PSYCHIATRIC MORBIDITY IN DRUG-NAIVE HYPOTHYROID PATIENTS

A CASE CONTROL STUDY

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CERTIFICATE

This is to certify that this dissertation entitled **PSYCHIATRIC MORBIDITY IN DRUG-NAIVE HYPOTHYROID PATIENTS"-A case control study**: is the bonafide original work of **Dr.I.SYED UMMAR** in partial fulfillment of the requirement for MD (Branch XVIII) Psychiatric examination of the Tamil Nadu Dr.MGR Medical University to be held in March 2008.

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CONTENTS

INTRODUCTION

Hypothyroidism results from inadequate production of thyroid hormone, and is classified as clinical or subclinical, 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. Subclinical 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. Subclinical hypothyroidism also predominates in women, occuring in approximately 7.5% of women and 3% in men. Elderly women are estimated to have upto 16% of subclinical hypothyroidism.

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 are cold intolerance, constipation, muscle cramps, menstrual disturbances (amenorrhoea or menorrhagia), weight gain, dyspnoea, husky voice, slowed DTRs, bradycardia, cardiomegaly, dizziness, syncope, poor appetite, normocytic, normochromic anemia.

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. 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. Approximately 40% of clinically hypothyroid patients have significant signs and symptoms of depression. 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 are the proposed hypotheses linking depressive symptoms in hypothyroidism.

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

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

The prevalence of major depression among hypothyroid patients is 33%-43%, Anxiety disorder is 20%-33%, cognitive impairement 29% and psychosis/delirium is 5%.

This study focusses on psychiatric morbidity among hypothyroid patients. Since correction of thyroid deficiency may reverse psychiatric manifestations, drug-naive hypothyroid patients were included. Only adult population were included in this study.

REVIEW OF LITERATURE

Many studies have focussed 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.

Barton et al. (1991)[4] did a retrospective study of 58 hypothyroid patients attending the Endocrine clinic, university hospital of West Indies, Jamaica between July and August 1989. Psychiatric symptoms were the major presenting symptoms along with hypothyroid symptoms and ranged (7-12)% of study patients.

Gulseran et al. (2006)[28] studied the effects of thyroid dysfunction on quality of life, levels of depression/anxiety. A total of 160 patients, consisting of an overt hypothyroidism group (n=33), a subclinical hypothyroidism group (n=43), an overt hyperthyroidism group (n=51), a subclinical hyperthyroidism group (n=13), and a healthy control group (n=20) were included in the study. The result of the study was, Anxiety and Depressive symptoms were more severe in patients with overt hypo and hyperthyroidism ($p<0.001$).

Constant et al. (2005)[12] studied the presence of anxiety and depressive symptoms in hypothyroidism, and examined the possible link between these symptoms and the cognitive disturbances. The result of this study was that the thyroid participants were more anxious and depressed than the controls. Contrary to what was expected, symptoms of anxiety and not symptoms of

depression interfered with the cognitive performance of participants in hypothyroidism.

Larisch et al. (2004)[52] did a prospective cross-sectional study to examine psychiatric symptoms in different thyroid function states. Among 254 patients, hypothyroid patients showed a significant mean score (17 + / - T, $p<0.001$, ANOVA). The study concluded that hypothyroidism represents a widely underestimated functional condition that may severely affect mental health.

Engum et al. (2002)[21] studied the association between depression, anxiety and thyroid dysfunction, a part of HUNT study. Individuals aged 40-89 years (n=30, 589) with thyroid assays and self-rated Hospital Anxiety and Depression Scale (HADS) were studied. In this large, unselected population, no statistical association between thyroid dysfunction and the presence of depression or anxiety disorder.

Baldini et al. (1997)[3] evaluated affective and cognitive dysfunctions in subjects with a marginal form of thyroid hypofunction, the authors studied a population of female goitre patients, divided into euthyroidism and subclinical hypothyroidism. In conclusion, subclinical hypothyroidism appeared to be associated only with memory impairment, while the impairment of affective functions described in previous studies comparing Subclinical Hypothyroid patients with euthyroid patients was not confirmed.

