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A STUDY OF PSYCHIATRIC MORBIDITY IN PATIENTS WITH THYROID DISORDERS- SIX MONTHS FOLLOW UP STUDY

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ABSTRACT

Background: Thyroid hormones have, from time immemorial, been known to have an impact mood and cognition. The thyroid hormones affect the neuronal functions at multiple levels- ranging from receptors, neurotransmitter systems, myelination, to intracellular genomic effects. Depression and anxiety are the most common mental conditions seen in thyroid disorders. There is also the possibility that the co-occurrence of psychiatric and thyroid diseases may be a result of shared genetic and biochemical abnormalities. There have been a multitude of studies exploring the quality of life and psychiatric co-morbidity, in patients afflicted with thyroid disorders.

Materials and methods: 147 patients with thyroid disorders who attended the outpatient Endocrinology Department at the hospital were evaluated for psychiatric morbidity. We estimated the severity and prevalence of depression and anxiety. We have followed up the patients for a period of six months, while they are receiving treatment for thyroid. We reassessed them for psychiatric morbidity during the follow up period and compared the prevalence rates and severity of depression and anxiety. We also did a correlation between demographic and illness variables with the presence and severity of psychiatric morbidity.

Results: Of the 147 participants, 93% were women. The average duration of thyroid dysfunction was 1.76 years. There was a significantly high prevalence of depression (59.2%) and anxiety(21.8%) in thyroid patients initially. After six months the prevalence rates decreased to 41.5% and 7.5% respectively .The psychiatric morbidity decreased significantly when the underlying thyroid dysfunction was corrected, without the use of any psychotropic medications.

Conclusion: There is a high prevalence of depression and anxiety in thyroid patients. There is a need for compulsory screening, follow up and review of these patients for psychiatric morbidity. The prevalence and severity depression and anxiety decrease significantly with appropriate and adequate management of the thyroid disorder, without any psychopharmacological intervention.

INTRODUCTION

The interplay between thyroid and psychiatry has always been a matter of intense research, debate and fascination. The history linking hypothyroidism and psychiatry dates back 1874, when George Murray successfully treated myxedema using thyroid extracts from sheep. Subsequently, a follow up study reported the presence of delusions and hallucinations in patients with advanced thyroid derangements. Years later, von Basedow first described a psychotic illness (probably mania), in a patient with exophthalmic goiter. Decades later, Asher coined the term "myxedema madness" to describe the psychosis in hypothyroidism[1].

The relationship between the thyroid gland and the brain is bidirectional. Thyroid hormones have a well known influence on the affective and cognitive functions. In turn, research has now proven the effect of psychosocial stress on the thyroid gland function. The mechanisms by which thyroid hormones influence the brain are manifold - ranging from neurotransmitter release to intracellular receptor binding and genomic effects.[4]. The effect of the thyroid hormones are more pronounced in the central nervous system than the peripheral nervous system.

It is now well established that thyroid disorders are more prevalent in women, ranging from two to as high as ten times the prevalence rates seen in men. In an Indian study, it has been estimated that around 42 million people suffer from thyroid disorders. (Desai PM et al 1997) [2]. Though hypothyroidism is more prevalent than hyperthyroidism, both disorders can cause profound changes in mood and intellectual functioning. Frequently, the thyroid abnormality is subclinical, and, a high degree of suspicion is required to diagnose the subclinical thyroid disorders.

The prevalence of psychiatric morbidity in thyroid disorders is nearly 60% [5]. Among hypothyroid patients, depression is more prevalent than anxiety, while in hyperthyroid patients they are equally prevalent. The vast majority of patients with depression do not have overt thyroid disease, although subclinical hypothyroidism has been detected in approximately 15% of patients (Nemeroff CB et al. 1985)[3]. In patients suffering from major depression, subclinical hypothyroidism may make them less responsive to antidepressant treatment. Thyroid hormone treatment has been shown to augment, accelerate, and complement anti depressant pharmacotherapy in refractory depression and refractory bipolar disorders. More recently, individual case reports have reported psychoses with depressive, manic, paranoid and schizophreniform features in hypothyroidism. Anti -thyroid antibodies have been found in 50% of patients with rapid cycling bipolar disorders (Joeffe et al.2001)[6] . In the Cochin study, about 53% of subjects with subclinical hypothyroidism had tested positive for anti-TPO antibodies. This was a population-based study, which employed cluster sampling strategy (Ambika Gopalakrishnan et al. 2011)[7].

