



CODEN [USA]: IAJPBB

ISSN: 2349-7750

**INDO AMERICAN JOURNAL OF  
PHARMACEUTICAL SCIENCES**<http://doi.org/10.5281/zenodo.1194803>Available online at: <http://www.iajps.com>

Research Article

**EVALUATION OF FREQUENCY AND SEVERITY OF  
ANXIETY AND MOOD DISORDERS  
AMONG PATIENTS WITH GRAVES' DISEASE.****Muhammad Iqbal<sup>1</sup>, Atif Ahmed<sup>2</sup>, Sohail Baig<sup>3</sup>, Hamid Nawaz Ali Memon<sup>4</sup> and  
Aatir H. Rajput<sup>5</sup>**<sup>1</sup>Department of Medicine - Liaquat University of Medical & Health Sciences, Jamshoro<sup>2</sup>Department of Medicine – Bilawal Medical College, Jamshoro<sup>3</sup>Department of Medicine - Liaquat University Hospital, Hyderabad<sup>4</sup>Zulekha Hospital – United Arab Emirates<sup>5</sup>Department of Psychiatry – Liaqua University of Medical & health Sciences, Jamshoro**Abstract:**

**Objective:** Graves' disease has been associated with an increased psychiatric morbidity. It is unclarified whether this relates to Graves' disease or chronic disease per se. The aim of our study was to evaluate the frequency and severity of anxiety and mood disorders in patients with Graves' disease.

**Methodology:** This cross-sectional analysis was conducted upon a total of 341 patients presenting to the medical out-patient department of Liaquat University Hospital, Hyderabad. Data was collected using a structured, interview based questionnaire comprising of 2 factions. One derived from the DAS-42 scale for anxiety and the standard Profile of Mood States (POMS) for mood disorders, after taking written informed consent. The data obtained was analyzed using MS. Excel 2017 and SPSS v. 21.0.

**Results:** Significantly greater frequency of social anxiety disorder, generalized anxiety disorder, total mood and anxiety disorders, as well as major depression and higher symptom scores on the POMS and DAS-42 scale, was found in the subjects. The difference in severity however, when gauged against published controls, was found non-significant.

**Conclusion:** The results confirm, without any doubt, that frequency of anxiety and mood disorders among patients of Graves' disease is greater than any found in other chronic disease (as per published evidence).

**Keywords:** Graves' disease, Social Anxiety, General Anxiety Disorder, Major Depression and Cghronic Illness.

**Corresponding author:****Dr. Muhammad Iqbal,**

Associate Professor of Medicine,

Liaquat University, Jamshoro

Email: [muhammadiqbalshah22@gmail.com](mailto:muhammadiqbalshah22@gmail.com)

Phone: +92-300-3034963

QR code



Please cite this article in press as Muhammad Iqbal et al., *Evaluation of Frequency and Severity of Anxiety and Mood Disorders among Patients with Graves' disease*, Indo Am. J. P. Sci, 2018; 05(02).

**INTRODUCTION:**

Graves' disease, an expression of an autoimmune process, is the most common cause of hyperthyroidism. [1] It is associated with various mental signs and symptoms, including anxiety, depression, mania and cognitive dysfunction and with discrete psychiatric disorders, including (but not limited to) mood disorders [2]. Increased prevalence of mood and anxiety disorders, diagnosed using psychiatric diagnostic criteria [3–5], as well as increased scores on depression and anxiety self-rating scales [4,6–8], has been consistently reported in untreated hyperthyroid patients.

Mood scores tended to be similar in patients with subclinical and overt hyperthyroidism [9]. Trzepacz et al. [10] found no associations between scores of anxiety or depression and serum concentrations of thyroid hormones in Graves' disease. In a similar way, no strict relationship was found between severity of symptoms of hyperthyroidism and degree of elevation in thyroid hormone concentration [11]. The effects of treatment of hyperthyroidism on mental symptoms also have been examined. In the short term, treatment was found to produce a parallel decrease in endocrine symptoms and in psychiatric symptoms [6, 12].

When prolonged treatment normalizes thyroid function some psychiatric symptoms and somatic complaints may persist [13–15]. Nevertheless, a recent study showed that remitted Graves' disease patients, in contrast to relapsed Graves' disease patients, showed no significant differences from healthy controls on standard psychometric tests [16].

These studies of treatment effects have been concerned only with the measurement of mood

ratings and not with the prevalence of discrete psychiatric entities. The studies cited above have taken patients with hyperthyroidism as their index populations. Many other studies have taken at their index populations patients with psychiatric disorders. Although strictly outside the purview of the present study, two such studies seem relevant. In patients with anxiety disorders, a history of hyperthyroidism was found unusually often [17, 18].

