Abstract

Objective: Sub-clinical hypothyroidism (SCH) is a common disorder. People with this condition may have symptoms which could affect their perception of health. Therefore, the perceived health status of people with SCH was assessed and compared with population-matched norms.

Design: A prospective cross-sectional survey.

Methods: Seventy-one adults with SCH, age range 18–64 years were studied. Perceived health status was measured by the Short Form-36 (SF-36) version 2 questionnaire, which has been validated in a UK population setting. The SF-36 has eight scales measuring physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional and mental health. Their SF-36 scores were compared with UK normative data after matching for age and sex and are reported as z-scores.

Results: Scores of all eight SF-36 scales were significantly lower in people with SCH compared with the normative population. A negative score (compared with zero of the normative population) indicates worse health status. The most significantly impaired aspects of health status were vitality and role limitations due to physical problems (role physical scale) with z-scores (95% confidence intervals) of \(-1.01 (\pm 0.74 \text{ to } -1.29)\) and \(-0.73 (\pm 0.43 \text{ to } -1.04)\) respectively. Thyroid autoimmunity did not influence the results.

Conclusion: Perceived health status is significantly impaired in people with SCH when compared with UK normative population scores. This needs to be taken into consideration by clinicians when managing patients with this disease.

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using the SF-36v2 and compared it with UK normative population scores.

Patients and methods

Patients

One hundred consecutive community living adults with SCH were recruited over a 5-month period from primary care practices after identification from the laboratory database. Inclusion criteria were people with SCH over 18 years of age. Exclusion criteria were people with ischaemic heart disease, cerebrovascular disease, neurological disease, diabetes mellitus, chronic renal impairment, known psychological illnesses such as schizophrenia, bipolar affective disorder and depression, previous history of thyroid disease or previous thyroxine therapy, asthma, and pregnancy, so as to reduce the effect of other co-morbid conditions on perceived health status. All participants except one had had at least three abnormal thyroid function tests (TSH >4 mU/l with normal fT4 levels) consistent with SCH, their thyroid status having been checked previously due to hypothyroid symptoms, or SCH was an incidental finding. All participants gave written informed consent and the Gateshead ethics committee approved the study. Only 71 patients (mean age (± S.D.) 48.7 years (± 9.67), range 23–64; 15 males) in the 18 to 64 year age group were considered for comparison with the UK SF-36v2 normative data, as normative data are not available for older adults. The mean TSH concentration was 6.6±2.5 mU/l, range 4.1–16 (normal reference range: 0.4–4.0 mU/l) and the mean fT4 concentration was 13.9±1.9 pmol/l, range 10.3–19 (normal reference range: 9–25 pmol/l). The frequency of other chronic diseases was: hypertension 9.5%, hypercholesterolaemia 1.3% and arthritis (osteoarthritis, gout or rheumatoid arthritis) 21.9%. Results of two participants found missing fT4. This, in turn, was calibrated using equilibrium dialysis. Thyroid autoimmunity was determined by the quantitative measurement of anti-thyroid peroxidase autoantibodies (anti-TPO) by ELISA (ORGENTEC Diagnostika GmbH, Mainz, Germany) with a cut-off value of 50 IU/ml.

Biochemical tests

The tests were performed at the Queen Elizabeth Hospital Biochemistry Laboratory. Serum was collected using standard sampling tubes containing separating gel. TSH and fT4 were measured by an electro-chemiluminescence immunoassay ‘ECLIA’ using Roche Elecsys E170 immunoassay analysers (Roche Diagnostics, UK). The Elecsys TSH test had been calibrated against the 2nd IRP WHO Reference Standard 80/558. The Elecsys fT4 test had been calibrated against Enzymuntest fT4. This, in turn, was calibrated using equilibrium dialysis. Thyroid autoimmunity was determined by the quantitative measurement of anti-thyroid peroxidase autoantibodies (anti-TPO) by ELISA (ORGENTEC Diagnostika GmbH, Mainz, Germany) with a cut-off value of 50 IU/ml.