Knezevic et al. (1990)[50] evaluated psychiatric manifestations in hypothyroidism. The results of this study indicate that the most frequent psychic changes are mild and atypical depression.

Demet et al. (2003)[17] studied the prevalence and severity of depression and anxiety in patients with hypothyroidism and to compare this with euthyroid patients. The study concluded that depression and anxiety were not outstanding features in hypothyroidism. However, depression was more significant in the hypothyroid than euthyroid group.

Weissel et al. (2003)[83] studied the possible consequences of subclinical hypothyroidism and concluded that treatment of 'symptoms' of subclinical hypothyroidism like depression should be done only in patients with TSH >10 mu/l to avoid unnecessary overdosage with the danger of eliciting atrial fibrillation.

McGaffee et al. (1981)[56] studied psychiatric manifestations of hypothyroidism. He emphasized that hypothyroid patients may present with depression, an organic mental disorder, apathy and / or frank psychosis. Psychiatric manifestations of the endocrinopathy will abate with thyroid hormone replacement therapy. He recommended that thyroid function screening is recommended for patients presenting with depression, psychosis or organic mental disorder.

Heinrich et al. (2003)[37] studied hypothyroidism presenting as psychosis. He presented a case of clinical hypothyroidism that came to clinical

attention due to psychotic symptoms consisting of auditary and visual hallucinations.

Flykesnes et al. (2000)[26] systematically reviewed Dementia and hypothyroidism. He concluded that when hypothyroidism is detected in a patients with suspected dementia, thyroxin should be tried, and if no improvement, the acetylcholine inhibitor may be tried.

Boillet et al. (1998)[8] published a case, with psychiatric manifestations as the only clinical sign of hypothyroidism. A 63 year old man, presented with behavioural disturbance, persecutary delusions and cognitive impairement. Hypothyroidism was documented and after thyroxine replacement therapy, all symptoms disappeared.

Heberfelner et al. (1993) reported a case of a young women, who was treated for one and a half years with psychotrophic drugs and psychotherapy until hypothyroidism was diagnosed. On administration of thyroid hormone, the patient was free of psychiatric and somatic symptoms within 3 months.

Baumgartner et al. (1993)[5] reviewed the literature on the interactions between thyroid hormones and psychiatric illness. He concluded that thyroid hormone disorders (hypo and hyperthyroidism) may induce any psychiatric symptom or syndrome. However, no disease of the thyroid causes symptom typical of a specific diagnosis.

Del Ser et al. (1990)[16] reviewed Neuro-psychological disorders in hypothyroid dementia. The study included a 70 year old patient suffering severe mental deterioration, cerebellopathy, myopathy and hypothyroidism.

The patient had low score in all neuropsychological tests which improved progressively with the treatment and it is also accompanied by a lack of language defects, nonconstructive apraxia or agnosia. The recovery involves the attentional field and memory.

Haggerty et al. (1990)[30] reviewed neuropsychiatric aspects of subclinical hypothyroidism. He concluded that there is a strong evidence that subclinical hypothyroidism may be associated with cognitive dysfunction, mood disturbance and diminished response to standard psychiatric treatments.

Hendrick et al. (1998)[38] reviewed two clinical cases of hypothyroidism presenting as Psychosis. He concluded that psychiatric complaints may be one of the earliest manifestations of hypothyroidism, they are often misdiagnosed as a functional psychiatric disorder, rather than a psychiatric disorder due to a general medical condition. This confusion leads to delayed treatment and a high likelihood of morbidity. This emphasizes the importance of a high degree of suspicion of thyroid dysfunction and the need for thyroid screening in psychiatric patients.

Gilbert et al. (1956)[27] reviewed mental disorder associated with thyroid dysfunction. He reported two clinical cases of psychosis associated with hypothyroidism. He concluded that with mental disorders secondary to hypothyroidism, mental condition dramatically improves following thyroid hormone replacement.