Thyroid status evaluation in patients with acute psychosis frequently reveals a high T 4 with normal TSH. In patients with mania, both total T4 and free T4 were often found to be elevated while in patients with depression, TSH may be low / high, with a high free T4 and low / high total T3. The degree of discrepancy in thyroid hormones in more pronounced in geriatric population suffering from psychiatric disorders[8].

Patients with thyroid disorders thus need a comprehensive, complete and regular psychiatric evaluation. Often, the thyroid patient fails to receive even a single psychiatric evaluation. Many a time, both the patient and the treating physician overlook the symptoms of depression and anxiety. Sometimes, these psychiatric symptoms remit on their own eventually, when the patient reaches euthyroid status. Sometimes, the symptoms become severe, and the patient may subsequently be referred to the psychiatrist.

The study aims to find the prevalence of common psychiatric disorders- depression and anxiety, in patients with thyroid disorders. The study attempts to examine the course of the psychiatric disorders and to observe the changes in the prevalence rates and severity of psychiatric morbidity, when the thyroid dysfunction is corrected. It is our contention that in thyroid patients with mild to moderate psychiatric morbidity, the psychiatric symptoms gradually subside when the underlying thyroid disorder is treated appropriately and adequately. This improvement is possible without any psychotherapeutic intervention. We have followed up the thyroid patients with psychiatric morbidity, over a period of 6 months, without any therapeutic intervention. Since we chose not to institute any therapeutic intervention, for ethical reasons, we did not recruit patients with psychotic disorders, and patients with suicidal ideation. Through this attempt, we can identify a specific group among the patients with thyroid disorders, who will have persistent psychiatric symptoms, thereby requiring psycho pharmacotherapy. This will then help us in formulating a protocol for long term management of psychiatric disorders in patients with thyroid dysfunction.

In patients suffering from multiple disorders, drug compliance has always been a long term problem, both for the patient and the physician. Hence in the management of co-morbidities, a careful choice is needed about adding a drug to an already loaded prescription. For these patients, a simple step such as refraining from adding a drug, to an existing list of medications, plays a significant role in sustaining compliance to treatment. This study will thus augment the effort to improve drug compliance in thyroid patients, by avoiding unnecessary psycho pharmacotherapy.

AIMS AND OBJECTIVES

The study aims to

1. estimate the prevalence and severity of psychiatric morbidity- depression and anxiety- in patients with thyroid disorders.
2. find the correlation, if any, between psychiatric morbidity and demographic variables in the patient.
3. find the course of the psychiatric morbidity over a 6 months period while the patients receive appropriate thyroid drugs.
4. estimate and compare the prevalence and severity of psychiatric morbidity after 6 months.

MATERIALS AND METHODS

Participants

The study was conducted at the Department of Psychiatry of the hospital. Consecutive patients attending the thyroid clinic at the Outpatient Department of Endocrinology, were screened for psychiatric morbidity using the General Health Questionnaire - 28 (GHQ-28)[9]. It is a screening tool first developed by Goldberg to detect those who are at risk or are likely to have mental disorders. It has 28 questions under 4 domains – anxiety, depression, somatic symptoms and social withdrawal. All items are rated on a Likert scale of 0 (not at all) to 3 (much more than usual). A score of 23/24 is significant.

Both hypothyroid and hyperthyroid patients having significant scores on General Health Questionnaire - 28 were then evaluated for psychiatric disorders based on ICD 10 diagnostic criteria. After diagnosis, the severity of the disorder was assessed using the Hamilton Depression Rating Scale, Montgomery Asberg Depression Rating Scale, and Hamilton Anxiety Rating Scale.

