Psychological and behavioural aspects in children and adolescents with congenital hypothyroidism diagnosed by neonatal screening: comparison between parents' and children's perceptions

Nicoletta Bisacchi, Milva Orquidea Bal, Laura Nardi, Ilaria Bettocchi, Graziana D’Addabbo, Veronica Conti, Sara Monti, Franco D’Alberton, Alessandro Cicognani and Alessandra Cassio

Department of Gynaecologic, Obstetric and Paediatric Sciences, S. Orsola-Malpighi Hospital, University of Bologna, Via Massarenti 11, 40138 Bologna, Italy

(Correspondence should be addressed to A Cassio; Email: alessandra.cassio@unibo.it)

Abstract

Objective: To compare the psychological adjustment and behaviour of congenital hypothyroidism (CH) children and their parents with a control group.

Study design: A cross-sectional study was carried out with 84 CH subjects diagnosed by neonatal screening (range 2.7–18.6 years), subdivided into four age groups: group 1 (2–5 years); group 2 (6–10 years); group 3 (11–13 years); and group 4 (14–18 years) and was compared with an age-matched control group. Patients were assessed using two questionnaires: Child Behaviour Checklist for parents and Youth Self-Report for children over 11 years of age.

Results: In groups 1, 3 and 4, total score (TS), internalising score (IS = problems within the self) and externalising score (ES = conflicts with other people) as reported by parents were not significantly different in CH patients and in controls. In group 2, parents of CH children showed values of TS ($P < 0.05$), IS ($P < 0.05$), ES ($P < 0.05$) and scores on other scales significantly higher than controls. In self-reports of groups 3 and 4, the behavioural scales were not significantly different in CH patients and in controls.

Conclusions: Paediatricians should be informed about the increased risk of the development of behavioural problems at primary school age in CH patients. At this age special attention should be paid to parental worries and anxiety. However, it can be reassuring for the patients and parents to know that the problems may be related to CH, and that they may spontaneously disappear.

Introduction

The introduction of neonatal screening for congenital hypothyroidism (CH) has successfully reduced severe neuropsychological effects in children with CH (1). However, previous studies have indicated that children who receive early treatment for CH have a normal intelligence quotient combined with attention problems (2, 3), motor deficits and defects in visuospatial skills, language and memory (4, 5). Several studies have correlated these problems with the severity of CH and others with the timing in starting treatment (6–11).

Although there are many studies about these cognitive and motor deficits in children with CH, there are fewer studies about the behavioural and emotional aspects of these patients. Some studies have evaluated the quality of life of young adults with CH diagnosed by neonatal screening but the results are controversial (12, 13). The limited literature has shown that children and adolescents with early-treated CH have more behavioural problems, particularly in the areas of introversion and social negativity, than normal controls (14).

In the literature, there is a growing interest in the effects of chronic diseases in the psychosocial and behavioural aspects of children and young adults. In fact, a chronic disease can represent a risk factor for such psychological disorders as anxiety, depression, affective problems and aggressive behaviour (15–17). CH is a chronic but latent condition: there are no clinical after-effects in the neonatal period and, although it can be treated, it cannot be cured. These aspects can influence the psychological development of children and their relationships with their parents (18).

On the other hand, communication of the diagnosis and the consecutive follow-up of these patients who need chronic treatment can influence the attitude of the parents. Therefore, it is important to take into
consideration the parents' attitudes towards their children's disease (19). However, the parents' point of view regarding their children's emotions and behaviour has not been thoroughly studied.

The objectives of this study were

i) to compare the psychological adjustment and behaviour of CH children and adolescents with a control group using self and parent questionnaires in order to evaluate the effects of a chronic disease that required lifelong treatment on these parameters;

ii) to analyse the possible influences of CH severity and initial treatment factors on the later psychological adjustment and behaviour of CH patients.

