Depression and anxiety among hyperthyroid female patients and impact of treatment

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Abstract

Background: The aim of the present study was to compare the presence of psychiatric disorders in people with hyperthyroidism and euthyroid patients attending the Endocrinology Outpatient Department at the Shri Maharaja Hari Singh Hospital in Kashmir, India. Seventy-five patients with hyperthyroidism and an equal number of euthyroid patients participated in the study. Participants were selected using stratified random sampling. All patients were female. There was no significant difference between the two groups in terms of demographic features. Hormonal screening was performed by immunoassay and haemagglutination method. For the mental health assessment, the Mini-International Neuropsychiatric Interview (MINI), Hamilton Depression Rating Scale [HAM-D], and Hamilton Anxiety Rating Scale [HAM-A] were used.

Results: There was a higher prevalence of psychiatric disorders among the hyperthyroidism group (60% versus 34.7%). In particular, there was a higher prevalence of major depressive disorder, suicidality, generalised anxiety disorder, panic attacks, and agoraphobia. In some cases, the prevalence of a psychiatric disorder diminished after endocrinological treatment.

Conclusions: Screening patients with hyperthyroid disorders for psychiatric symptoms and disorders, and providing timely care when necessary, can go a long way in improving the quality of life of this population. It is imperative to establish routine screening and timely care of mental health symptoms and disorders in patients with hyperthyroidism.

Keywords: Hyperthyroidism, Mental health, Liaison psychiatry, Anxiety, Depression

Background

Hyperthyroidism is one of the most common thyroid disorders. Hyperthyroidism can often manifest with symptoms consistent with mental illnesses; plus, it is not uncommon for people with hyperthyroidism to meet psychiatric disorders' diagnostic criteria [1, 2]. At the same time, people with hyperthyroidism will likely present symptoms such as tension and other autonomic symptoms that could resemble a mental illness [3]. It is important, then, to pay attention to the presence of these symptoms and assess and address them promptly and adequately, as they can have a clear impact on the person's well-being.

Various psychiatric disorders have been associated with hyperthyroidism. Over 150 years ago, Basedow had already described a manic psychosis illness in a patient with exophthalmic goitre [4]. Psychotic disorders, however, are an uncommon presentation of hyperthyroidism [4–6]. Symptoms of anxiety and depression, on the other hand, are more common [7, 8], as well as increased scores on depression and anxiety self-rating scales [9].
Suicidality also seems to be more common in people with hyperthyroidism [7], which further emphasises the importance of acknowledging mental health symptoms and disorders in this population.

Despite the reported high prevalence of psychiatric symptoms and disorders among people with hyperthyroidism, no previous study in India has explored this issue. To have a better understanding of this comorbidity could improve the ways in which these patients are assessed and supported. Therefore, the present study was set out to explore the prevalence of psychiatric disorders in patients with hyperthyroidism attending an Endocrine Outpatient Clinic in the North of India.

Methods
The present is a cross-sectional, comparative study including case and control arms, with follow-up on the case arm, and compared the presence of various psychiatric disorders among people with hyperthyroidism, with and without treatment, and people without hyperthyroidism. The study was conducted between March 2017 and March 2019.

Participants
The study targeted people over 15 years of age with hyperthyroidism who attended the Endocrinology Outpatient Department at the Shri Maharaja Hari Singh Hospital in North India. Participants were selected using stratified random sampling, choosing every alternate female patient with hyperthyroidism. The control group was people over 15 years of age without any present or past thyroid disease and family history of thyroid disease. The case group also included hyperthyroid patients assessed after 2 months of treatment. Thyroid status was checked using a thyroid function test (TFT) that included an estimation of serum triiodothyronine (T3), tetra-iodothyronine (T4), and thyroid-stimulating hormone (TSH) and clinical profile of the patient were monitored to see the effect of endocrinological medications in the follow-up of hyperthyroid patients. Sampling of participants was conducted for a period of 6 months. The assessment of patients before and after treatment was done and those who did not improve were referred for psychiatric treatment. Exclusion criteria were the presence of pregnancy or a history of pregnancy in the last 6 months, and the use of steroids or other drugs known to interfere with thyroid function. The control group was taken from another Outpatient Department of the same hospital and was subjected to the same laboratory investigation for confirmation.