The Hamilton Rating Scale for Depression (HAM-D) consists of 21 items, though the rating is based on the first 17 items. Eight of the items are rated on a five point scale as 0- 4, and nine items are rated as 0- 2. It is observer rated. A score of more than 7 is significant.

The Hamilton Rating Scale for Anxiety (HAM- A) has 14 items corresponding to both psychic and somatic symptoms of anxiety. Each item is scored on a five point scale of 0 – 4. A score of more than 7 is significant.

The Montgomery Asberg Depression Rating Scale (MADRS) has 10 items each of which is rated on a seven point rating from 0- 6. Of these, the ratings of 0,2,4,6 are well defined. The rater has to decide, during the course of the interview, whether the patient can be awarded the intermediate points of 1, 3, and 5 for any item. This scale has many items corresponding to psychological symptoms of depression rather than the somatic components[10].

In addition, we used the Mini Mental Status Examination (MMSE) to evaluate patients who complained of impairment in memory, at the time of screening. It is the gold standard screening tool for cognitive impairment. Developed by M. Folstein, the scale has a total of 11 items. The cut -off point indicative of cognitive impairment is 23 – 24. However, none of the participants had a significant score on MMSE.

Ethical committee approval was obtained. Statistical analysis was done using SPSS software.

Exclusion criteria- patients with symptoms of psychotic nature, patients having suicidal risk, patients previously or currently on psychiatric medications, patients with poor general medical condition, patients with any other general medical condition receiving medications other than thyroid drugs.

Informed consent was obtained from all the participants.

Clinical evaluation

170 thyroid patients of either gender, belonging to age group between 15 and 65 were chosen and recruited for the study. All thyroid patients had undergone a baseline thyroid status evaluation including the TSH, T4 assay in the Department of Biochemistry. The Endocrinology Department protocol requires that the patients come for follow-up once every four weeks, and undergo the thyroid hormonal status evaluation as requested by the treating endocrinologist. The same protocol was followed for all the participants. We interviewed the patient at the time of psychiatric screening using the GHQ-28 tool. Subsequently, we diagnosed the psychiatric morbidity using ICD-10 criteria. Severity rating was done using the rating scales mentioned. Psychiatric evaluation was continued at each subsequent visit to the thyroid clinic. During the interview the patients were re-assessed for severity of symptoms, and screened for new symptoms. We did not employ any structured or unstructured psychotherapy at any point during the study. No psychiatric medications were prescribed and the participants were observed for a period of six months. Out of 170 patients who entered the study, 147 participants had come for regular follow up till the completion of six months.

RESULTS

1.Demographic variables

The age wise distribution among the participants is shown in Table 1. The mean age of the participant was 33.18 years. Of the 147 participants, 137 were women (93.2% of the participants). Average duration of thyroid illness was 1.76 years.

Table 1 Age distribution among thyroid patients

Age in years	10- 19	20-29	30-39	40-49	50-59	60-69	Mean in years
Thyroid patients	13	53	38	26	12	5	33.18

2.Thyroid dysfunction pattern distribution among thyroid patients

Among the participants, majority (76%) had hypothyroidism (Table 2). We further classified the thyroid dysfunction as clinical and subclinical varieties. We observed that 74% of hypothyroid patients had subclinical hypothyroidism and 74% of hyperthyroid patients had overt hyperthyroidism (Table 2).

Table 2 Type of thyroid disorder among patients.

Thyroid patients			
Hyperthyroid patients		Hypothyroid patients	
35 (24%)		112 (76%)	
Subclinical	Overt	Subclinical	Overt
9 (25.7%)	26 (74.3%)	83(74.1%)	29 (25.9%)

3.Psychiatric morbidity

All the 147 participants were initially evaluated for psychiatric morbidity- namely depression and anxiety. The study showed that psychiatric morbidity was seen in 119 patients (81%) (Table 3). The prevalence rate was statistically significant. Depression was much more common than anxiety.