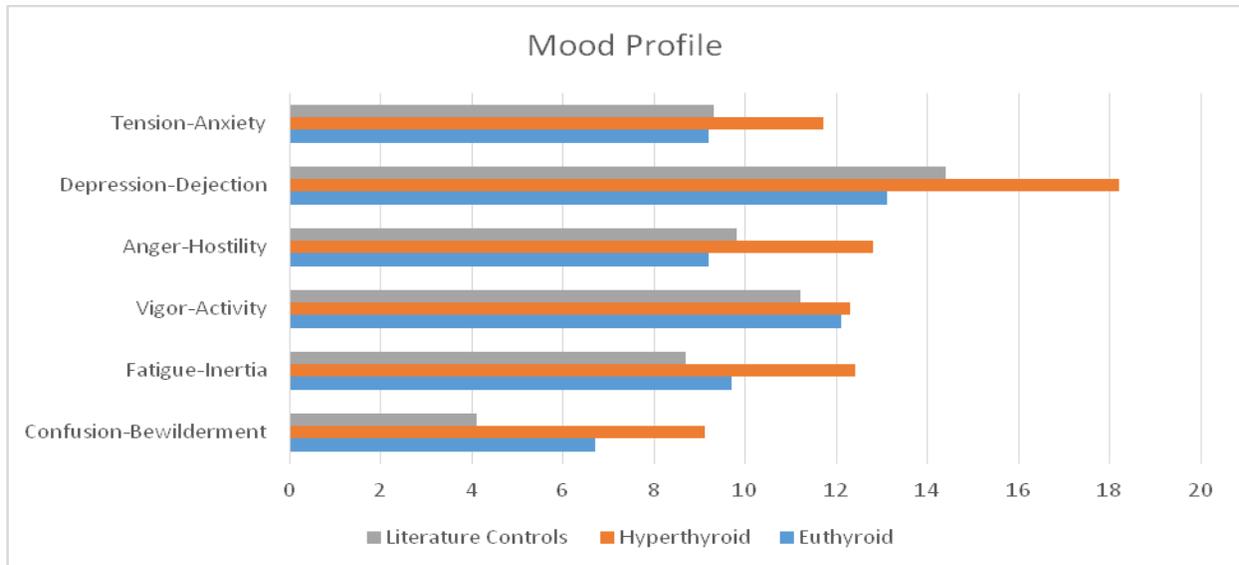
The aim of our study was to evaluate the frequency and severity of anxiety and mood disorders in untreated patients with Graves' disease presenting at our study setting.

**METHODOLOGY:**

This cross-sectional analysis was conducted upon a total of 341 patients presenting to the medical out-patient department of Liaquat University Hospital, Hyderabad. Data was collected using a structured, interview based questionnaire comprising of 2 factions. One derived from the DAS-42 scale for anxiety and the standard Profile of Mood States (POMS) for mood disorders, after taking written informed consent. The data obtained was analyzed using MS. Excel 2017 and SPSS v. 21.0.

**RESULTS:**

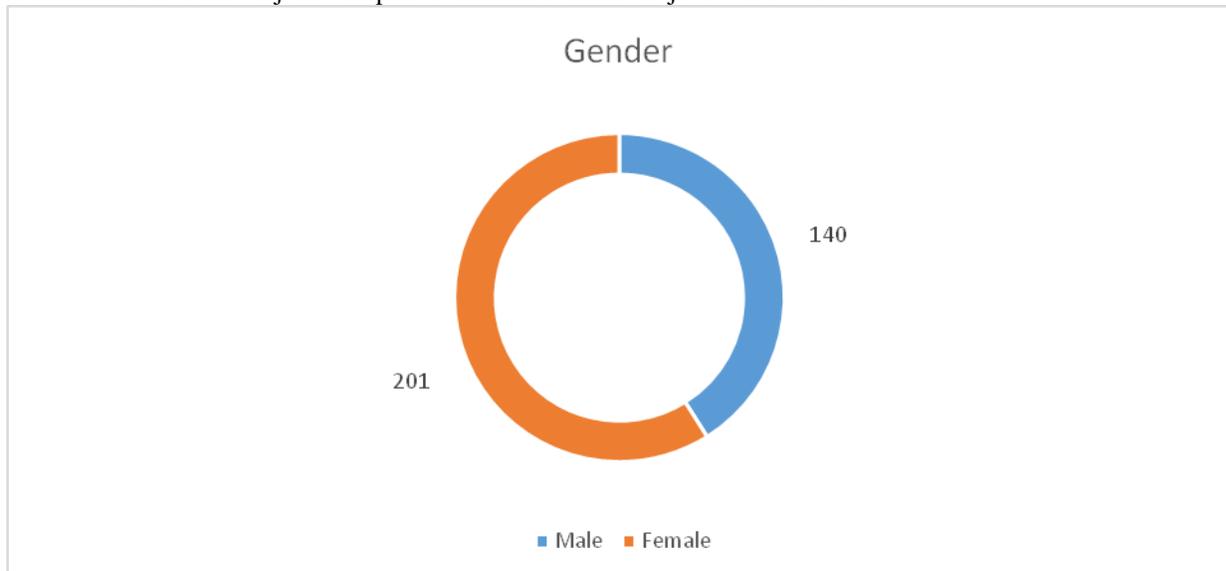
Significantly greater frequency of social anxiety disorder, generalized anxiety disorder, total mood and anxiety disorders, as well as major depression and higher symptom scores on the POMS and DAS-42 scale, was found in the subjects. The difference in severity however, when gauged against published controls, was found non-significant.



