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# Incidence of Psychiatric Morbidities in Drug Naive Hypothyroid Patients: A Case Control Study

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## ABSTRACT

***Background:*** Hypothyroidism is one the etiology of emerging psychiatric illness. The present study is an attempt to find out the incidence of psychiatric morbidity in drug-naïve hypothyroid patients and to find the correlation between patient's sociodemographic variable, symptom duration, varying thyroid profile, subtype of hypothyroidism and psychiatric morbidity. ***Materials and Methods:*** This is a case-control study. The sample in this study consists of 75 hypothyroid patient and 75 euthyroid patients from Endocrinology out-patient department, matched for age and sex, after obtaining informed consent. ***Results:*** There was no statistical difference between cases and controls, with regard to sociodemographic variables. The psychiatric morbidity in hypothyroid patients is higher than euthyroid population ($\chi 2$ =32.9, p=0.001). The incidence and severity of depression (I - $\chi 2$=7.29, p=0.004), (severity- $\chi 2$ =10.42, p=0.02), anxiety (I- $\chi 2$ =3.84, p=0.05), (severity- $\chi 2$ =4.81, p=0.03) and cognitive impairment (I- $\chi 2$ =10..9, p=0.001), (severity- $\chi 2$ =13.04, p=0.001) are higher in hypothyroid patient when compared with controls. But the incidence of Psychosis is not statistically significant between groups. Among hypothyroid patients various parameters like symptom duration, varying thyroid profile and subtype of hypothyroidism did not reveal any significant statistical difference between patients with and without psychiatric morbidity. ***Conclusion:*** Incidence and severity of psychiatric morbidity in hypothyroid patients is higher than euthyroid population in our study. Hypothyroidism is one of the reversible etiologies of psychiatry disorder which is most often overlooked. Early diagnosis and treatment of hypothyroidism may alter the course of psychiatric illness and reduce the morbidity of these illnesses among patients.

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**H**ypothyroidism results from inadequate production of thyroid hormone, and is classified as clinical or sub clinical, depending on the degree of clinical severity and the extent of abnormalities in thyroid indices. In overt or clinical hypothyroidism, thyroid hormone levels are low, and TSH is elevated. Sub clinical hypothyroidism describes a condition in which T 3 and T 4 levels are normal but TSH is elevated, or the TSH response to TRH infusion is exaggerated. The prevalence of clinical hypothyroidism is approximately 2% in women and less than 0.1 % in men.[1] Sub clinical hypothyroidism also predominates in women, occurring in approximately 7.5% of women and 3% in men.[1]

Hashimoto's thyroiditis is the most common cause of clinical hypothyroidism. Other causes are idiopathic atrophy of thyroid gland, iodine deficiency, hypopituitarism, iatrogenic hypothyroidism. Symptoms of hypothyroidism are cold intolerance, constipation, muscle cramps, menstrual disturbances (amenorrhoea or menorrhagia), weight gain, dyspnoea, husky voice, slowed DTRs, bradycardia, cardiomegaly, dizziness, syncope, poor appetite and normocytic normochromic anemia.[2]

Psychiatric symptoms most commonly related to thyroid deficiency include forgetfulness, fatigue, mental slowness, inattention and emotional lability. The predominant affective disorder experienced is depression. Delusions and hallucinations may occur as the disease progresses. The prevalence of major depression among hypothyroid patients is 33%-43% [3], Anxiety disorder is 20%-33%[4], cognitive impairment 29%[5] and psychosis/delirium is 5%[2]. No correlation, however, appears to exist between the degree of thyroid dysfunction and psychiatric symptoms that subsequently develop.

Depression has been the major affective illness described in hypothyroid patients. Although the relationship between subclinical hypothyroidism and depression remains controversial, a more firmly established relationship exists between treatment resistant depression and subclinical hypothyroidism. A central serotonergic deficiency, brain catecholamine deficiency, Inhibition of type-II 5-deiodinase enzyme, a state of relative cerebral hypothyroidism is the proposed hypotheses linking depressive symptoms in hypothyroidism.[3]

Psychosis typically emerges after the onset of physical symptoms, often after a period of years or months. Manifestations include delusions (often paranoid), visual or auditory hallucinations, perseveration and loosening of association. These psychotic symptoms can occur without delirium or dementia [2].