TABLE 3 Prevalence of psychiatric morbidity in thyroid patients at initial Evaluation

Psychiatric morbidity in thyroid patients at initial evaluation							
Depression				Anxiety			
Nil	Present	Chi-square	p value	Nil	Present	Chi-square	p value
60	87	69.879	0.000**	113	32	11.493	0.000**

**Statistically significant

Prevalence of Depressive disorder was 59.2% and the prevalence of anxiety disorder was 21.8% (Table 3). The psychiatric disorder was further categorized as mild, moderate and severe (Table 4).

Table 4 Categorization of severity of psychiatric morbidity

Severity of psychiatric morbidity at initial evaluation							
Depression				Anxiety			
Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
41	41	5	87	5	23	6	34

After instituting appropriate medication for the corresponding thyroid disorder, psychiatric morbidity gradually improved. All the patients were serially evaluated for psychiatric symptoms and followed up over a period of six months. We found a decrease in the prevalence rates for both depressive disorder (41.5%) and anxiety disorder (7.5%) (Table 5). However the prevalence of psychiatric morbidity after six months was still statistically significant.

Table 5 Prevalence of Psychiatric morbidity in thyroid patients after six months

Psychiatric morbidity in thyroid patients after six months							
Depression				Anxiety			
Nil	Present	Chi square	p value	Nil	Present	Chi square	p value
86	61	38.218	0.000**	136	11	11.493	0.000**

** statistically significant

After six months, the depression and anxiety were again categorized based on severity as mild, moderate and severe (Table 6). There was a decrease in the number of patients in each group (Figure 1) (Figure 2).

Table 6 Categorization of severity of psychiatric morbidity

Severity of psychiatric morbidity after six months							
Depression				Anxiety			
Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
34	24	3	61	6	4	1	11

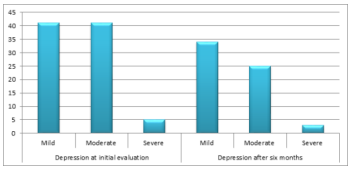


FIGURE 1 Comparison of depression severity and prevalence initially and after six months

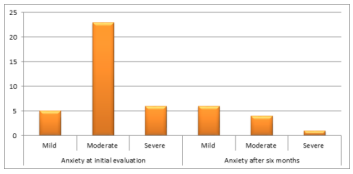


FIGURE 2 Comparison of anxiety severity and prevalence initially and after six months

We then compared the prevalence rates of depression and anxiety in thyroid patients –prevalence at the initial evaluation and prevalence after of six months (Table 7). We observed that there was a statistically significant difference. The prevalence rates decreased for both anxiety and depression (Figure 3).

TABLE 7 Comparison of prevalence of psychiatric morbidity in thyroid patients

Comparison of prevalence of psychiatric morbidity in Thyroid patients				
	Depression		Anxiety	
	Nil	Present	Nil	Present
Initial evaluation	60	87	113	34
After six months	86	61	136	11
	Chi square 207.674		Chi square 68.147	
	p value 0.000**		p value 0.000**	

**statistically significant

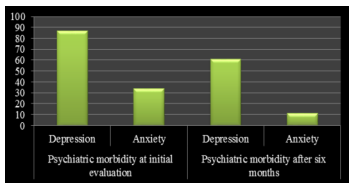


FIGURE 3 Comparison of prevalence of psychiatric morbidity

4.Correlation between demographic variables, illness variables and psychiatric morbidity

We examined the correlation between the patient variables (viz age and gender), and the presence as well as severity of psychiatric morbidity (Table 8). We found a statistically significant positive correlation between age and severity of psychiatric symptoms. Higher the age, more severe is the psychiatric morbidity. There was no statistically significant correlation to gender.

We did a correlation analysis between duration of illness among the participants and the presence as well as the severity of psychiatric morbidity. There was no statistically significant correlation.

