

# Subclinical hypothyroidism: psychiatric disorders and symptoms

## Hipotireoidismo subclínico: transtornos e sintomas psiquiátricos

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### Abstract

**Objective:** To evaluate the prevalence of psychiatric disorders and symptoms in patients with subclinical hypothyroidism. **Method:** Ninety-four outpatients with at least two elevated serum thyrotrophin levels ( $> 4 \mu\text{U/ml}$ ) and normal  $\text{FT}_4$ , and 43 euthyroid outpatients, both groups from HUCFF-UFRJ, were evaluated. Psychiatric diagnosis was based on the Structured Clinical Interview Diagnostic for the DSM-IV axis I (SCID-I/DSM-IV), the psychopathological symptoms on Hamilton anxiety and depression scales, and the Beck Inventory. **Results:** Our data showed an increased prevalence of psychiatric disorders in the subclinical hypothyroidism patients when compared to the euthyroid group (45.7% vs 25.6%;  $p = 0.025$ ), mood disorders being the most frequent. The prevalence of depressive symptoms based on Beck's Scale among subclinical hypothyroidism patients was about 2.3 times higher than among euthyroid ones (45.6% vs 20.9%,  $p = 0.006$ ). Anxiety symptoms were also more frequent among subclinical hypothyroidism patients (87.0% vs 60.5%,  $p < 0.001$ ), mainly clinical anxiety (44.6% vs 23.3%;  $p = 0.001$ ). **Conclusion:** Our results showed a significant association of subclinical hypothyroidism with psychiatric disorders and an increased frequency of subsyndromic depression and anxiety symptoms in subclinical hypothyroidism in relation to the euthyroid group.

**Descriptors:** Hypothyroidism; Anxiety disorders; Mood disorders; Symptoms; Prevalence

### Resumo

**Objetivo:** Avaliar a prevalência de sintomas e alterações psiquiátricas em pacientes com hipotireoidismo subclínico. **Método:** Foram estudados 94 pacientes ambulatoriais com pelo menos duas dosagens plasmáticas elevadas de tireotropina ( $> 4 \mu\text{U/ml}$ ) e com  $\text{T}_4$  livre normal e, 43 eutireoidianos, ambos os grupos do HUCFF-UFRJ. Para diagnóstico psiquiátrico foi utilizada a entrevista clínica estruturada do eixo I (SCID-I/DSM-IV) e, para sintomas psicopatológicos, as escalas de ansiedade e depressão de Hamilton (HAM-A e HAM-D) e inventário de Beck. **Resultados:** Encontramos uma prevalência aumentada de transtornos psiquiátricos no hipotireoidismo subclínico em comparação ao grupo eutireoidiano (45,7% vs 25,6%;  $p = 0,025$ ), sendo o transtorno do humor o de maior frequência. Sintomas de depressão no grupo com hipotireoidismo subclínico foram cerca de 2,3 vezes mais frequentes que entre os eutireoidianos (45,6% vs 20,9%;  $p = 0,006$ ) quando o instrumento utilizado foi a escala de Beck. Da mesma forma, sintomas de ansiedade também foram mais frequentes no hipotireoidismo subclínico (87,0% vs 60,5%;  $p < 0,001$ ), principalmente ansiedade clínica (44,6% vs 23,3%;  $p = 0,001$ ). **Conclusão:** Os resultados indicaram uma associação do hipotireoidismo subclínico com os transtornos psiquiátricos, além de uma frequência aumentada de sintomas de depressão e ansiedade subsindrômicos em relação ao grupo eutireoidiano.

**Descritores:** Hipotireoidismo; Transtornos da ansiedade; Transtornos do humor; Sintomas; Prevalência

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## Introduction

The expression subclinical hypothyroidism (SH) is applied to individuals with supranormal serum TSH levels and normal free fractions of thyroid hormones. It may be inappropriate because of occasional presence of signs and symptoms that may be attributable to hormonal deficiency and most commonly of neuropsychiatric and muscular origin.<sup>1</sup> The most frequently cited symptoms are memory deficit, despondency, symptoms of depression and anxiety.<sup>2</sup> A few authors, however, could not find an increased prevalence of these manifestations,<sup>3-6</sup> others found cognitive alterations,<sup>7-8</sup> and there is even one study that found better scores in patient with SH.<sup>9</sup> We found one study showing an increased prevalence of previous depressive episodes in patients with SH<sup>3</sup> but could not find specific studies of psychiatric disorder (PD) in patients with SH. Placidi et al. looked at 93 patients with different thyroid dysfunctions and found 63% with a psychiatric diagnosis.<sup>10</sup> In Brazil, a multicentric study of morbidity in the general population found 18% prevalence of anxiety disorder and 3-10% of depression but no correlation with thyroid function was made.<sup>11</sup>

In spite of the growing interest in the relation between thyroid dysfunction and neuropsychiatric alterations, no consensus has been reached. We investigated the prevalence of psychiatric disorders and the presence of subsyndromic symptoms of depression and anxiety in patients with SH.

## Method

This is a cross-sectional study that evaluated patients with SH as they were diagnosed sequentially at the Endocrine Clinic of the Hospital Universitário Clementino Fraga Filho of the Universidade Federal do Rio de Janeiro (HUCFF-UFRJ) during a 3-year period.

SH was defined as a serum TSH level above the upper reference limit (4  $\mu$ U/ml) with a serum free T<sub>4</sub> level in the normal range (0.8-1.8 ng/dl). Results had to be confirmed with at least one month interval between blood collections.