### Subjects and methods

#### Subjects

We examined 84 consecutive CH children and adolescents (33 males) with chronological age (CA) 9.6 ± 4.4 years (range: 2.7–18.6 years; age at starting therapy: 8–53 days) diagnosed in our centre by neonatal screening and their parents (73 mothers and 61 fathers). In all the patients, aetiological diagnosis of CH was obtained at recall on the basis of abnormal serum TSH and free thyroxine (FT4) values and by means of thyroid ultrasound and/or scintiscan. The gland morphology was as follows: 19 patients with athyreosis (22.6%), 44 with ectopic gland (52.3%) and 21 with gland in situ (25.1%).

The CH patients were classified into two subgroups: 'severe CH' and 'moderate/mild CH', according to bone maturation at birth evaluated by X-ray assessment of the distal femoral epiphysyeal ossification centre at the confirmation of diagnosis (severe CH: bony nucleus absent or its diameter < 3 mm; moderate/mild CH: bony nucleus diameter ≥ 3 mm) (20). This indicator of prenatal CH severity was preferred to neonatal FT4 cutoff level according to pre-therapy serum FT4 concentration (21), because it was considered a more reliable indicator of foetal thyroid hormone supply during the pregnancy (10, 11, 20). However, Table 1 shows that bone maturation at birth was related to FT4 serum levels at confirmation; therefore, they were both good parameters for the estimation of prenatal CH severity.

The subjects and their families were selected among a cohort of 148 patients with permanent CH diagnosed between January 1987 and December 2002 in our regional screening for CH programme: 44 patients out of 148 moved to other clinical centres and were lost to follow up. Among the remaining 104 patients who came to our paediatric centre for clinical and hormonal follow-up during 2005–2006, 84 were enrolled in the study. The inclusion criteria at the moment of the testing and filling in the questionnaires were as follows: written consent to the study by the parents and/or the patients, good compliance and adequacy of the levothyroxine (L-T4) treatment assayed by regular evaluations of TSH and FT4 and intelligence quotient (IQ) in the normal range (low average 80–89; average 90–109; high average 110–119; 4 patients with IQ < 80 and 7 with IQ > 119 were excluded).

The L-T4 dose was adjusted in order to maintain a euthyroid status defined as TSH serum levels ranging from 0.5 to 4.5 mU/l and FT4 normal values according to normal range values for our laboratory for the age.

To evaluate age-related differences, patients were subdivided into four age groups: group 1, infancy

### Table 1 Clinical and hormonal parameters at diagnosis in CH patients subdivided according to the age group and to the severity of CH (values are reported as median and ranges).