Data collection
Data collection included demographic information, such as age, sex, residence, and economic status.

Endocrine evaluation
Endocrinologists evaluated all study and control subjects. This evaluation included a detailed haemogram, erythrocyte sedimentation rate (ESR), and serum biochemistry in the form of blood glucose, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase, and cholesterol. All participants also had a thyroid function test (TFT) that included an estimation of serum triiodothyronine (T3), tetra-iodothyronine (T4), and thyroid-stimulating hormone (TSH). The diagnosis of hyperthyroidism was made based on clinical criteria and confirmed by the elevated serum T3 and/or T4 and suppressed TSH (< 0.1 IU/mL). Participants with laboratory confirmation of hyperthyroidism had done a technetium scan of the thyroid gland using 99mTc-pertechnate. Graves’ disease (GD) diagnosis was based on diffuse goitre with increased radioactive iodine uptake (RAIU) at 24 h.

Different treatments were given for different thyroid conditions with different diagnoses. Patients with hyperthyroidism were treated by surgery, antithyroid drug (ATD) medication, or radioactive iodine (RAI). Local traditions, severity of the disease, sex, and age are some of the factors that influenced the type of treatment chosen.

Mental status evaluation
The psychiatric history was taken using a pretested semi-structured interview. The interviewer was blind to the participants’ endocrinological diagnosis. These interviews were conducted using the mood and anxiety modules of the Mini-International Neuropsychiatric Interview (MINI) [10] and the diagnostic criteria for depression and anxiety of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition [11]. In addition, all participants were evaluated using both observer-rated and self-rated scales. A psychiatrist applied Hamilton Depression Rating Scale (HAM-D) and Hamilton Anxiety Rating Scale (HAM-A) [12, 13].

Hormones of the hypothalamic–pituitary–thyroid axis
Venous blood was drawn for the measurement of serum thyrotropin (TSH), thyroxine (T4), and total T3 (T3T). All hormones were estimated by commercially available chemiluminescence assay (CLA); antithyroid peroxidase antibody (anti-TPO) was estimated by immunofluorescence technique (ELISA).
Data analysis
Data were keyed into Microsoft Excel 2016 and after cleaning exported to Statistical Package for the Social Science® (SPSS Inc., IL, USA) for further analysis. Numbers and percentages were used to present categorical data. Mean (± standard deviation) was used for normally distributed continuous data. The significance of differences between the two groups was examined by Student’s t-test or Mann-Whitney U test (as appropriate). The χ² test of independence was used for qualitative variables (Yates’ correction and Fisher’s exact test were used wherever appropriate). Correlations and association between various variables were studied using the Pearson and/or Spearman test. A probability level of P <.05 was taken as significant.

Results
In total, 75 patients with hyperthyroidism and an equal number of euthyroid patients participated in this study (Tables 1 and 2). The age of the subjects (cases and controls) ranged from 20 to 70 years with a mean of 33.37±7.61. All the studied subjects were females. Overall, 60% (n = 45) of the participants with hyperthyroidism showed signs of a psychiatric disorder, against 34.7% (n = 26 patients) of participants in the control group (Table 3).

About 10.7% of the participants with hyperthyroidism met the criteria for major depressive disorder, versus 6.7% of the control group participants. Of the total of participants with hyperthyroidism, 4% presented suicidality, a number that dropped to almost 0% after endocrinological treatment (see Table 4). No significant difference was noticed in the presence of depression after treatment, with results remaining consistent at 10.7%. As for the Hamilton Depression Scale (HAM-D), scores for the hyperthyroidism and euthyroid groups were 21 and 16, respectively, with a P value of < 0.001. Participating in the hyperthyroidism group were treated by surgery, antithyroid drug (ATD) medication, or radioactive iodine (RAI). The presence of psychiatric disorders was reduced in some cases after endocrinological treatment. No case of psychosis or bipolar affective disorder (BAD) were reported in the study.