Statistical analyses

Data were analysed by one researcher (SR). Means±S.D. were used to report descriptive data and 95% confidence intervals (95% CI) were used to report the difference in the means between the study participants and the normative population. A 95% CI is significant if the interval range does not cross zero, signifying that the two populations are different (21). Student’s unpaired t-test was used to compare the subgroup means and Bonferroni’s post hoc multiple comparison test for observed means was carried out to ensure that multiple t-tests did not show a significant difference where none exists, i.e. to reduce type I error (22).
Z-scores were also used to report transformed scores as discussed previously. A mean z-score < 0.2 was considered clinically non-significant, between 0.2 and 0.5 as a small difference, between 0.5 and 0.8 as a moderate difference and > 0.8 as a large difference (23, 24).

Correlation analysis (Spearman’s rho for non-parametric data or Pearson’s r for parametric data) was used to assess the relationship between each SF-36 scale measured and biochemical and demographic parameters. Internal consistency reliability - that is, the extent to which there is a correlation between items on a scale – was assessed by Cronbach’s alpha, an inter-item correlation statistic, with a value range of 0–1 (25). Levels of >0.9 are usually agreed to signify excellent internal consistency reliability (26). A P value of <0.05 was taken as statistically significant. SPSS version 11.0 was utilised for computing the statistics (SPSS Inc., Chicago, IL, USA).

Results

In comparison with a large UK population reference group, scores on all eight scales of the SF36v2 were found to be significantly reduced (Table 1). The difference was attenuated but still significant when people with SCH and other chronic diseases (e.g. arthritis, hypertension and hypercholesterolaemia) were excluded from the analyses (n = 24). Z-scores for all 71 participants studied were significantly lower than the normative data for all scales of the SF-36 but only the vitality (VT) scale showed a large difference, that is > 0.8 (Fig. 1).

The rest of the z-scores showed either moderate (role physical (RP), general health (GH), social functioning (SF) and role emotional (RE)) or small (physical functioning (PF), bodily pain (BP) and mental health (MH)) differences. When analysed separately for men (n = 15) and women (n = 56), the results of the z-score analysis showed that women tended to have lower scores for all scales compared with men, although not significantly so (Fig. 2). Men had significantly lower z-scores in all scales except PF when compared with men from the UK norms (Fig. 2) whereas women had significantly lower scores on all scales.

Health status scores did not differ in people with thyroid autoimmunity, as determined by the presence of antitPO antibodies (n = 39), although the two groups were well matched for age, sex and biochemical thyroid function tests. None of the scales of the SF-36v2 correlated with either TSH or fT4 levels. As expected, TSH values correlated significantly with fT4 (r = −0.35, P = 0.002), which was statistically significant after Bonferroni correction requiring a P value of 0.006 (0.05/8). Comparison of absolute scores of older people with SCH (aged 65–80 years) (n = 27) with the younger group studied (n = 71) showed that the older group had significantly impaired health status only for the PF, RP and BP scales except PF when compared with men from the UK norms (Fig. 2) whereas women had significantly lower scores on all scales.

Health status in subclinical hypothyroidism

Figure 1 SF-36v2 scale scores of patients with SCH (mean with 95% confidence interval) compared with age- and sex-matched controls in a UK cohort (zero line). Note: a negative z-score indicates lower health status in the SCH group compared with normative data. PF, physical functioning; RP, role physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role emotional; MH, mental health.

Table 1 Differences in absolute SF-36 scores in patients with SCH compared with age- and sex-matched normative data.