Aszalos-Z et al. (2007)[2] reported 14 cases of hypothyroidism with psychosis, within a period of four years (nine of them showed dramatic improvement with administration of thyroid).

Jurish et al. (1993)[45] described psychotic symptoms occuring several months after subtotal thyroidectomy, which responded promptly to appropriate medications.

Sait Gonen et al. (2001)[72] assessed anxiety in subclinical thyroid disorders. Eighty five outpatients were enrolled in this study. One-way ANOVA showed that both of the subclinical hypothyroid and subclinical hyperthyroid groups had significantly higher anxiety scores than euthyroid group ($F:11.4$, $p<0.001$). He also concluded that mood changes especially anxiety due to subclinical thyroid dysfunction may have an important impact on the patient's quality of life.

Heinrich et al. (2003)[37] published an article of a case presenting with psychotic symptoms consisting of auditary and visual hallucinations due to clinical hypothyroidism, which responded to appropriate thyroid hormone supplementation.

Adam et al. (2005)[1] reviewed common executive dysfunctions between hypothyroidism and major depression. The study examined attentional and executive functions as well as the intensity of anxiety and depressive symptoms in hypothyroidism and major depression and the possible link between these symptoms and cognitive disturbances. This study confirmed the existance of psychomotor slowing associated with attentional and executive disturbance in

major depression as well as in hypothyroidism. While the hypothyroid state is accompanied by anxiety, depressive symptoms, it seems that the latter are too discrete for an attentional bias to be observed with material with a negative emotional valance.

Chureive et al. (2004)[11] reviewed the risk for depression in subclinical hypothyroid elderly patients. His study group consisted of 323 individuals over 60 years old, and were interviewed for mood disturbances. He studied both euthyroid and hypothyroid population. He concluded that subclinical hypothyrodism increases the risk for depression and emphasized the importance of thyroid screening tests in the elderly.

Thomsen et al. (2002)[79] reviewed increased risk of developing affective disorder in patients with hypothyroidism. The study was a prospective cohort study using historical data from Danish registers (1977-1999). The study concluded that patients hospitalised with hypothyroidism have a greater risk of readmission with depression or bipolar disorder than control patients.

Rogers et al. (2001)[71] examined anxiety disorders in patients with thyroid hormone disturbances. He concluded that hypothyroid patients had significantly higher incidence of anxiety disorders than euthyroid population.

Srikanth. S and Nagaraja AV (2005)[76] did a prospective study of reversible dementias-frequency causes and their clinical presentations. A total of 129 patients who met DSM criteria for Dementia were considered in the study. The study concluded that a high proportion of patients (18%) had

reversible dementia and B12 deficiency, hypothyroidism, CNS infections were the leading causes.

Patel R. et al. (2004)[63] did a study, some observations on the spectrum of dementia and concluded that B12 deficiency and hypothyroidism constituted a significant proportion of reversible dementias.

AIM AND OBJECTIVES

AIM OF THE STUDY

To study the incidence of psychiatric morbidity in drug-naive hypothyroid patients.

OBJECTIVES

1. To study the incidence of psychiatric morbidity in drug-naive hypothyroid patients and to compare with euthyroid population.

2. To compare the sociodemographic variables between euthyroid and hypothyroid population

3. To study the socio demographic variables among drug-naive hypothyroid patients with and without psychiatric manifestations.

4. To compare the incidence of psychiatric morbidity between clinical and subclinical hypothyroid patients.

5. To compare the severity of psychiatric manifestations in drug-naive hypothyroid patients with varying thyroid profile.

6. To study the incidence of psychiatric morbidity with varying symptom duration of hypothyroidism.

HYPOTHESIS

1. The psychiatric morbidity, is more common in hypothyroid patients, when compared to euthyroid population.

2. The incidence of Depressive episode is more common in drug-naive hypothyroid, patients when compared to euthyroid population.