Discussion
In the present study, we compared the presence of psychiatric disorders among people with hyperthyroidism and euthyroid patients. Overall, the study found that 60% of the participants with hyperthyroidism showed signs of a psychiatric disorder, against 34.7% of participants in the control group. Patients with hyperthyroidism were treated by surgery, antithyroid drug (ATD) medication, or radioactive iodine (RAI). The presence of psychiatric disorders was reduced in some cases after endocrinological treatment. No case of psychosis or bipolar affective disorder (BAD) were reported in the study.

Table 1 Clinical and laboratory variables among cases and controls (n = 150)

| Variable                  | Hyperthyroid group (n = 75) | Euthyroid group (n = 75) | P value |
|---------------------------|-----------------------------|--------------------------|---------|
| Age (years)               | 33.37±7.61*                 | 33.37±7.61               | 1.0     |
| T3 (ng/ml)                | 3.49±1.05                   | 2.38±1.54                | <0.001  |
| T4 (mcg/dl)               | 16.89±2.24                  | 7.02±1.51                | <0.001  |
| TSH (mIU/l)               | 0.9±0.08                    | 2.88±1.66                | <0.001  |
| HAM-A scores              | 27.1±6.14                   | 15.5±6.11                | <0.001  |
| HAM-D scores              | 21±5.66                     | 16±6.1                   | <0.001  |
| Duration of symptoms (months) | 8.12±0.17               |                          |         |
| Underlying aetiology of hyperthyroidism |                  |                          |         |
| Graves’ disease           | 30 (40%)                    |                          |         |
| Toxic nodular hyperthyroidism | 9 (12%)                   |                          |         |
| Indeterminate aetiology   | 36 (48%)                    |                          |         |

* Values are expressed as mean ± SD unless specified otherwise
There are various studies reporting a higher prevalence of anxiety disorders in people with hyperthyroidism [2, 14, 15]. The present study found higher rates of certain anxiety disorders in people with hyperthyroidism when compared with euthyroid patients. These were generalised anxiety disorder, panic attack, and agoraphobia. A study conducted by Simon and colleagues [14] also found a higher prevalence of generalised anxiety disorder and panic disorder among patients with thyroid dysfunction, and as the present study, they found a minimal correlation with social phobia. Endocrinological treatment reduced the number of participants with agoraphobia almost in half, and it also reduced the number of participants with panic attack, although at a lower level. It did not, however, reduced the number of participants with generalised anxiety disorder in a statistically

Table 2 Reported symptoms and signs of hyperthyroidism

| Symptoms of hyperthyroidism | Weight loss (56%) | Weight gain (8%) | Heat intolerance (60%) | Palpitations (57%) | Tremor (54%) | Increased bowel movement (24%) | Neck enlargement (22%) | Shortness of breath (10%) | Eyes symptoms (12%) | Psychological symptoms (44%) |
|----------------------------|-------------------|------------------|------------------------|-------------------|-------------|--------------------------------|----------------------|-----------------------|-----------------------|--------------------------|
| Reported signs of hyperthyroidism | Signs of atrial fibrillation (4%) | Thyroid eye disease (TED) in a patient with Graves' disease | Tremor (40%) | No sign of TED (NOSPECS 0) (36%) | Palpable goitre (62%) | Mild TED (NOSPECS 1) (20%) | Moderate TED (NOSPECS 2–3) (40%) | Severe TED (NOSPECS ≥4) (3.3%) |