<table>
<thead>
<tr>
<th>CH severity</th>
<th>Number of patients</th>
<th>Age at confirmation of diagnosis (days)</th>
<th>Initial T4 dose (μg/kg per day)</th>
<th>TSH spot value (mIU/l)</th>
<th>TSH serum value at confirmation (mIU/l)</th>
<th>FT4 serum value at confirmation (pmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>6 (30.0%)</td>
<td>14 (8–29)</td>
<td>8.1 (6.3–10.6)</td>
<td>145 (50–300)</td>
<td>465 (170–1400)</td>
<td>3.5 (2.1–4.9)</td>
</tr>
<tr>
<td>Moderate/mild</td>
<td>14 (70.0%)</td>
<td>15 (9–31)</td>
<td>8.0 (6.0–10.1)</td>
<td>91 (23–200)</td>
<td>232 (25–980)</td>
<td>7.9 (3.1–16.2)</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
<td>15 (9–31)</td>
<td>8.1 (6.0–10.6)</td>
<td>108 (23–300)</td>
<td>348 (25–1400)</td>
<td>5.8 (2.1–16.2)</td>
</tr>
<tr>
<td>Group 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>9 (31.0%)</td>
<td>20 (12–47)</td>
<td>7.4 (4.4–10.1)</td>
<td>190 (80–275)</td>
<td>414 (158–965)</td>
<td>3.6 (1.9–5.4)</td>
</tr>
<tr>
<td>Moderate/mild</td>
<td>20 (69.0%)</td>
<td>17 (13–44)</td>
<td>6.5 (3.6–9.4)</td>
<td>93 (47–450)</td>
<td>169 (30–800)</td>
<td>8.9 (2.9–18.9)</td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
<td>17 (12–47)</td>
<td>7.0 (3.6–10.1)</td>
<td>129 (47–450)</td>
<td>204 (30–965)</td>
<td>6.8 (3.0–18.9)</td>
</tr>
<tr>
<td>Group 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>6 (37.5%)</td>
<td>18 (11–51)</td>
<td>9.0 (6.7–10.0)</td>
<td>210 (150–816)</td>
<td>251 (191–595)</td>
<td>2.1 (0.1–5.0)</td>
</tr>
<tr>
<td>Moderate/mild</td>
<td>10 (62.5%)</td>
<td>17 (12–67)</td>
<td>7.3 (5.0–8.9)</td>
<td>149 (50–374)</td>
<td>195 (50–370)</td>
<td>5.7 (3.3–14.0)</td>
</tr>
<tr>
<td>Total</td>
<td>16</td>
<td>17 (11–67)</td>
<td>7.7 (5.0–10.0)</td>
<td>172 (50–816)</td>
<td>198 (50–595)</td>
<td>4.3 (0.1–14.0)</td>
</tr>
<tr>
<td>Group 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>5 (26.3%)</td>
<td>20 (15–22)</td>
<td>5.5 (4.3–7.1)</td>
<td>293 (200–800)</td>
<td>274 (118–740)</td>
<td>1.3 (0.7–2.6)</td>
</tr>
<tr>
<td>Moderate/mild</td>
<td>14 (73.7%)</td>
<td>30 (16–53)</td>
<td>4.4 (2.6–7.0)</td>
<td>183 (71–392)</td>
<td>138 (65–430)</td>
<td>9.1 (2.6–15.3)</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>23 (15–53)</td>
<td>5.0 (2.6–7.1)</td>
<td>201 (71–800)</td>
<td>138 (65–740)</td>
<td>8.6 (0.7–15.3)</td>
</tr>
</tbody>
</table>

*P < 0.05 versus moderate/mild groups 1 and 2. †P < 0.05 versus severe groups 1, 2 and 3. ‡P < 0.001 versus total groups 1 and 2. §P < 0.01 versus moderate/mild groups 1, 2 and 3. ¶P < 0.01 versus total groups 3 and 4. aP < 0.05 versus total group 4.
(pre-school age, range 2–5 years, n = 20; CA 4.2 ± 0.9 years, parents, n = 38); group 2, latency (primary school age, range 6–10 years, n = 29; CA 7.9 ± 1.4 years, parents, n = 44); group 3, pre-adolescence (middle school age, range 11–13 years, n = 16; CA 12.1 ± 0.9 years, parents, n = 23); and group 4, adolescence (high school age, range 14–18 years, n = 19; CA 15.9 ± 1.3 years, parents, n = 29) (22).

CH subjects were compared with a control group of otherwise healthy children from different schools in Bologna, matched (1:1) by age, sex and parent’s socio-economic status (SES CH patients: 27.2 ± 10.7; SES controls: 27.9 ± 9.6).

The SES of the families was calculated according to the Hollingshead Socio-Economic Status (Hollingshead, Four Factor Index of Social Status, Department of Sociology, Yale University, New Haven, CT, USA, unpublished paper, 1975), taking into consideration the educational level and employment of parents.

Informed written consent from parents and/or subjects for participating in the study was obtained.

**Methods**

Behavioural and emotional aspects were analysed in our patients and their parents with a structured questionnaire. The parents of the patients of all the four groups and the patients of groups 3 and 4 filled in the questionnaire.

The parents of the subjects in group 1 were assessed using the Achenbach’s and Rescorla’s Child Behaviour Checklist (CBCL) for ages 1.5–5 (23), which was designed to be filled in by parents. The parents of groups 2, 3 and 4 were assessed using the Achenbach’s and Rescorla’s CBCL for ages 6–18 (24). Patients of groups 3 and 4 completed the Youth Self-Report (YSR) (25), which was designed for youths from 11 to 18 years of age.