Cognitive dysfunction also may be a result of hypothyroidism, most commonly, psychomotor slowing, deficits in memory, visuoperceptual skills and constructional dexterity[5]. Cognitive decline secondary to thyroid deficiency may represent dementia, which is reversible with thyroxin replacement therapy.

Many studies have focused on specific psychiatric disorders like Depression, Anxiety, cognitive deficits and psychosis in Hypothyroidism. But, unfortunately there are only few studies emphasizing overall psychiatric morbidity in hypothyroidism. So we proposed to do this study to focus on psychiatric morbidity among drug-naive hypothyroid patients, since correction of thyroid deficiency may reverse psychiatric manifestations. The study aims to estimate the incidence of psychiatric morbidity in drug-naive hypothyroid patients and study the association of each psychiatric disorder and its severity with duration of hypothyroidism, varying thyroid profile and subtype of hypothyroidism.

## MATERIALS AND METHODS

***Selection of sample:***

In study sample group age greater than 18 yrs, patients diagnosed to have hypothyroidism by blood parameters and not initiated on thyroxine replacement therapy were included and patients who were initiated thyroxine replacement therapy for hypothyroidism, patients with history of psychiatric or neurological illness, patients on drugs causing hypothyroidism (eg. Lithium, Amiodarone, etc) and patients who had underwent surgery of thyroid gland were excluded from our study. Patients with age greater than 18 yrs and Blood parameters revealing euthyroid status were included in control group. 75 drug-naive hypothyroid patients fulfilling the inclusion and exclusion criteria were taken as study-sample group. Another 75 euthyroid individuals fulfilling eligibility criteria were taken as control population. Written informed consent was obtained from all patients and their relatives participating in our study.

***Tools used :***

1. Semistructured proforma
2. ICD-10 diagnostic criteria
3. Hamilton Depression Rating Scale (HDRS)
4. Hamilton Anxiety Rating Scale (HARS)
5. Brief Psychiatric Rating Scale (BPRS)
6. Mini Mental Status Examination (MMSE)

### HAMILTON RATING SCLAE FOR DEPRESSION

The Hamilton Rating Scale for Depression (HAMD, HRSD) is an observer-rated scale to assess the symptoms of depression consists of 17 to 21 items.

### HAMILTON RATING SCALE FOR ANXIETY

The HAM-A widely utilized assessment scale for anxiety symptoms, consists of 14 items, and each item is rated on a 0 to 4 scale.

### THE MINI MENTAL STATE EXAMINATION (MMSE)

The Mini-Mental Status Examination (MMSE) is a valid and reliable 30-point questionnaire that is used extensively in clinical and research settings to measure cognitive impairment. The cut-off point to indicate cognitive impairment is less than 24.

### BRIEF PSYCHIATRIC RATING SCLAE (BPRS)

The BPRS is an 18 item brief scale that measures major psychotic and nonpsychotic symptoms in individuals with a major psychiatric disorder, particularly schizophrenia.

***Procedure of study:***

The study was carried out in Endocrinology outpatient department at Stanley Medical Hospital, after getting approval from the ethical committee. This is a Case control study. A total of 75 drug-naive hypothyroid patients and 75 euthyroid controls, who fulfill the inclusion and exclusion criteria were taken for study. A written informed consent was obtained. The two groups were equally matched for comparison in terms of age, sex, religion, marital status, education, occupational status, family status and Income. The HAMD, HAM-A, MMSE and BPRS scales were administered after clinically evaluating as per ICD-10 diagnostic criteria.

## STATISTICAL METHOD

The sociodemographic variables and HDRS, HAM-A, BPRS, MMSE, Scores were given in frequencies with their percentages. HDRS, HAM-A, BPRS and MMSE scores differences between cases and controls were analyzed using chi-square test. The proportion of subjects in cases and control in HDRS, HAM-A, BPRS, HMSE were analyzed using chi-square test. The overall incidence of psychiatric disorder differences between cases and control were analyzed using chi-square test. The association between sociodemographic, thyroid subtype, thyroid profile variables and psychiatric disorders were analyzed using chi-square test. The incidence of psychiatric morbidity among hypothyroid patients were given in percentage with 95% confidence interval.