We included outpatients of both sexes, 18 years old or older, with at least 3 years of schooling (mandatory in the case of self-administered tests). We excluded patients with severe or chronic illnesses and who were using drugs that might interfere with thyroid function or hormonal determination. Patients with serum TSH levels above 20  $\mu$ U/ml were also excluded, even if they presented normal T<sub>4</sub> level.

This study was approved by the Research Ethics Committee (n. 012/01) of the HUCFF-UFRJ and all participants signed an informed consent form.

A group of individuals of the same sex and schooling level, free of thyroid disease and negative for anti thyroperoxidase antibodies (anti-TPO) comprised the euthyroid group for comparison. These outpatients were selected through advertisement in the same hospital environment and submitted to the same selection criteria.

All patients went through clinical examination and their previous medical history was investigated regarding psychiatric aspects. Blood was collected at the same time for hormonal determinations and anti-TPO antibodies. Psychiatric tests were administered during a 30-day period.

A prevalence of 45% of PD in the patients was assumed based on the literature and a prevalence ratio of 2.25 in relation to the euthyroid group. Considering *alpha* and *beta* errors of 5% and 20%, respectively, we calculated a sample size of 96 SH patients and 48 euthyroid individuals. We used the EPI-INFO program, version 6.04.

## 1. Instruments

Psychiatric evaluation was performed by a single investigator through a structured clinical interview for axis I (SCID-I) psychiatric diagnosis based on the Diagnostic and Statistical Manual for Mental Disorders, 4<sup>th</sup> edition (DSM-IV).

For evaluation of the intensity of psychopathological symptoms, we used Hamilton Depression and Anxiety Scales (HAM-D and HAM-A), and Beck's Depression Inventory (BDI).

## 2. Statistical analysis

For comparison of continuous variables, Student's t-test and Mann-Whitney's test were used, respectively, for those with normal and asymmetrical distribution. The latter was also employed for analyses involving comparison of ordinal variables between both groups. For proportion comparison between the groups, the chi-square and Fisher's exact test were used, and also calculations of chance ratios and the respective 95% confidence intervals. Significance was established at the 5% level ( $p < 0.05$ ).

## Results

Ninety-four patients (89 females) with SH and 43 euthyroid individuals (40 females) were studied. The mean ages ( $49.1 \pm 10.3$  and  $44.8 \pm 9.6$ , respectively) were significantly different at a  $p = 0.024$  level but this was not considered of clinical relevance. Schooling level had a similar distribution between the groups.

A great prevalence of PD was found in the SH group when compared to the euthyroid group, 45.7% vs 25.6%, respectively ( $p = 0.025$ ), mood disorders being the most frequent.

Twenty-six percent of the SH patients had a high HAM-D score ( $> 7$ ). Depressive symptoms were about 1.5 times more frequent in the SH patients than in the euthyroid group with no statistical significance. Regarding HAM-A, anxiety symptoms (score  $> 5$ ) were present in 87% of patients with SH against 60.5% of the euthyroid individuals ( $p < 0.001$ ), a prevalence about 1.4 times greater. Among subjects with anxiety symptoms, 44.6% of SH patients presented clinical anxiety versus 23.3% of the euthyroid individuals ( $p = 0.001$ ).

According to Beck's Inventory, most euthyroid individuals (79.1%) see themselves as free of depressive symptoms vs. 54.4% of the SH subjects. Symptoms of depression were 2.3 times more prevalent in SH patients than in euthyroid individuals (45.6 vs 20.9%,  $p = 0.006$ ) and symptomatic SH patients (68.3%) could be classified as having mild symptoms of depression.

## Discussion

The selection of patients in a hospital environment might explain a higher prevalence of psychiatric symptoms in general. Nevertheless, the prevalence was higher (45.7 vs 25.6%,  $p = 0.025$ ) than that of the euthyroid group selected in the same circumstances. PD are more prevalent in thyroid disorders according to Placidi et al., who used DSM-III-R and found panic disorder as the most frequent disorder, followed by generalized anxiety disorder and major depressive disorder, single episode. No correlation was made with types of thyroid dysfunction.<sup>10</sup>

Through the administration of Hamilton scales, we found differences between SH patients and the euthyroid group in both the depression and anxiety scores, but such a difference was only significant in the latter. Two other studies using these

scales<sup>3,5</sup> could not find any difference between the groups. Baldini et al., studying patients with goiter, found higher mean scores than we did in our sample, albeit not different from controls.<sup>4</sup> Our scores in the HAM-A scale are, in turn, higher than those found in the Baldini et al. study.

Differently from our results, Jorde et al. did not find any differences between SH subjects and controls when applying Beck's scores.<sup>9</sup> They considered SH patients with a serum TSH in a more restricted interval (between 3.5 and 10  $\mu$ U/ml) and selected the patients from a general population sample.

When comparing these few published studies with our study, it is possible to conclude that most divergences in the results may be a consequence of different methodologies, specifically sample composition, inclusion and exclusion criteria, and standardization of evaluation instruments. It is important to be cautious when generalizing the results of our study, given the nature of the sampling process, which was based on a convenience sample.

### Conclusion

Our results support the evidence of an increased prevalence of depression and anxiety symptoms in subclinical hypothyroidism. Definitive proof of these symptoms resolution through specific therapy may be provided by intervention trials.

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