The thyroid status of the subjects was as tabulated below:

	<i>Euthyroidism</i>	<i>Hyperthyroidism</i>	<i>All</i>	<i>Normal Range</i>
<i>Thyroid Stimulating Hormone (mU/L)</i>	1.84	0.07	1.22	0.17 – 4
<i>Free T4 (pmol/L)</i>	17.8	34.7	26.22	11.5 – 23

A main faction of the subjects comprised of females. Male subjects were scarce.



### DISCUSSION:

In Graves' disease, presumably as a result of some failure of autoimmune regulation, the TSH receptor, a normal element of the HPT axis, becomes an antigen. Its excessive stimulation in thyroid gland by TSH receptor antibodies results in hyperthyroidism. The TSH receptor is also found in extrathyroidal tissues

such as orbital muscle and brain. Stimulation of the TSH receptor in brain increases type II deiodinase activity, which is responsible for local triiodothyronine production. Cortex and hippocampus are rich in TSH receptors and play an important role in mood regulation and cognition.

Thus, the excessive production of triiodothyronine in these regions may occur in Graves' disease and may contribute to its typical mental symptoms. A full understanding, however, of the causes of mental disability in Graves' disease awaits a full description of the effects on neural tissue of thyroid hormones as well as of the underlying autoimmune process.

The results of this study demonstrate a high prevalence of mood and anxiety disorders in subjects as assessed by our research tools. Mental disorders among women with Graves' disease were significantly more frequent than among men. It should be noted, however, that prevalence of mental disorder among women with gynecologic disease was also quite high. This observation is consistent with the findings of other studies [19, 20].

Hyperthyroid study subjects demonstrated a significantly higher prevalence of current mood episodes and specific anxiety disorders in comparison with the euthyroid patients. These findings are consistent with reports concerning psychiatric morbidity in studies, such as that conducted by Kathol and Delahunt. [3] These studies, like many others, however, of their era, failed to employ standard psychiatric diagnostic criteria.

Despite these limitations, there was general agreement that hyperthyroid patients tend to show a high rate of anxiety. The later studies, using standard psychiatric diagnostic criteria, confirmed earlier findings. Trzepacz *et al.* [4] studied 13 patients with untreated Graves' disease, using the Schedule for Affective Disorders and Schizophrenia and applying Research Diagnostic Criteria. They found that every patient met Research Diagnostic Criteria for at least one psychiatric diagnosis, most often anxiety. Placidi *et al.* [5] studied 93 hyperthyroid patients, using a version of the Structured Clinical Interview for DSM, Revised Third Edition criteria (SCID). They found that one third of patients suffered from panic disorder and nearly as many from generalized anxiety disorder. Brownlie *et al.* [21] studied 18 patients who, over the course of 20 years, had been considered to be thyrotoxic and, at some time, psychotic.

Scores on only one mood factor, the subscale of confusion and bewilderment, were significantly higher in hyperthyroid subjects with treated Graves' disease. This finding corresponds to data from Whybrow *et al.* [6], showing prominent confusion in patients with hyperthyroidism. Scores of other subscales of the POMS may have been blunted by the drugs in use; Propranolol, benzodiazepines and antidepressants. [13, 15]

#### CONCLUSION:

The results confirm, without any doubt, that frequency of anxiety and mood disorders among patients of Graves' disease is greater than any found in other chronic disease (as per published evidence).