## RESULTS

***General characteristics of the study population:***

The population with age group more than 18 years were included in the study. Table 1 sets out the sociodemographic profile of these patients. Among the 150 participants, 50% were cases (drug–navie hypothyroid patients) and remaining 50% were controls. Most of participants belonged to age group of 31-50 in both case and control group. Majority of the participants from both groups were females (85.3% cases and 78.7% controls). Among religion, Hindu's

constituted highest percentage among cases and control groups. There was no significant statistical difference in variables Marital Status, Education, Occupation, Family System and socioeconomic status (p= 0.62, 0.26, 0.18, 0.25, 0.56 respectively) between cases and controls. There was no significant statistical difference between cases and control group in the sociodemographic profile.

***Psychiatric morbidity:***

Among 75 cases, 38 patients had psychiatric disorder (50.6%) and 6 patients (8%) in control group [Table 2]. Chi square value was 32.9, with p value 0.001 indicating statistical significance. Among the psychiatric morbidity, depression was the most common disorder, in the study (20%) and in the control group (5.3%), followed by anxiety disorder (12% in study group and 2.7% in control group). There was no patient with cognitive impairment or psychosis among control, while 16% and 2.7% respectively in study population. Chi-square test showed statistical significance for Depression, Anxiety disorder and cognitive impairment, but there was no statistical significance for psychosis between cases and controls [Table 3]. There was significant statistically difference in the severity of depression ($\chi 2$ =10.42, p=0.02), anxiety ( $\chi 2$ =4.81, p=0.03) and cognitive impairment ($\chi 2$ =13.04, p=0.001) between cases and controls[Table 4].

There is no significant statistically difference between patient with psychiatric morbidity and patients without psychiatric morbidity in terms of duration of symptoms among hypothyroid patient ($\chi 2$ =0.59, p= 0.74). Thyroid profile (free T4, TSH) also did not have statistical difference between two groups ($\chi 2$ =1.08, p= 0.58 & $\chi 2$ =0.22,p= 0.63 respectively). Subtype of hypothyroidism – clinical or subclinical did not have statistical difference between two groups ($\chi 2$ =0.04, p= 0.74) [Table 5].

## DISCUSSION

The two groups - cases and controls were compared over various sociodemographic profiles. They were compared over variables for age, sex, religion, marital status, education, occupational status, family status and Income. The two groups were compared using chi-square test and no significant statistical difference was found between the two groups.

Among hypothyroid patients (75 patients), 38 had psychiatric morbidity, accounting for 50.6% of total study population [Table 2]. The above results go in accordance with the study[6] which concluded that psychiatric symptoms were the major presenting symptoms ranging (7-12%) in 58 hypothyroid patients .

Among 75 hypothyroid patients, 15 patients had depressive episode, accounting to 20% of study population, statistically significant when compared with control (p= 0.004). Among depressive patients majority (10 out of 15, 13.4% of total study group) had severe depressive episode. The above results is in accordance with results of previous studies [7],[8], which concluded that

depression was more significant in hypothyroid than euthyroid group. However, another study[9] concluding, the most frequent psychiatric changes were mild depression, was not in accordance with our study as majority of patients had severe depressive episode.

12% of study population had anxiety disorder (p=0.05), majority had severe anxiety symptoms. The above results is in accordance with the previous studies[4],[10],[11] which concluded that hypothyroid patients had significantly higher incidence of anxiety disorders than euthyroid population.12 patients had cognitive impairment, accounting for 16% of study group. In contrary, none of the euthyroid population had cognitive impairment, p=0.001. The above results is in accordance with literature [12],[13],[14] which concluded that hypothyroidism is a significant cause of dementia.Only 2 patients had psychosis , in contrary to earlier studies [15],[16],[17] which emphasized that psychosis is highly significant among hypothyroid patients.

Earlier studies [18,19] concluded that subclinical hypothyroidism patients are more prone for psychiatric morbidity. Another study [20] concluded clinical hypothyroidism patients were vulnerable for psychiatric morbidity. But, in our study, there was no statistical significance between the subtype of hypothyroidism (clinical and subclinical hypothyroidism) and psychiatric morbidity.