The CBCL and YSR provide a standardised description of behavioural problems and competence in children. The CBCL and YSR are broken down into cross-informant syndrome and Diagnostic and Statistical manual of mental disorders (DSM)-oriented scales. The instruments generate a total problem score (TS), which is an index of psychopathological severity, an internalising score (IS), which is an index of problems within the self, and an externalising score (ES), which is an index of conflicts with others.

The scores provided by the instruments are sub-divided into three ranges: normal range scores (for all scales < 64; for TS, IS and ES < 60); borderline range scores (for all scales 65–69; for TS, IS and ES 60–63); and pathological range scores (for all scales ≥ 70; for TS, IS and ES ≥ 64).

The cross-informant syndrome scales from the CBCL 1.5–5 are emotionally reactive, anxious/depressed, somatic complaints, withdrawn, sleep problems, attention problems and aggressive behaviour. The five DSM-oriented scales are affective problems, anxiety problems, pervasive developmental problems, attention deficit/hyperactivity problems and oppositional defiant problems.

In CBCL 1.5–5, internalising symptoms include emotionally reactive, anxious/depressed, somatic complaints and withdrawn. Externalising symptoms include attention problems and aggressive behaviour.

The cross-informant syndrome scales from the CBCL 6–18 and YSR are anxious/depressed, withdrawn/depressed, somatic complaints, social problems, thought problems, attention problems, rule-breaking behaviour and aggressive behaviour. The six DSM-oriented scales are affective problems, anxiety problems, somatic problems, attention deficit/hyperactivity problems, oppositional defiant problems and conduct problems.

In the CBCL 6–18 and YSR, internalising symptoms include anxious/depressed, withdrawn/depressed and somatic complaints. Externalising symptoms include rule-breaking behaviour and aggressive behaviour.

In the CBCL 1.5–5, CBCL 6–18 and YSR, scales with higher scores suggest greater problems. The Italian versions of the CBCL 1.5–5, CBCL 6–18 and YSR were translated and validated in 2000 (26).

To assess the IQ in CH children, we used the Stanford–Binet Scale (30 months–5 years) (27) and the Wechsler Intelligence Scale for Children – Revised (6–18 years) (28).

**Statistical analysis**

All statistical analyses were performed using SPSS for Windows, version 13.0 (SPSS Inc., Chicago, IL, USA). Data distribution was analysed by Skewness and Kurtosis coefficients and the Kolmogorov–Smirnov test. For normally distributed data, the statistical significance was assessed using Student’s t-test and one-way ANOVA. Descriptive statistics are reported as means ± s.d., median and ranges or numbers (percentages). For non-normally distributed data, the Mann–Whitney U test and χ² test were used. Non-normally distributed data are expressed as medians and interquartile range. Correlations among the variables were determined by Spearman’s correlation test. The following parameters were taken into account for the correlations: TSH spot and serum values; l-T4 dose at confirmation, in the first years of treatment and at the time of the psychological interview; age at the onset of therapy; and IQ. A P value < 0.05 was considered statistically significant.

**Results**

Tables 1 and 2 show the clinical and hormonal features at diagnosis of CH and the IQ values at the moment of testing in CH patients and controls according to the age group and to the severity of CH. In group 4 patients, the diagnosis of CH dated back to the first period of our screening programme and the initial l-T4 dose was the
lowest of all the groups, particularly in severe CH patients. There were no significant differences in CA at diagnosis in severe CH patients of different age groups. The increase in serum TSH values from group 4 to group 1 was inconsistent with the decrease in TSH spot values according to the improvement of the age at diagnosis. Probably, this pattern was related to technical reasons and it should be defined as ‘a methodological artefact’. In fact, in the initial phases of the screening programme, our laboratory did not routinely report the real TSH serum concentration after dilution of the sample in all subjects with TSH serum levels above the maximum detectable value for the assay. This maximum detectable value was assumed as the true TSH serum value in laboratory reports and in our database. CH children showed IQ values not significantly different from controls: only in group 1, the IQ of CH children was lower than controls, but this difference was not significant (t=2.043; P=0.05).