3. The incidence of Anxiety Disorder is more common in drug-naive hypothyroid patients, when compared to euthyroid population.

4. The incidence of cognitive impairement is more common in drug-naive hypothyroid patients when compared to euthyroid population.

5. The incidence of psychosis is more common in drug-naive hypothyroid patients when compared to euthyroid population.

6. The psychiatric morbidity in hypothyroid patients does not depend on socio demographic variables.

7. Psychiatric manifestations are more common among clinical hypothyroid patients when compared to subclinical hypothyroid patients.

8. There is no significant correlation between the severity of psychiatric manifestations in drug-naive hypothyroid patients with varying thyroid profile.

9. The incidence of psychiatric morbidity increases with increasing symptoms duration of drug-naive hypothyroidism.

MATERIALS AND METHODS

SETTING OF STUDY

The study was carried out in Endocrinology outpatient department at Stanley Medical Hospital, which is conducted every Wednesdays.

PERIOD OF STUDY

January 2007 to July 2007 (Seven Months)

DESIGN OF STUDY

Case control study

SELECTION OF SAMPLE

75 drug-naive hypothyroid patients fulfilling the inclusion criteria were taken as study-sample group.

75 euthyroid individuals fulfilling inclusion criteria were taken as control population.

INCLUSION CRITERIA

Case

1. Age greater than 18 yrs.
2. Patients diagnosed to have hypothyroidism by blood parameters
3. Patients not initiated thyroxine replacement therapy

4. Patients who are willing to participate in the study and have given written consent.

Control

1. Age greater than 18 years.
2. Blood parameters revealing euthyroid status.
3. The people who are willing to participate in the study and given their written consent.

EXCLUSION CRITERIA

Case

1. Age less than 18 years of age.
2. Patients initiated thyroxine replacement therapy for hypothyroidism.
3. Patients with history of psychiatric or neurological illness.
4. Patients on drugs causing hypothyroidism (eg: Lithium, Amiodarone, etc).
5. Patients who had underwent surgery of thyroid gland.

Control

1. Age less than 18 years of age
2. Patients with history of psychiatric or neurological illness.

3. Patients on drugs causing hypothyroidism (eg: Lithium, Amiodarone etc)

4. Patient who had underwent surgery of thyroid gland.

TOOLS USED

1. Self innovated 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 SCALE FOR DEPRESSION

The Hamilton Rating Scale for Dpression (HAMD, HRSD), developed by M.Hamilton, is the most widely used rating scale to assess the symptoms of depression. The HAM-D is an observer-rated scale consisting of 17 to 21 items (including two 2-part items, weight and diurnal variation). Ratings are based on clinical interview, plus any additional available information such as nursing or family member report. The items are rated on either a 0 to 4 spectrum or a 0 to 2 spectrum.

The HAM-D also relies quite heavily on the clinical interviewing skills and the experience of rater in evaluating individuals with depressive illness. As most patients score zero on rare items in depression (depersonalization, obsessional and paranoid symptoms), the total score on the HAM-D generally consists of only the sum of first 17 items. The strength of HAM-D is its excellent validation/research base, and ease of administration. Its use is limited in individuals who have psychiatric disorders other than primary depression.

HAMILTON RATING SCALE FOR ANXIETY

The HAM-A, developed by M.Hamilton, is the most widely utilized assessment scale for anxiety symptoms, and was originally intended to be used to evaluate individuals who are already diagnosed with anxiety disorders. The HAM-A may be less useful in evaluating anxiety symptoms in those with other psychiatric disorders. The HAM-A consists of 14 items, and like the HAM-D, is heavily focused on somatic symptoms, with a great reliance on the patient's subjective report. Each item is rated on a 0 to 4 scale with a final item which rates behaviour at interview. Strengths of the scale include its brevity and widely accepted use. Limitations include its lack of generalizability to anxiety symptoms in other psychiatric disorders and the predominant focus on somatic, self-reported symptoms.