Literature shows[21] statistical significance between varying Free $T_4$ levels and psychiatric morbidity. Another study[22] emphasized prevalence of psychiatric morbidity more in patients with TSH levels > 10 uIU/ml, when compared to euthyroid population. In contrary our study showed no statistical significance between varying thyroid profile (free T4, TSH) and psychiatric morbidity (p= 0.58). Among 38 hypothyroid patients with psychiatric morbidity, majority (60.5%) had symptoms for less than 6 months duration. Earlier studies[23] concluded that patients with longer duration of hypothyroidism are more prone for psychiatric morbidity, which differs with our study.

In this study we were able to collectively compare various parameters to find the association between psychiatric morbidity and hypothyroidism which was strength of our study. Limitations in our study were small sample size, hence the study cannot be generalized to population. The study did not include diagnosis of Mental Retardation and Mania. Literature suggests a small percentage of hypothyroid population with these disorders. Only Free $T_4$ and TSH were considered for thyroid profile. Inclusion of Free $T_3$, would have strengthened this study. Treatment of psychiatric morbidity patients either with Psychotrophic drugs or Thyroxine replacement therapy and follow-up later would have made this study more informative.

## CONCLUSION

Our study is among the very few epidemiological studies with respect to studying various psychiatric morbidities in one study and its association with various parameters like sociodemographic profile, severity of psychiatric disorders, duration of hypothyroidism, varying

thyroid profile and subtype of hypothyroidism. Our study concluded that 50.6% of the subjects were suffering from diagnosable psychiatric disorder. The incidence of Depression, Anxiety Disorders and cognitive impairment is higher in hypothyroid patients than euthyroid population. The incidence of psychiatric morbidity in hypothyroid patients does not depend on socio demographic variables, sub type of hypothyroidism, varying thyroid profile (Free T 4 and TSH) and duration of hypothyroidism.

The clinical presentations of thyroid hormone deficiency are diverse and complicated which is often overlooked. It is one of the reversible etiologies of psychiatry disorders. Early diagnosis and treatment of hypothyroidism may alter the course of psychiatric illness and reduce the morbidity of these illnesses among patients.

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***Conflict of Interests:*** The author declared no conflict of interests.

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***Table 1: Sociodemographic Profile***

| Variable | Group | | | | $\chi 2$ value | P value |
|---|---|---|---|---|---|---|
| | Case (n) | % | Control (n) | % | | |
| **Age (Year)** | | | | | | |
| 18-30 | 34 | 45.3% | 25 | 33.3% | 3.59 | 0.31 |
| 31-50 | 35 | 46.7% | 39 | 52.0% | | |
| 51-65 | 6 | 8.0% | 10 | 13.3% | | |
| >65 | 0 | 0 | 1 | 1.3% | | |
| **Sex** | | | | | | |
| Male | 11 | 14.7% | 16 | 21.3% | 1.13 | 0.29 |
| Female | 64 | 85.3% | 59 | 78.7% | | |

| Variable | Group | | | | $\chi 2$ value | P value |
|---|---|---|---|---|---|---|
| | Case (n) | % | Control (n) | % | | |
| **Religion** | | | | | | |
| Hinduism | 58 | 77.3% | 50 | 66.7% | 4.49 | 0.11 |
| Islam | **11** | 14.7% | 10 | 13.3% | | |
| Christianity | 9 | 8.0% | 15 | 20.0% | | |
| **Marital status** | | | | | | |
| Married | 65 | 86.7% | 67 | 89.3% | 0.25 | 0.62 |
| Unmarried | 10 | 13.3% | 8 | 10.7% | | |
| **Education** | | | | | | |
| Illiterates | 26 | 34.7% | 24 | 32.0% | 1.16 | 0.26 |
| Upto 8th Std | 31 | 41.3% | 29 | 38.7% | | |
| 9th-12th Std | 16 | 21.3% | 21 | 28.0% | | |
| Higher Studies | 2 | 2.7% | 1 | 1.3% | | |
| **Occupation** | | | | | | |
| Unemployed | 40 | 53.3% | 43 | 57.3% | 3.47 | 0.18 |
| Manual labourer | 10 | 13.3% | 16 | 21.3% | | |
| Others | 25 | 33.4% | 16 | 21.3% | | |
| **Family system** | | | | | | |
| Nuclear | 42 | 56% | 35 | 47% | 1.13 | 0.25 |
| Joint | 33 | 44% | 40 | 53% | | |
| **Income** | | | | | | |
| < Rs. 1500 | 38 | 50.7% | 44 | 58.7% | 1.16 | 0.567 |
| Rs 1501- Rs 5000 | 35 | 46.7% | 30 | 40% | | |
| >Rs 5000 | 2 | 2.7% | 1 | 1.3% | | |