Table 3 Proportion of psychiatric disorders among patients with hyperthyroidism

| Variable | Group | No psychiatric illness | Psychiatric disorder | Chi-square | P-value |
|----------|-------|------------------------|----------------------|------------|---------|
| Any psychiatric disorder | Euthyroid | 49 (65.3%) | 26 (34.7%) | 9.65 | 0.003 |
| | Hyperthyroid | 30 (40%) | 45 (60%) | 0.38 | 0.56 |
| MDD | Euthyroid | 70 (93.3%) | 5 (6.7%) | 0 | 1.0 |
| | Hyperthyroid | 67 (89.3%) | 8 (10.7%) | 0.21 | 0.65 |
| Dysthymia | Euthyroid | 73 (97.3%) | 2 (2.7%) | 0 | 1.0 |
| | Hyperthyroid | 73 (97.3%) | 2 (2.7%) | 0.56 | 1.0 |
| Suicidality | Euthyroid | 73 (97.3%) | 2 (2.7%) | 0.21 | 0.65 |
| | Hyperthyroid | 72 (96%) | 3 (4%) | 0.65 | 1.0 |
| Agoraphobia | Euthyroid | 74 (98.7%) | 1 (1.3%) | 0 | 1.0 |
| | Hyperthyroid | 73 (97.3%) | 2 (2.7%) | 0.56 | 1.0 |
| Panic attack | Euthyroid | 71 (94.7%) | 4 (5.3%) | 6.31 | 0.02 |
| | Hyperthyroid | 61 (81.3%) | 14 (18.7%) | 14 | 1.0 |
| Alcohol use | Euthyroid | 74 (98.7%) | 1 (1.3%) | 0 | 1.0 |
| | Hyperthyroid | 74 (98.7%) | 1 (1.3%) | 0 | 1.0 |
| OC spectrum | Euthyroid | 73 (97.3%) | 2 (2.7%) | 0.21 | 1.0 |
| | Hyperthyroid | 72 (96%) | 3 (4%) | 0.65 | 1.0 |
| Social phobia | Euthyroid | 75 (100%) | 0 (0%) | 0 | 1.0 |
| | Hyperthyroid | 75 (100%) | 0 (0%) | 0 | 1.0 |
| Premenstrual dd | Euthyroid | 72 (96%) | 3 (4%) | 0.65 | 1.0 |
| | Hyperthyroid | 73 (97.3%) | 2 (2.7%) | 0.56 | 1.0 |
| GAD | Euthyroid | 70 (93.3%) | 5 (6.7%) | 1.85 | 0.28 |
| | Hyperthyroid | 65 (86.7%) | 10 (13.3%) | 0.85 | 1.0 |
significant number. The study also found an overall higher score in the HAM-A scale among these participants, a result that echoes the literature [9], as well as a slightly higher prevalence of obsessive–compulsive spectrum disorders (4% versus 2.7%).

Previous authors have also suggested a potential association between hyperthyroidism and depression [2, 8, 15, 16]. The present study also found a higher rate of major depressive disorder in participants with hyperthyroidism (10.7% vs 6.7%), as well as a higher rate of suicidality (4% vs 2.7%). Also, as previously reported by Demet and colleagues [9], the study found higher scores for the HAM-D in participants with hyperthyroidism. After endocrinological treatment, the number of participants with hyperthyroidism showing suicidality dropped down to almost 0%. Radanović-Grgrurić and colleagues had previously discussed the importance of timely diagnosis of depression among people with thyroid dysfunction, a point further supported by the present study [17].

Sub-clinical and overt hyperthyroidism can be associated with various mental health symptoms, although the casual relationship can be sometimes unclear [3]. Moreover, some of the characteristic symptoms of hyperthyroidism may resemble the clinical presentation of a mental health disorder. The relationship between the clinical presentation of hyperthyroidism and anxiety, as well as its precipitating role in the development of an anxiety disorder, is somewhat clear [3]; however, the relationship between it and depression is less certain [3]. Despite their potential causal relationship, it is important to assess and address both, the thyroid dysfunction and mental health symptoms. Previous authors have also pointed out that endocrinological treatment may be accompanied by an improvement of the mental health symptoms [1, 18]. Still, it could be necessary to provide further pharmacological and psychosocial support when this is not the case [1].