Table 3 shows the differences in psychological adjustment between parents of all CH subjects. CH subjects of groups 3 and 4 and controls.

**Table 2** Intelligence quotient (IQ) in CH patients subdivided according to the age group and to the severity of CH and in controls at the moment of the study (values are reported as median and ranges).

<table>
<thead>
<tr>
<th>CH severity</th>
<th>Group 1 (n=20)</th>
<th>Controls (n=84)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age at testing</td>
<td>IQ</td>
</tr>
<tr>
<td></td>
<td>(years)</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>4.4 (2.8–6.6)</td>
<td>94 (80–117)</td>
</tr>
<tr>
<td>Moderate/mild</td>
<td>4.2 (2.7–5.8)</td>
<td>99 (87–115)</td>
</tr>
<tr>
<td>Total</td>
<td>4.3 (2.7–5.8)</td>
<td>97 (80–117)</td>
</tr>
<tr>
<td>Severe</td>
<td>7.4 (6.5–9.9)</td>
<td>106 (85–119)</td>
</tr>
<tr>
<td>Moderate/mild</td>
<td>8.0 (6.0–10.3)</td>
<td>109 (91–119)</td>
</tr>
<tr>
<td>Total</td>
<td>8.0 (6.0–10.3)</td>
<td>108 (85–119)</td>
</tr>
</tbody>
</table>

*P<0.05 versus total group 2. †P<0.01 versus total group 3. ‡P<0.01 versus moderate/mild group 2. §P<0.05 versus moderate/mild group 3.

**Group 1**

TS, IS and ES as reported by parents were not significantly different in CH patients (both evaluated as a whole and subdivided according to CH severity) and in controls. In the total group, parents of CH children reported significantly higher scores than controls in the Pervasive Developmental Problems scale (56.0 (12.0) vs 52.0 (5.0), P<0.05).

TS was in the borderline area or in the pathological area in 25.0% of CH patients and in 12.9% of controls, but this difference was not significant.

There were no significant differences between patients with severe or moderate/mild CH.

TSH spot values (r=0.45, P<0.05) and TSH serum values at confirmation (r=0.48, P<0.01) showed a significant positive correlation with IS. There was a significant positive correlation between mean t-T4 dose in the first year of treatment and TS (r=0.38, P<0.05), IS (r=0.46, P<0.01) and ES (r=0.37, P<0.05). There were no significant correlations between IQ of CH children, SES and psychological and behavioural scales.

**Group 2**

The parents of CH children showed values of TS (54.0 (14.5) vs 51.0 (11.0), P<0.05), IS (54.0 (17.5) vs 50.0 (16.5), P<0.05) and ES (54.0 (12.5) vs 49.0 (9.5), P<0.05) significantly higher than in controls. Regarding the cross-informant syndrome scales, scores on attention problems (57.0 (13.5) vs 53.0 (5.0), P<0.05) and rule-breaking behaviour (53.0 (7.5) vs 52.0 (5.0), P<0.05) were significantly higher than in controls. Regarding the DSM-oriented scales, scores on affective problems (56.0 (11.0) vs 52.0 (6.0), P<0.05), attention deficit/hyperactivity problems (56.0 (9.0) vs 51.0 (5.5), P<0.05), oppositional defiant problems (55.0 (8.0) vs 52.0 (5.0), P<0.01) and conduct problems (52.0 (7.0) vs 52.0 (2.0), P<0.05) were significantly higher than in controls.