***Table 2: Psychiatric morbidity***

| Psychiatric Morbidity | Group | | | | $\chi 2$ value | P value |
|---|---|---|---|---|---|---|
| | Case (n) | % | Control (n) | % | | |
| Present | 38 | 50.6% | 6 | 8% | 32.9 | 0.001 |

***Table 3: Specific Psychiatry Disorders***

| Psychiatric Morbidity | Group | | | | $\chi 2$ value | P value |
|---|---|---|---|---|---|---|
| | Case (n) | % | Control (n) | % | | |
| Depression | 15 | 20% | 4 | 5.3% | 7.29 | 0.004 |
| Anxiety Disorder | 9 | 12% | 2 | 2.7% | | 0.05 |
| Cognitive Impairment | 12 | 16% | 0 | 0% | 3.84 | 0.001 |
| Psychosis | 2 | 2.7% | 0 | 0% | 10.9<br>0.53 | 0.47 |

***Table 4: Severity of psychiatric morbidity***

| Severity of psychiatric morbidity | Psychiatric disorder | | | | $\chi 2$ value | P value |
|---|---|---|---|---|---|---|
| | Cases(n=75) (n) | % | Controls(n=75) (n) | % | | |
| Depression | (n=15) | | (n=4) | | | |
| Mild | 1 | 1.3 | 2 | 2.7 | | |
| Moderate | 4 | 5.3 | 1 | 1.3 | 10.42 | 0.02 |
| Severe | 10 | 13.4 | 1 | 1.3 | | |
| Anxiety | (n=9) | | (n=2) | | | |
| Mild | 1 | 1.3 | 1 | 1.35 | | |
| Moderate | 2 | 2.7 | 1 | 1.35 | 4.81 | 0.03 |
| Severe | 6 | 8 | 0 | 0 | | |
| Cognitive impairments | (n=12) | | (n=0) | | | |
| Mild | 0 | 0 | 0 | 0 | 13.04 | 0.001 |
| Moderate | 12 | 16 | 0 | 0 | | |
| Severe | 0 | 0 | 0 | 0 | | |

*Table 5 : Psychiatric mortifies and associated variable*

| Variables | Psychiatric disorder | | | | $\chi 2$ value | P value |
|---|---|---|---|---|---|---|
| | Present (n) | % | Absent (n) | % | | |
| **Symptom duration** | | | | | | |
| <6 months | 23 | 60.5% | 20 | 54.1% | | |
| 6 months-1 year | 11 | 28.9% | 11 | 29.7% | 0.59 | 0.74 |
| >1 Year | 4 | 10.5% | 6 | 16.2% | | |
| **Subtype of Hypothyroidism** | | | | | | |
| Clinical | | | | | | |
| Subclinical | 29 | 76.3% | 29 | 78.4% | | |
| **Free T4 level (ng/dl)** | 9 | 23.7% | 8 | 21.6% | | |
| <0.6 | | | | | 0.04 | 0.74 |
| 0.6-0.8 | | | | | | |
| 0.8-2.0 | | | | | | |
| | 26 | 68.4% | 26 | 70.3% | | |
| **TSH levels** | | | | | | |
| (uIU/ml) | 4 | 10.5% | 6 | 16.2% | | |
| 6.16-10.0 | | | | | 1.08 | 0.58 |
| >10 | 8 | 21.1% | 3 | 13.5% | | |
| | 10 | 26.3% | 8 | 21.6% | | |
| | 28 | 73.7% | 29 | 78.4% | 0.22 | 0.63 |

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