THE MINI-MENTAL STATE EXAMINATION (MMSE)

The Mini-Mental Status Examination (MMSE), developed by M.Folstein in 1975, is a screening instrument that gives a brief assessment of an individual's orientation to time and place, recall ability, short memory and

arithmetic ability. The MMSE has been extensively used in clinical settings. This instrument should not be used to diagnose dementia, but, rather, is utilized as a bed side instrument to assess the cognitive function of a patient.

The 11-item MMSE is divided into two sections. The first section requires verbal responses to orientation, memory, and attention questions. The second section requires reading, writing and the ability to copy a geometric figure (a polygon). The test can be scored immediately with a maximum of 30 (no impairement). The cut-off point to indicate cognitive impairement is generally between 23-25. The MMSE is brief, easy to use, can be administered by nonprofessional. It has been reported to potentially miss mild impairements and individuals with limited education tend to give false-positive responses.

BRIEF PSYCHIATRIC RATING SCALE (BPRS)

The BPRS, developed by JE overall and DR Gorham, is a very widely used, relatively brief scale that measures major psychotic and nonpsychotic symptoms in individuals with a major psychiatric disorder, particularly schizophrenia. The 18-item BPRS is perhaps the most researched instrument in psychiatry. Strengths of the scale include its brevity, ease of administration, wide use, and well-researched status.

PROCEDURE OF 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 HAMD, HAM-A, MMSE and BPRS

scales were administered after clinically evaluating as per ICD-10 diagnostic criteria.

ETHICAL COMMITTEE APPROVAL

The study was submitted for the approval of the ethical committee meeting held on 17.05.2007 at Dean's chamber at Govt. Stanley Hospital and approval was obtained.

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

OBSERVATIONS AND RESULTS

A. SOCIO DEMOGRAPHIC CHARACTERISTICS OF SAMPLE AND CONTROL GROUPS

1) Age distribution

TABLE-1

AGE DISTRIBUTION

Age (Year)	GROUP				Chi-square test
	Case		Control		
	n	%	n	%	
18-30	34	45.3%	25	33.3%	$\chi^2 = 3.59$
31-50	35	46.7%	39	52.0%	p = 0.31
51-65	6	8.0%	10	13.3%	Not significant
>65	0	0%	1	1.3%	

The population with age group more than 18 years were included in the study. There was no significant statistical difference among age distribution between cases and control group.

2) Sex distribution

TABLE-2

SEX DISTRIBUTION

Sex	GROUP				Chi-square test
	Case		Control		
	n	%	n	%	
Male	11	14.7%	16	21.3%	$\chi^2 = 1.13$, $p = 0.29$
Female	64	85.3%	59	78.7%	Not significant

There was no significant statistical difference between cases and control in sex distribution. Females predominated both in control (78.7%) and in cases (85.3%).

3) Religion

TABLE-3

RELIGION

Religion	GROUP				Chi-square test
	Case		Control		
	n	%	n	%	
Hinduism	58	77.3%	50	66.7%	$\chi^2 = 4.49$
Islam	11	14.7%	10	13.3%	p = 0.11
Christianity	9	8.0%	15	20.0%	Not significant

Among religion, there was no significant statistical difference between cases and control group. Hindu's constituted highest percentage among cases and control groups.

4) Marital Status

TABLE-4

MARITAL STATUS

Marital Status	GROUP				Chi-square test
	Case		Control		
	n	%	n	%	
Married	65	86.7%	67	89.3%	$\chi^2 = 0.25$; p = 0.62
Unmarried	10	13.3%	8	10.7%	Not significant

There was no significant statistical difference between cases and control group in marital status. Majority of the patients in cases and control group were married.

5) Educational Status

TABLE-5

EDUCATIONAL STATUS

Education	GROUP				Chi-square test
	Case		Control		
	n	%	n	%	
Illiterates	26	34.7%	24	32.0%	$\chi^2 = 1.16$
Upto 8th Std	31	41.3%	29	38.7%	p = 0.26
9th-12th Std	16	21.3%	21	28.0%	Not significant
Higher Studies	2	2.7%	1	1.3%	

There was no significant statistical difference in educational status between cases and controls.