Parents of severe CH patients reported significantly higher score than controls in TS (55.5 (17.3) vs 49.0 (15.0), P<0.05), IS (54.0 (16.0) vs 43.0 (23.0), P<0.01), and in scales anxious/depressed (54.0 (10.8) vs 50.0 (4.0), P<0.01), withdrawn/depressed (60.0 (12.0) vs 50.0 (6.0), P<0.05), somatic
complaints (53.0 (1.0) vs 50.0 (3.0), P<0.05), affective problems (54.0 (14.3) vs 52.0 (2.0), P<0.05), somatic problems (53.0 (7.0) vs 50.0 (0.0), P<0.05) and attention deficit/hyperactivity problems (55.0 (10.5) vs 50.0 (2.0), P<0.05). Parents of moderate/mild CH patients reported significantly higher score than controls in ES (54.5 (12.5) vs 49.0 (10.5), P<0.05), and in scales thought problems (54.0 (11.0) vs 51.0 (5.0), P<0.05), rule-breaking behaviour (53.0 (8.0) vs 51.5 (2.6), P<0.05), affective problems (56.0 (8.0) vs 52.0 (6.0), P<0.05) and oppositional defiant problems (55.0 (7.0) vs 51.0 (5.0), P<0.01).

TS was in the borderline area or in the pathological area in 29.73% of CH patients and in 13.21% of controls, but this difference was not significant.

There were no significant differences between patients with severe or moderate/mild CH.

No significant correlation was found between psychological and behavioural scales and hormonal values, l-T4 dose in the first year of treatment, IQ of CH children and SES.

**Group 3**

**Parents’ report** TS, IS and ES were not significantly different in parents of CH patients (both evaluated as a whole and subdivided according to CH severity) and in controls. In the total group, regarding the cross-informant syndrome scales, score on thought problem (54.0 (8.5) vs 51.0 (1.0), P<0.05) was significantly higher in CH patients than in controls. Regarding the DSM-oriented scales, score on somatic problem (56.5 (9.5) vs 56.0 (8.5), P<0.05) was significantly higher in CH patients than in controls.

There were no significant differences between patients with severe or moderate/mild CH.

There was a significant positive correlation between TSH spot value and TS (r = 0.54, P < 0.05) and ES (r = 0.49, P < 0.05). No other significant correlations between hormonal values, treatment, SES, IQ and behavioural scales were found.

**Self-report** The behavioural scales were not significantly different in CH patients and in controls.

There were no significant differences between patients with severe or moderate/mild CH.

**Group 4**

**Parents’ report** The behavioural scales were not significantly different in parents of CH patients (both evaluated as a whole and subdivided according to CH severity) and in controls.

TS, IS and ES were not significantly different in patients with severe or moderate/mild CH. The score in the anxious/depressed scale was significantly higher in severe CH than in moderate/mild CH patients (65.0 (16.0) vs 55.0 (10.0), P<0.05).

**Self-report** The behavioural scales were not significantly different in CH patients and in controls.

Adolescents with severe CH had significantly higher scores than adolescents with moderate/mild CH in IS (63.5 (17.0) vs 50.0 (14.0), P<0.05) and in scales

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**Table 3** Differences in psychological adjustment between congenital hypothyroidism subjects of groups 2, 3 and 4 and controls.