**Conclusions**

Screening patients with hyperthyroid disorders for psychiatric symptoms and disorders, and providing timely care when necessary, can go a long way in improving the quality of life of this population. Still, the present study suggests the usefulness of a longitudinal study exploring the temporal correlation between psychiatric symptoms and hyperthyroidism, as it could shed further light into this topic. Moreover, further epidemiological studies are necessary to gauge the degree of the problem. Therefore, the implementation of a routine screening for mental illness would prove further useful in facilitating a better

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**Table 4** Status of treatment and its association with psychiatric symptoms among cases (n = 75)

| Psychiatric symptoms                  | Treatment status | No psychiatric illness | Psychiatric disorder | Chi-square | P-value |
|---------------------------------------|------------------|------------------------|----------------------|------------|---------|
| Overall psychiatric disorders         | Under treatment  | 8 (72.73%)            | 3 (27.27%)           | 5.75       | .02     |
|                                       | No               | 22 (34.4%)            | 42 (65.6%)           |            |         |
| Dysthymia                             | Under treatment  | 11 (100%)             | 0 (0%)               | 1.54       | .59     |
|                                       | No               | 56 (87.5%)            | 8 (12.5%)            |            |         |
| Suicidality                           | Under treatment  | 11 (100%)             | 0 (0%)               | 0.54       | .0      |
|                                       | No               | 61 (95.3%)            | 3 (4.7%)             |            |         |
| Agoraphobia                           | Under treatment  | 10 (90.9%)            | 1 (1.6%)             | 2.05       | .27     |
|                                       | No               | 63 (98.4%)            | 1 (1.6%)             |            |         |
| Panic attack                          | Under treatment  | 10 (90.9%)            | 1 (9.1%)             | 0.78       | .68     |
|                                       | No               | 51 (79.7%)            | 13 (20.3%)           |            |         |
| Alcohol abuse                         | Under treatment  | 11 (100%)             | 0 (0%)               | 0.17       | .0      |
|                                       | No               | 63 (98.4%)            | 1.6 (%)              |            |         |
| OC spectrum                           | Under treatment  | 11 (100%)             | 0 (0%)               | 0.54       | .0      |
|                                       | No               | 61 (95.3%)            | 3 (4.7%)             |            |         |
| Social phobia                         | Under treatment  | 11 (100%)             | 0                    | –          | –       |
|                                       | No               | 64 (100%)             | 0                    |            |         |
| Premenstrual dysphoric disorder       | Under treatment  | 11 (100%)             | 0 (0%)               | 0.35       | .0      |
|                                       | No               | 62 (96.9%)            | 2 (3.1%)             |            |         |
| GAD                                   | Under treatment  | 9 (81.8%)             | 2 (18.2%)            | 0.26       | .61     |
|                                       | No               | 56 (87.5%)            | 8 (12.5%)            |            |         |
understanding of the relationship between thyroid dysfunction and mental health disorders.

**Limitation of study**
In addition to the small sample size, all findings of laboratory and clinical profile of the case group mentioned were not used in any correlation in the study although of importance.

**Abbreviations**
- MINI: Mini-International Neuropsychiatric Interview
- HAM-D: Hamilton Depression Rating Scale
- HAM-A: Hamilton Anxiety Rating Scale
- TFT: Thyroid function test
- T3: Serum triiodothyronine
- T4: Tetra-iodothyronine
- TSH: Thyroid-stimulating hormone

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**Authors' contributions**
SS, JA, and MAW all contributed in conceiving the presented idea, developed the methodology and data collection, drafted the article, and helped shape the research, analysis, and manuscript. SS obtained the ethical approval, performed computations, verified the analytical methods and data tabulation, and contributed to manuscript writing, editing, and critical revision. IU, RR, and SW contributed to editing and critical revision. All authors have read and approved the manuscript.

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**Availability of data and materials**
All data generated or analysed during this study are included in this published article.

**Declarations**

**Ethics approval and consent to participate**
All participants included in the study provided informed consent, and the Ethical Committee of Government Medical College, Srinagar, Kashmir, India (GMC-3217 March 2017), approved the study. Proper written informed consent was obtained from study participants.