6) Occupation

TABLE-6

OCCUPATION

Occupation	GROUP				Chi-square test
	Case		Control		
	n	%	n	%	
Unemployed	40	53.3%	43	57.3%	$\chi^2 = 3.47$
Manual labourer	10	13.3%	16	21.3%	p = 0.18
Others	25	33.4%	16	21.3%	Not significant

There was no significant statistical difference in occupation status between cases and controls.

7) Family System

TABLE-7

FAMILY SYSTEM

Family System	GROUP				Chi-square test
	Case		Control		
	n	%	n	%	
Nuclear	42	56.0%	35	47%	$\chi^2 = 1.13$; p=0.25
Joint	33	44.0%	40	53%	Not significant

There was no significant statistical difference between cases and controls in family system.

8) Socioeconomic Status

TABLE-8

SOCIOECONOMIC STATUS

Socioeconomic status (Income/Month)	GROUP				Chi-square test
	Case		Control		
	n	%	n	%	
<Rs.1500	38	50.7%	44	58.7%	$\chi^2 = 1.16$
Rs.1501-Rs.5000	35	46.7%	30	40.0%	p = 0.567
>Rs.5000	2	2.7%	1	1.3%	Not significant

There was no significant statistical difference in socioeconomic status between cases and control population.

9) Sociodemographic variables among hypothyroid patients

TABLE-9

SOCIODEMOGRAPHIC VARIABLES AMONG CASES

S.No.	Parameters	Subtype	With Psychiatric Morbidity		Without Psychiatric Morbidity		Chi-square test
			n	%	n	%	
1	Sex	Male	5	13.2%	6	16.2%	χ^2 = 0.14, p=0.71
		Female	33	86.8%	31	83.8%	Not significant
2.	Age	18-30 Yrs	18	47.4%	16	43.2%	χ^2 = 1.03
		31-50 Yrs	16	42.1%	19	51.4%	p =0.59
		51-65 Yrs	4	10.5%	2	5.4%	Not significant
3	Religion	Hindu	32	84.2%	26	70.3%	χ^2 = 3.37
		Islam	5	13.2%	6	16.2%	p =0.19
		Christian	1	2.6%	5	13.5%	Not significant
4	Marital status	Married	32	84.2%	33	89.2%	χ^2=0.40, p =0.08
		Unmarried	6	15.8%	4	10.8%	Not significant
5	Education	upto 8th Std	14	36.8%	17	45.9%	χ^2 = 6.37
		9th-12th Std	5	13.2%	11	29.7%	p =0.08
		Higher Studies	1	2.6%	1	2.7%	Not significant
		Illeterates	18	47.4%	8	21.6%	
6	Occupation	Unemployed	22	57.9%	18	48.6%	χ^2 = 0.83
		Manual labourer	4	10.5%	6	16.2%	p =0.66
		Others	12	31.6%	13	35.1%	Not significant
7	Family system	Nuclear	23	60.5%	19	51.4%	χ^2 = 0.64, p=0.42
		Joint	15	39.5%	18	48.6%	Not significant
8	Income	<Rs.1500	23	60.5%	23	62.2%	χ^2 = 2.32
		Rs.1501-5000	15	39.5%	12	32.4%	p =0.31
		>Rs.5000	0	0%	2	5.4%	Not Significant

There was no significant statistical difference in variables such as Age, Sex, Religion, Marital Status, Education, Occupation, Family System and socioeconomic status between patients with psychiatric disorders and without psychiatric disorders among hypothyroid patients.

B) Psychiatric morbidity among hypothyroid patients

TABLE-10

OVERALL PSYCHIATRIC MORBIDITY

Psychiatric Morbidity	GROUP				Chi-square test
	Case (75)		Control (75)		$\chi^2 = 32.9$
	n	%	n	%	p = 0.001
	38	50.6%	6	8.0%	Significant

Among 75 cases, 38 patients had psychiatric disorder (50.6%). Among the control group, 6 had psychiatric disorder (8%). Chi square value was 32.9%, with 'P' value 0.001, indicating statistical significance.