<table>
<thead>
<tr>
<th>CBCL 6–18 and YSR scales</th>
<th>Group 2 (age 6–10 years)</th>
<th>Group 3 (age 11–13 years)</th>
<th>Group 4 (age 14–18 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Parents (n=44)</td>
<td>Self</td>
<td>Parents (n=23)</td>
</tr>
<tr>
<td>Cross-informant syndrome scales</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxious/depressed</td>
<td>NS</td>
<td>–</td>
<td>NS</td>
</tr>
<tr>
<td>Withdrawn/depressed</td>
<td>NS</td>
<td>–</td>
<td>NS</td>
</tr>
<tr>
<td>Somatic complaints</td>
<td>NS</td>
<td>–</td>
<td>NS</td>
</tr>
<tr>
<td>Social problems</td>
<td>NS</td>
<td>–</td>
<td>NS</td>
</tr>
<tr>
<td>Thought problems</td>
<td>NS</td>
<td>–</td>
<td>P&lt;0.012</td>
</tr>
<tr>
<td>Attention problems</td>
<td>P&lt;0.019</td>
<td>–</td>
<td>NS</td>
</tr>
<tr>
<td>Rule-breaking behaviour</td>
<td>P&lt;0.049</td>
<td>–</td>
<td>NS</td>
</tr>
<tr>
<td>Aggressive behaviour</td>
<td>NS</td>
<td>–</td>
<td>NS</td>
</tr>
<tr>
<td>DSM-oriented scales</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Affective problems</td>
<td>P&lt;0.022</td>
<td>–</td>
<td>NS</td>
</tr>
<tr>
<td>Anxiety problems</td>
<td>NS</td>
<td>–</td>
<td>NS</td>
</tr>
<tr>
<td>Somatic problems</td>
<td>NS</td>
<td>–</td>
<td>P&lt;0.024</td>
</tr>
<tr>
<td>Attention deficit/hyperactivity problems</td>
<td>P&lt;0.027</td>
<td>–</td>
<td>NS</td>
</tr>
<tr>
<td>Oppositional defiant problems</td>
<td>P&lt;0.002</td>
<td>–</td>
<td>NS</td>
</tr>
<tr>
<td>Conduct problems</td>
<td>P&lt;0.046</td>
<td>–</td>
<td>NS</td>
</tr>
<tr>
<td>Total score (TS)</td>
<td>P&lt;0.022</td>
<td>–</td>
<td>NS</td>
</tr>
<tr>
<td>Internalising score (IS)</td>
<td>P&lt;0.030</td>
<td>–</td>
<td>NS</td>
</tr>
<tr>
<td>Externalising score (ES)</td>
<td>P&lt;0.026</td>
<td>–</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values in boldface are statistically significant (P<0.05). NS, not significant.
anxious/depressed (61.0 (17.8) vs 50.0 (5.5), P<0.05), affective problems (63.5 (15.5) vs 52.0 (5.0), P<0.05) and anxiety problems (62.0 (15.75) vs 52.0 (9.0), P<0.05).

No significant correlation was found between psychological and behavioural scales and hormonal values. t-T4 doses in the first year of treatment, SES and IQ.

Discussion

CH is a chronic disease, which influences patient’s life because of hospital visits, daily T4 administration and the necessary regular dose adjustments. T4 administration protects patients from the manifestation of the disease, but creates a state of dependence. Moreover, cognitive and motor deficits can affect the social life, self-esteem, emotional, behavioural and psychological functioning of CH patients (12). A chronic disease represents a risk factor for psychological and behavioural problems in patients and their families. Psychological disorders could be attributable to children’s neurobiological deficits and to difficult family relationships, as congenital diseases can generate a sense of guilt in parents. Parents know that CH could cause cognitive and motor deficits later in life: therefore, CH is a threat for parents, a condition that will sooner or later reveal that their child is different from other children (18).

To our knowledge, this is the first study in literature, which considers the state of psychological adjustment in different age groups and takes into account both the parents’ and the children’s point of view. Moreover, we have to point out that, according to the inclusion criteria, our CH patients were enrolled in the study only if their IQ was above the normal range limit to stress the influence of psychological adjustment and behaviour parameters also in CH patients with normal intellectual outcome. This selection may partly explain our results in disagreement with Simoneau-Roy et al. (11), who found subtle but relevant differences in intellectual performances between CH patients and controls and between severe and moderate/mild forms of CH. However, at least in our cohort of selected CH patients, the age at the beginning of treatment and the initial T4 dose did not seem to be the critical factors for the later intellectual outcome (Tables 1 and 2).

According to the data from recent literature (14, 18), parents of children in the latency age reported the most behavioural problems. There may be different reasons to explain this increase in behavioural problems in parents’ opinion: it is likely that at this age, starting school emphasises the problem of comparison with healthy peers in terms of scholastic performance requiring cognitive competence. This comparison worries parents who highlight and amplify every small difficulty their children have. In fact, parents are anxious about attention problems, rule-breaking behaviour, affective problems, attention deficit/hyperactivity problems, oppositional defiant problems and conduct problems. Moreover, the learning of reading and writing skills could highlight specific deficits such as learning disabilities. Previous studies have found an association between CH and attention problems (2, 3), motor deficits, defects in visuospatial skills, language, memory (4, 5) and the development of specific learning disabilities (29). These behavioural and emotional problems do not seem to be related to CH severity, in fact, they are experienced almost in the same way by parents of children with both severe and moderate/mild CH.