TABLE 8 Correlation analysis of demographic and illness variables with psychiatric morbidity in thyroid patients

	Demographic and illness variables in Thyroid patients		
	Age	Gender	Duration of illness
Presence of psychiatric morbidity	0.024 (p value 0.193)	0.063 (p value 0.448)	0.035 (p value 0.673)
Severity of psychiatric morbidity	0.212 (p value 0.023**)	0.069 (p value 0.228)	0.042 (p value 0.342)

**statistically significant

5.Correlation between hormonal status and psychiatric morbidity

We attempted to find correlation if any, between the hormonal levels, viz serum T4, serum TSH and the psychiatric morbidity. We tabulated the baseline TSH and T4 levels of all thyroid patients in the study and evaluated the psychiatric morbidity of the patients at baseline. We found that, there was a statistically significant correlation between serum T4 and serum TSH levels with the presence and severity of depression and anxiety in thyroid patients (Table 9). The serum level of TSH had a statistically significant positive correlation with presence as well as the severity of psychiatric morbidity. Likewise the serum levels of T4 had a statistically significant negative correlation with the presence as well as the severity of psychiatric morbidity.

TABLE 9:Correlation between hormonal levels and psychiatric morbidity in thyroid patients at initial evaluation

	Hormonal levels in Thyroid patients	
	Serum T4	Serum TSH
Presence of psychiatric morbidity	-0.533 (p value 0.000**)	0.372 (p value 0.000**)
Severity of psychiatric morbidity	-0.331 (p value 0.002**)	0.261 (p value 0.003**)

** statistically significant

During follow up, over the period of six months, we continued to examine this correlation. We again tabulated the serum levels of TSH and T4, and psychiatric morbidity in patients. After six months, we found that the there was a statistically significant positive correlation between serum TSH levels and the presence as well as the severity of psychiatric morbidity-depression and anxiety (Table 10). However, there was no statistically significant correlation with serum T4.

TABLE 10 Correlation between thyroid hormonal levels and psychiatric morbidity in thyroid patients after six months

	Hormonal levels in Thyroid patients	
	Serum T4	Serum TSH
Presence of psychiatric morbidity	-0.023 (p value 0.756)	0.392 (p value 0.000**)
Severity of psychiatric morbidity	-0.018 (p value 0.123)	0.411 (p value 0.000**)

** statistically significant

This finding suggests that serum TSH is a better indicator of the presence as well as the severity of depression and anxiety disorders in thyroid patients. Higher the level of TSH, higher is the risk and greater is the severity of psychiatric morbidity. This positive correlation remained statistically significant over a period of six months, long after the correction of serum T4 levels.

Numerous biological studies in the past, have established that, subsequent to treatment of the thyroid abnormality, the serum T4 levels return to normal ranges, much rapidly than serum TSH levels. Hence, serum TSH level is more sensitive indicator of psychiatric morbidity than serum T4. Serum TSH levels reflect the thyroid status within the central nervous system. Thus the changes in serum TSH are closely related to the changes happening in the cortical and sub-cortical circuits, which are clinically manifested as psychiatric symptoms of depression and anxiety.

DISCUSSION

The prevalence of depression in general population varies from 11.8% to 58%. The prevalence of anxiety in the general population varies from 5% to 45%. In a hospital based study, the prevalence of psychiatric disorders in patients with thyroid dysfunction was estimated at 58.33% (Jain and Gautam et al. 1988)[11].

In our study, the prevalence of depression in thyroid patients was 59.2% and the prevalence of anxiety in thyroid patients was 21.8%. Based on severity, mild and moderate depression was more prevalent than severe depression in the study group. Likewise, mild and moderate anxiety was more prevalent than severe anxiety. As the thyroid status was corrected, over a period of six months, the prevalence of depression decreased to 41.5% and the prevalence of anxiety fell to 7.5%. The decrease in prevalence was statistically significant.

Many preclinical studies have discussed about depressive symptoms and glucose metabolism. Depressive symptoms in hypothyroidism were extrapolated to regional differences in glucose metabolism, particularly in the peri-genual anterior cingulate cortex region and the hippocampus in a glucose-PET study. After 3months of T4 substitution therapy, activity patterns started normalizing (Baeur et al. 2009) [12]. Likewise, it is now known that psychiatric symptoms in hyperthyroidism, such as anxiety, appear to be mediated by beta-adrenergic hyperactivity.