#### REFERENCES:

1. Vanderpump MPJ, Tunbridge WMG. The epidemiology of thyroid diseases. In: Braverman LE, Utiger RD, editors. *Werner & Ingbar's thyroid: a fundamental and clinical text*. 8th ed. Philadelphia: Lippincott Williams & Wilkins; 2000. p. 465–73.
2. Whybrow PC, Bauer M. Behavioral and psychiatric aspects of thyrotoxicosis. In: Braverman LE, Utiger RD, editors. *Werner & Ingbar's thyroid: a fundamental and clinical text*. 8th ed. Philadelphia: Lippincott Williams & Wilkins; 2000. p. 673–8.
3. Kathol RG, Delahunt JW. The relationship of anxiety and depression to symptoms of hyperthyroidism using operational criteria. *Gen Hosp Psychiatry* 1986;8:23–8.
4. Trzepacz PT, McCue M, Klein I, Levey GS, Greenhouse J. A psychiatric and neuropsychological study of patients with untreated Graves' disease. *Gen Hosp Psychiatry* 1988;10:49–55.
5. Placidi GPA, Boldrini M, Patronelli A, *et al.* Prevalence of psychiatric disorders in thyroid diseased patients. *Neuropsychobiology* 1998;38: 222–5.
6. Whybrow PC, Prange Jr AJ, Treadway CR. Mental changes accompanying thyroid gland dysfunction. *Arch Gen Psychiatry* 1969;20:48–63.
7. MacCrimmon DJ, Wallace JE, Goldberg WM, Streiner DL. Emotional disturbance and cognitive deficits in hyperthyroidism. *Psychosom Med* 1979;41:331–40.
8. Demet MM, Ozmen B, Deveci A, *et al.* Depression and anxiety in hyperthyroidism. *Arch Med Res* 2002;33:552–6.
9. Schlote B, Nowotny B, Schaaf L, *et al.* Subclinical hyperthyroidism: physical and mental state of patients. *Eur Arch Psychiatry Clin Neurosci* 1992;241:357–64.
10. Trzepacz PT, Klein I, Roberts M, Greenhouse J, Levey GS. Graves' disease: an analysis of thyroid hormone levels and hyperthyroid signs and symptoms. *Am J Med* 1989;87:558–61.
11. Larsen PR. Thyroid–pituitary interaction: feedback regulation of thyrotropin secretion by thyroid hormones. *N Engl J Med* 1982;306: 23–32.
12. Trzepacz PT, McCue M, Klein I, Greenhouse J, Levey GS. Psychiatric and neuropsychological response to propranolol in Graves' disease. *Biol Psychiatry* 1988;23:678–88.
13. Bommer M, Eversmann T, Pickardt R, Leonhardt A, Naber D. Psychopathological and neuropsychological symptoms in patients with

subclinical and remitted hyperthyroidism. *Klin Wochenschr* 1990;68:552–8.

14. Stern RA, Robinson B, Thorner AR, et al. A survey study of neuropsychiatric complaints in patients with Graves' disease. *J Neuropsychiatry Clin Neurosci* 1996;8:181–5

15. Fahrenfort JJ, Wilterdink AM, van der Veen EA. Long-term residual complaints and psychosocial sequel after remission of hyperthyroidism. *Psychoneuroendocrinology* 2000;25:201–11.

16. Fukao A, Takamatsu J, Murakami Y, et al. The relationship of psychological factors to the prognosis of hyperthyroidism in antithyroid drug-treated patients with Graves' disease. *Clin Endocrinol* 2003;58:550–5.

17. Orenstein H, Peskind A, Raskind MA. Thyroid disorders in female psychiatric patients with panic disorder or agoraphobia. *Am J Psychiatry* 1988;145:1428–30.

18. Simon NM, Blacker D, Korbly NB, et al. Hypothyroidism and hyperthyroidism in anxiety disorders revisited: new data and literature review. *J Affect Disord* 2002;69:209–17.

19. Sundstrom IM, Bixo M, Bjorn I, Astrom M. Prevalence of psychiatric disorders in gynecologic outpatients. *Am J Obstet Gynecol* 2001;184:8–13.

20. Scholle SH, Haskett RF, Hanusa BH, Pincus HA, Kupfer DJ. Addressing depression in obstetrics/gynecology practice. *Gen Hosp Psychiatry* 2003;25:83–90.

21. Brownlie BEW, Rae AM, Walshe JWB, Wells JE. Psychoses associated with thyrotoxicoses — bthyrotoxic psychosesQ. A report of 18 cases, with statistical analysis of incidence. *Eur J Endocrinol* 2000;142:438–44.