In this primary school age it may be advisable to make the teachers aware of a child’s CH. However, in our opinion, they should also be prepared by specific training concerning the new perspectives of the disease and its complications. In this way the teachers will be able to plan correct educational approaches.

In the first years of secondary school, CH patients’ parents, compared with controls’ parents, reported only thought and somatic problems. In this period, preadolescents often use their bodies to express themselves and this normal tendency could be read by parents in relation to CH. However, these problems were not reported by adolescents’ parents. We hypothesise that normal psychophysical development in children and adolescents is likely to ease parental anxieties and gradually eliminate their perception of problems. However, all CH patients and their parents had, since the first months of life, yearly psychological sessions. In these sessions, psychological problems and cognitive competence were assessed in the children and a chance to express themselves and their worries were offered to the parents. This assessment allowed us to understand whether in some cases a psychological support to the parents was needed.

The findings that emerged from the comparison between children’s reports did not overlap those that emerged from the comparison of parents’ report. Self-report questionnaires of CH pre-adolescents and adolescents show that they have no psychological and behavioural problems and they see themselves as healthy peers.

The results of this study seem to have an important clinical implication. In our centre, the communication of diagnosis is regarded as the main procedure, which needs careful management, but parental concerns towards the consequences of the disease were still present in the years following this communication. Therefore, although a correct communication of the CH diagnosis remains a crucial step, further follow-up visits and counselling for the parents are needed until school age.

This study has several limitations. The sample size, although substantial for the overall analyses, was small for subgroup comparisons according to the age and to the severity of the disease. The reliability of the results
may be partly affected and the lack of differences between some subgroups may have represented statistical limitations rather than a true lack of effect. The significant correlations between behavioural scales and some determinants of CH severity (i.e. neonatal TSH levels and L-T4 dose) may underline the possible influence of this parameter on the psychological adjustment. However, we found significant differences in affective mood disorders only in group 4: adolescents with severe CH were more anxious, depressed and had more affective problems than subjects with moderate/mild CH. Recent reports stressed the importance of better and earlier treatment to eliminate the neurocognitive gap between moderate and severe CH (30–32). I n our adolescent patients of group 4, the diagnosis of CH dated back to the first period of our screening programme and the initial dose of L-T4, in particular in severe CH patients, was significantly lower than in the other age groups of patients. However, a longitudinal design and follow-up data with a greater number of patients are needed to understand better the differences reported earlier in the different age groups to draw definitive conclusions.

The cross-sectional design of the study does not allow us to confirm the transient or permanent character of the behavioural problems experienced by parents of group 2. Certainly, our professional approach to CH patients has changed over time and we cannot exclude that this phenomenon should be associated at least in part with some different variables related to the disease severity or to therapeutic approach at diagnosis. However, we would like to emphasise that all patients were diagnosed and followed up in the same centre with sufficiently homogeneous criteria.

The mean IQ of the subjects in group 1 was significantly lower than in those of groups 2 and 3. These results are partially in disagreement with previous studies (30–32) and the explanation appears questionable at present. It is probable that the cross-sectional design of the study and the comparison between different IQ scales could play a role. However, we have to point out that the comparison of IQs between patients and their matched controls showed no significant differences.

In summary, this study underlines that, although CH children have a normal psychophysical development, the assessment of psychological and behavioural aspects in these children and in their parents represents an important part of the evaluation during the follow-up. In particular, paediatricians should be informed about the increased risk of the development of behavioural problems in CH patients at primary school age. At this age, special attention should be paid to parental worries and anxiety. However, it can be reassuring for the patients and parents to know that the problems may be related to CH, and that they may spontaneously disappear.

**Declaration of interest**

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

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