TABLE-11

SPECIFIC PSYCHIATRIC DISORDERS

Psychiatric Morbidity	GROUP				Chi-square test		
	Case (75)		Control (75)				
	n	%	n	%	$\chi^2 = 32.9$	p = 0.001	Significant
Depression	15	20%	4	5.3%	7.29	0.004	Significant
Anxiety Disorder	9	12%	2	2.7%	3.84	0-.05	Significant
Cognitive impairment	12	16%	0	0%	10.9	0.001	Significant
Psychosis	2	2.7%	0	0%	0.53	0.47	Not Significant

Among the psychiatric morbidity, Depression was the most common disorder, in study group (20%) and in control group (5.3%), followed by Anxiety Disorder (12% in study group and 2.7% in control group). There was no patients with cognitive impairment or psychosis among controls. (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 between cases and controls for psychosis.

TABLE-12

DEPRESSION AMONG HYPOTHYROID PATIENTS

Severity of depression	GROUP				Chi-square test
	Case (75)		Control (75)		
	n	%	n	%	
Absent	60	80.0%	71	94.7%	$\chi^2 = 10.42$
Mild	1	1.3%	2	2.7%	p = 0.02
Moderate	4	5.3%	1	1.3%	Significant
Severe	10	13.4%	1	1.3%	

There was significant statistical difference in the severity of depressive symptoms between cases and controls.

TABLE-13

ANXIETY DISORDER IN HYPOTHYROID PATIENTS

Anxiety Disorder	GROUP				Chi-square test
	Case (75)		Control (75)		
	n	%	n	%	
Present	9	12%	2	2.7%	χ^2=4.81 p=0.03
Absent	66	88%	73	97.3%	Significant

There was significant statistical difference in the severity of anxiety symptoms between cases and controls.

TABLE-14

COGNITIVE IMPAIRMENT AMONG HYPOTHYROID PATIENTS

Severity of cognitive impairment	GROUP				Chi-square test
	Case (75)		Control (75)		
	n	%	n	%	
Mild	0	0%	0	0%	χ^2=13.04
Moderate	12	16%	0	0%	p=0.001
Severe	0	0%	0	0%	Significant
Absent	63	84%	75	100%	

There was significant statistical difference in the severity of cognitive impairment between cases and controls.

TABLE-15

PSYCHOSIS IN HYPOTHYROID PATIENTS

Psychosis	GROUP				Chi-square test
	Case (75)		Control (75)		
	n	%	n	%	
Present	2	2.7%	0	0%	χ^2=0.51, p=0.47
Absent	73	97.3%	7%	100%	Not Significant

There was no significant difference between cases and control in the severity of psychosis.

C) Symptoms duration and psychiatric morbidity

TABLE-16

SYMPTOMS DURATION AND PSYCHIATRIC MORBIDITY

Symptom Duration	GROUP				Chi-square test
	With Psychiatric Disorder		No Psychiatric Disorder		
	n	%	n	%	
<6 months	23	60.5%	20	54.1%	$\chi^2 = 0.59$
6 months-1 year	11	28.9%	11	29.7%	p = 0.74
>1 Year	4	10.5%	6	16.2%	Not Significant

There was no significant statistical difference between patients with psychiatric morbidity and patients without psychiatric morbidity in terms of duration of symptoms among hypothyroid patients.

D) Subtype of hypothyroidism and psychiatric morbidity

TABLE-17

Sub type of Hypothyrodism	Psychiatric Morbidity				Chi-square test
	Present		Absent		
	n	%	n	%	
Clinical	29	76.3%	29	78.4%	$\chi^2 = 0.04$; p = 0.74
Subclinical	9	23.7%	8	21.6%	Not Significant

There was no significant statistical difference between patients with and without psychiatric morbidity in terms of subtype of hypothyroidism.