<table>
<thead>
<tr>
<th>SCH subjects (mean±s.d.; n = 71)</th>
<th>UK normative population (mean±s.d.; n = 8660)</th>
<th>Difference in means (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PF 76.05±24.98</td>
<td>87.99±19.65</td>
<td>11.94 (7.4–16.48)</td>
</tr>
<tr>
<td>RP 68.32±29.74</td>
<td>87.17±22.01</td>
<td>18.85 (13.76–23.94)</td>
</tr>
<tr>
<td>BP 68.63±27.02</td>
<td>78.8±23.01</td>
<td>10.17 (4.86–15.48)</td>
</tr>
<tr>
<td>GH 60.07±22.26</td>
<td>71.06±20.43</td>
<td>10.99 (6.28–15.7)</td>
</tr>
<tr>
<td>V 37.15±23.81</td>
<td>58.04±19.69</td>
<td>20.89 (16.37–25.41)</td>
</tr>
<tr>
<td>SF 69.52±27.47</td>
<td>82.77±23.24</td>
<td>13.25 (7.89–18.61)</td>
</tr>
<tr>
<td>RE 72.48±26.84</td>
<td>85.75±21.18</td>
<td>13.27 (8.38–18.16)</td>
</tr>
<tr>
<td>MH 63.35±18.85</td>
<td>71.92±18.15</td>
<td>8.57 (4.39–12.75)</td>
</tr>
</tbody>
</table>

SF-36 score range: 0 to 100 (poor to excellent health status). PF, physical functioning; RP, role physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role emotional; MH, mental health.
scales (difference in means (95% CI): 17.72 (6.4–29.04), 13.93 (1.32–26.54) and 14.93 (2.97–26.89) respectively). Cronbach’s alpha coefficient ranged from 0.91 to 0.93 signifying excellent internal consistency reliability for all eight SF-36 scales in this sample of patients with SCH.

Discussion

Perceived health status is more than just the presence or absence of disease or symptoms and encompasses social, physical and emotional dimensions. Clinicians do not routinely assess patients’ perceptions of their health status, but it is increasingly being argued that the patient’s perspective is as valid as that of the clinician in evaluation of a medical condition and its outcomes (27). We have shown for the first time that patients with SCH perceive significant impairment of their health status, as measured by all eight scales of the SF-36v2. The normative data in this study for comparison of scores for all scales comprised a random sample from the general population and not a disease-free population. Hence it is probable that some of these individuals had thyroid disease and therefore the results obtained in this study may well be an underestimation of the true value. This is all the more likely since 36.6% of the normative population reported chronic long-standing illness (patients with chronic diseases are more likely to respond to a postal health survey than disease-free individuals), whereas patients with such conditions, apart from hypertension, arthritis and hypercholesterolaemia, were excluded in the present study.

Bianchi and colleagues recently reported that there were no differences in perceived health status (as measured by the SF-36 and the Nottingham Health Profile instruments) between their Italian patients with SCH, and age- and sex-matched Italian population norms (20). The results reported in this paper are different from their observations. This may be due to the different population and normative data used in the analysis as well as the fact that the comparison sample in the present study was younger owing to the lack of normative data for people older than 64 years in the UK.

Limitations of this study are that patients were not identified from a screening programme and were recruited from primary care practices. Thus patients with presence of symptoms at the higher end of the scale and/or with other co-morbidities were more likely to have been included. However, the results obtained still remain significantly different from the normative scores even when data were analysed after excluding people with other chronic conditions. It is quite possible that some conditions such as hypertension and hypercholesterolaemia are ‘silent’ and hence affect health status the least (28). Also, it would seem that men tend not to have any impairment of physical functioning as compared with normative scores for men of the same age. We have no direct explanation for this and further research is required. Also, older people (> 64 years) with SCH have significantly lower scores on the physical scales (PF, RP and BP) when compared with younger people. This was not an unexpected finding as others have obtained significant age gradients in some SF-36 subscales (29), but the lack of normative data for comparison with this older group is disappointing, especially since SCH is more prevalent in older people (30). There is some recent evidence that SCH may not adversely affect the very old in terms of disability, cognitive function and survival (31).

Although it is clear from this study that people with SCH have impaired perceived health status, it is yet to be clarified whether normalizing serum TSH level would improve it. Previous studies have had conflicting results in improving symptoms and health-related quality of life (4, 7, 32–34). It has also been shown that people on adequate doses of l-thyroxine exhibit improved psychological well-being (35).

In conclusion, we have shown that perceived health status is significantly impaired in people presenting with SCH and this should be considered when managing this condition.

Acknowledgements

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