAH, which was also reported in England (22). Before newborn screening started in Sweden in 1986, the prevalence of CAH was also higher for girls than for boys (21, 23). This is intriguing, since CAH is an autosomal recessive trait with expected equal sex ratio, and may be interpreted as increased neonatal male mortality because of adrenal crises, as male infants are less readily diagnosed and treated than female infants (22).

Another explanation may be that some boys with the SV form of CAH remain undiagnosed in adult age (24).

The impaired health perception as indicated by the SF-36 and QOLS scores corresponds well with the reduced working ability. The impairment of GH and VT perception were most pronounced and equalled those of Norwegian patients with Addison’s disease (25). Our results contrast those of the Finnish study in 32 men and women, which showed a better health-related QOL than the general Finnish population (11). However, the Finnish investigators did not provide data for the men separately, and their response rate (55%) was lower than in our study.

Some published studies report good psychological adjustment for the CAH patients (8, 10–12). The largest previous study found no significant differences on any measure between CAH females and unaffected females in any age group, or CAH males in childhood compared with controls (8). However, adolescent and adult age males with CAH had unfavourable emotionality scores. One study from Taiwan including 11 young CAH women showed increased psychiatric morbidity (26), and a Danish study including 40 women found impaired QOL compared with a control group (27).

Recent studies of 60 adult women with CAH in Sweden showed that type of mutation and surgical procedure affected long-term psychosexual aspects of QOL, which correlated with satisfaction with genitalia, and fertility (28). Pregnancy and delivery rates were reduced, most likely due to psychosocial reasons (14).

The impairment of subjective health status in our study could be underestimated as we have fewer patients with SW among the respondents than in the total patient population. Other studies have shown that non-responders in such surveys tend to be older and less healthy than the responders (16). Furthermore, patients with chronic diseases tend to adjust their health-related quality of life (HRQoL) responses (response shift), in some cases appreciating life more despite health deficiencies (29). Most likely the cause of the impaired subjective health perception is complex, including the hormonal disturbances and the steroid treatment as well as psychological issues. The discrepancy between the effects on SF-36 and those on QOLS indicates that the SF-36 scales target the
particularly problematic QOL issues in CAH better than the QOLS does, and that the impaired health perception does not impact all the various aspects of psychological well-being.

Some limitations apply to our analysis of the HRQoL responses; most importantly, we were not able to correct for socioeconomic status. Early diagnosis and treatment are likely to improve the long-term outcome, and our historical cases may not represent the outcome of patients diagnosed more recently. The normative data were 10 years older than the patient data; the recent data from Addison’s disease, however, showed no drift of responses compared with scores obtained in 2001–2002 (30).

Our data confirm the findings by others that the CAH women are more often single, and have fewer children than the normal population (14): single status was more frequent in women with SW than SV. CAH women had only 21% of the expected number of children, which is similar to reported pregnancy and child birth rates in previous studies of females with classic 21-OH deficiency (12). The low birth rate could have various reasons; some patients have decreased sexual activity due to genital malformations (31), and higher frequency of homosexuality and single status is noted among the CAH women (10). Furthermore, the potential for conception may be reduced due to polycystic ovary syndrome and hyperandrogenism, which inhibits the ovarian hormone cycle resulting in anovulation (14).

The data on fertility in men with CAH are conflicting. We found that the fraction of childless males with CAH over 45 was roughly the same as in the general population. Testicular adrenal rest tumours, occurring in one-third of classic CAH males, may result in oligoazoospermia or Leydig cell failure, and have been associated with reduced male fertility (32, 33). On the other hand, Urban et al. (34) found approximately normal fertility in 18 of 20 patients evaluated by paternity and/or sperm count. A study in 29 adult Finnish male patients found significantly reduced birth rate compared with age-matched controls (35).

Treatment differences in different countries may explain some of the contrasting results on subjective health status and fertility. Swedish CAH women had lower androgens (testosterone, androstendione and DHEAS) than the controls (36), indicating possible over-treatment with glucocorticoids. A much lower proportion of the Norwegian than the Swedish CAH women received fludrocortisone therapy (82% in Sweden versus 38% in Norway) (36). Fludrocortisone is recommended in all patients with CAH at the time of diagnosis, but in many adults fludrocortisone therapy can be tapered down (3). It is not unlikely that the age at diagnosis and choice of treatment could impact subjective health, working ability and fertility, but the number of patients in this study is too low to address this issue specifically. Further research is needed to determine whether novel treatments such as modified-released hydrocortisone tablets (4) and CSHI (5) will improve subjective health and fertility in these patients.

Conclusion

In this population-based survey, we found impaired subjective health status in adult Norwegian patients with CAH and reduced fertility in the female patients. Significantly more patients received disability benefit. These results suggest that there is a need for improvement of the therapy, the general care and psychological follow-up in CAH.

Supplementary data

This is linked to the online version of the paper at http://dx.doi.org/10.1530/EJE-10-0284.

Declarations of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

Funding

This work was supported by the Faculty Division, Akershus University Hospital, University of Oslo and the Regional Health Authorities of Western Norway.

Acknowledgements

We thank our colleagues Kristian J Fougner, St Olavs University Hospital, Thomas Schreiner and Tore Juulsberg Berg, Oslo University Hospital, John Cooper, Stavanger University Hospital, Bjarne Mella, Østfold Hospital, Helge Kapelrud, ‘Imlandet’ Hospital and Synnøve Emblem Holte ‘Sørlandet’ Hospital for help with identifying the patients and Dag Hofoss, Akershus University Hospital for help with the statistics. Robert Bjerknes at The Department of Clinical Medicine is thanked for valuable advice during the planning of the study.

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Received 10 June 2010
Accepted 15 June 2010