**Consent for publication**
Not applicable

**Competing interests**
The authors declare that they have no competing interests.

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**References**
1. Bunevicius R, Prange AJ Jr (2010) Thyroid disease and mental disorders: cause and effect or only comorbidity? Curr Opin Psychiatry 23(4):363–368. https://doi.org/10.1097/YCO.0b013e3283387b50
2. Greer S, Parsons V (1968) Schizophrenia-like psychosis in thyroid crisis. Br J Psychiatry 114(516):1357–1362. https://doi.org/10.1192/bjp.114.516.1357
3. Gagliardi JP, Clay GL (2002) Treatment of thyrotoxicosis-induced psychosis. Psychopharmacology (Berl) 167:13–17
4. Brownlie B, Rae A, Walse J, Wells J (2000) Psychoses associated with thyrototoxic-thyrotoxic psychosis.’ A report of 18 cases, with statistical analysis of incidence. Eur J Endocrinol 142:438–444
5. Zader SJ, Williams E, Buryk MA (2019) Mental health conditions and hyperthyroidism. Pediatrics 144(5):e20182874. https://doi.org/10.1542/peds.2018-2874
6. Bunevicius R, Velickene D, Prange AJ Jr (2005) Mood and anxiety disorders in women with treated hyperthyroidism and ophthalmopathy caused by Graves’ disease. Gen Hosp Psychiatry 27(2):133–139. https://doi.org/10.1016/j.genhosppsych.2004.10.002
7. Demet MM, Özen A, Deveci A, Boyvada S, Adıgüzel H, Aydemir O (2002) Depression and anxiety in hyperthyroidism. Arch Med Res 33(6):552–556. https://doi.org/10.1016/S0188-4409(02)00410-1
8. Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, Hergueta T, Baker R, Dunbar GC (1998) The Mini-International Neuropsychiatric Interview (MINI): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry 59:22–32
9. American Psychiatric Association (1994) Diagnostic and statistical manual of mental disorders: DSM-IV, 4th edn. American Psychiatric Association, Washington (DC)
10. Hamilton MA (1960) Rating scale for depression. J Neurol Neurosurg Psychiatry 23(1):56–62. https://doi.org/10.1136/jnnp.23.1.56
11. Hamilton M (1959) The assessment of anxiety states by rating. Br J Med Psychol 32(1):50–55. https://doi.org/10.1111/j.2044-8341.1959.tb00467.x
12. Simon NM, Blacker D, Koroby NB, Sharma SG, Worthington JJ, Otto MW, Pollack MH (2002) Hypothyroidism and hyperthyroidism in anxiety disorders revisited: new data and literature review. J Affect Disord 69(1-3):209–217. https://doi.org/10.1016/S0165-0327(01)00378-0
13. Bové KB, Watt T, Vogel A, Hegedüs L, Bjørner JB, Groenvold M, Bonnema SJ, Rasmussen ÅK, Feldt-Rasmussen U (2014) Anxiety and depression are more prevalent in patients with Graves’ disease than in patients with nodular goitre. Eur J Endocrinol 169(3):173–178. https://doi.org/10.1530/EJE-13-0321
14. Ittermann T, Völzke H, Baumeister SE, Appel K, Grabe HJ (2015) Diagnosed thyroid disorders are associated with depression and anxiety. Soc Psychiatry Psychiatr Epidemiol 50(9):1417–1425. https://doi.org/10.1007/s00127-015-1435-0
15. Radanović-Grujić L, Filaković P, Baričić J, Mandić N, Kamer I, Smoje J (2003) Depression in patients with thyroid dysfunction. Eur J Psychiatry 17:133–144
16. Gülseren S, Gulseren L, Hekimsoy Z, Cetinay P, Ozen C, Tokatlioglu B (2006) Depression, anxiety, health-related quality of life, and disability in patients with overt and subclinical thyroid dysfunction. Arch Med Res 37(1):133–139. https://doi.org/10.1016/j.arcmed.2005.05.008

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