In the study, we did not do any psychiatric intervention or therapy. Hence the fall in prevalence can solely be attributed to the correction of thyroid status. The study thus indicates that psychiatric morbidity is significantly high in thyroid patients. There is a need for compulsory screening of thyroid patients for depression and anxiety. The study highlights that a major chunk of patients with psychiatric morbidity, do improve significantly when their hormonal status is corrected. We can thus plan a strategy of regular follow up including serial screening and observation, for those patients with depression and anxiety. For patients with mild and moderate depression/ anxiety we can adopt a wait and watch approach, rather than initiate a psycho-pharmacological or psychotherapeutic intervention. We can thus avoid unnecessary use of psychotropic medications. However, it should be borne in mind that should any patient show a hint of worsening of psychiatric symptoms, drug therapy can and must be initiated without delay.

The association between thyroid deficiency and psychiatric presentation is commonly missed unless one exercises a high degree of suspicion while evaluating the behavioral, affective, and cognitive changes seen in the patient (Benvenga Set al. 2003)[13].The study thus emphasizes the need for regular screening, evaluation and the follow up of patients with psychiatric symptoms in this special population.

In the study we did the correlation analysis between the presence and severity of depression and anxiety, and serum levels of TSH and serum T4. We found that serum TSH correlated well with psychiatric morbidity throughout the study. The positive correlation was statistically significant and thus serum TSH rather than serum T4, proved to be a more

sensitive indicator of the presence and severity of depression and anxiety. Serum TSH level has been considered as a marker of the severity of 'brain hypothyroidism' in past studies too (Schraml et al., 2011) [14].

In future, we can possibly design a study to evaluate and compare the effects of non pharmacological intervention versus pharmacological intervention, on the prevalence and course of psychiatric morbidity in thyroid patients. We will then be able to examine how effective is psychotherapy and drug therapy in decreasing the psychiatric morbidity, specifically for those patients with clinically mild depression and anxiety. We will also be better define and categorize those thyroid patients who will require pharmacotherapy for their psychiatric symptoms.

It is well known that thyroid patients manifest with multiple symptoms of somatic nature. Some of the vegetative symptoms are common to both thyroid dysfunction and depression. We hence wanted to make sure that the nonspecific somatic symptoms in patients with depression were indeed related to depression and not a result of the underlying hypo/ hyperthyroidism. During our study, while evaluating all patients with depression, we had rated the severity of depression using two instruments- HAM-D and MADRS. We found that there was a high degree of concurrence between the two scales in rating the severity of depression.

Several studies have reported that both higher and lower TSH levels within the physiological 'normal'(euthyroid) range are associated with poor cognitive performance despite the absence of clinically evident thyroid disease (Bolger MD et al. 1986)[15]. Prompt recognition and treatment may reverse the cognitive and functional deficits. Neuro-psychologically, several cognitive defects in the domains of general intelligence, psychomotor speed, visuo-spatial skills, working memory and long-term memory have been observed ranging in degree from minimal to severe. It was suggested that hypothyroid-related memory defects are not attributable to deficit in attention or encoding, but rather to specific retrieval deficits (Miller K et al. 2003)[16]. In the study, we did a screening for memory impairment using the MMSE scale. We did not find cognitive impairment in any of the participants.

CONCLUSIONS

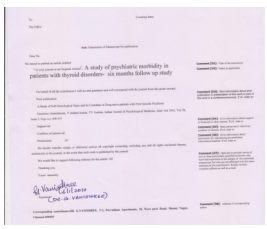
There is a need to devise a protocol for screening, evaluation, follow up and review patients with thyroid disorders, for the presence and severity of depression and anxiety. Psychiatric morbidity undergoes significant remission in response to treatment of the underlying hypo/hyperthyroidism, thus precluding the use of psychotropic medications.

LIMITATIONS

The study was designed to simply do a screening and regular follow-up, without resorting to any psychotherapeutic intervention. Hence, for ethical reasons, we did not include thyroid patients with severe depression and suicidal ideas and thyroid patients with psychotic disorders. The results of this study thus pertain only to those thyroid patients with depression and anxiety. This is a limitation.

CONFLICTS OF INTEREST

None



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