E) Varying thyroid profiles and psychiatric morbidity

TABLE-18

FREE T_4 LEVELS AND PSYCHIATRIC MORBIDITY

Free T_4 level (ng/dl)	Psychiatric Morbidity				Chi-square test
	Present		Absent		
	n	%	n	%	
<0.6	26	68.4%	26	70.3%	$\chi^2 = 1.08$
0.6-0.8	4	10.5%	6	16.2%	p = 0.58
0.8-2.0	8	21.1%	5	13.5%	Not Significant

There was no significant statistical difference between patients with and without psychiatric morbidity and varying free T_4 levels.

(* Normal value of Free T4 (0.8-2) ng/dl)

TABLE-19

TSH Levels and Psychiatric morbidity

TSH levels (μIU/ml)	Psychiatric Morbidity				Chi-square test
	Present		Absent		
	n	%	n	%	
6.16-10.0	10	26.3%	8	21.6%	$\chi^2 = 0.22$, p=0.63
>10	28	73.7%	29	78.4%	Not Significant

There was no significant statistical difference between patients with and without psychiatric morbidity and varying TSH levels.

Normal value of TSH (0.39-6.16) μIU/ml.

DISCUSSION

The two groups of patients 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. So the two groups were equally matched for comparision (Table 1 to Table 8).

Now, let as discuss the results of the study with literature background and compare with the hypothesis.

HYPOTHESIS - 1

(The pyschiatric morbidity, is more common in hypothyroid patients, when compared to euthyroid population).

Among hypothyroid patients (75 patients), 38 had psychiatric morbidity, accounting for 50.6% of total study population (Table - 11). Among euthyroid patients (75 controls), only 6 had psychiatric disorders, accounting for 8% of control group. Chi-square test revealed χ^2 value of 32.9, `p' value 0.001, which is statistically highly significant. 95% confidence interval for overall psychiatric morbidity is between 39% to 62%.

The above results go in accordance with the study by Barton et al.,[4] (1991), with 58 hypothyroid patients, which concluded that psychiatric symptoms were the major presenting symptoms, ranging (7-12%).

Larisch et al., (2003)[52], studied 254 hypothyroid patients, concluding significant statistical difference (p = 0.001) of the incidence of pychiatric morbidity. The above results, with `p' value 0.001, favour our study.

HYPOTHESIS - 2

(Depressive episode is more common in hypothyroid than euthyroid population).

Among 75 hypothyroid patients, 15 patients had depressive episode, accounting to 20% of study population. Among euthyroid patients, 4 had depressive episode, accounting for 5.3% of study group. This result was statistically significant with `p' value 0.004 (Table - 10).

Among hypothyroid patients with depressive episode, majority (10 out of 15, 13.4% of total study group) had severe depressive episode. In control group, distribution of severity of depressive episode was almost even. Moreover, there was significant statistical difference between cases and controls in the severity of depressive symptoms (`p' value - 0.02) (Table - 12).

The above results is in accordance with results of Constant et al., (2005)[12], Engum et al., (2002)[21] and Demet et al., (2003)[17] studies, which concluded that depression was more significant in hypothyroid than euthyroid group.

However, the study by Knezevic et al., (1990)[50], concluding, the most frequent psychiatric changes were mild depression, was not in accordance with our study (as majority of patients had severe depressive episode).

Depression was the most common psychiatric manitestation (20% of study group) is in accordance with the study of Engum et al.,[21]

HYPOTHESIS - 3

(Anxiety Disorder is more common in hypothyroid group than euthyroid population).

Among 75 hypothyroid patients, 9 patients had anxiety disorder, constituting 12% of study population. Among euthyroid population, 2 patients had anxiety disorder, accounting for 2.7% of study group. This result was statistically significant with `p' value 0.05 (Table - 10).

Among hypothyroid patient with anxiety disorder, majority had severe anxiety symptoms, with chi-square test revealing `p' value of 0.03, with statistical significance (Table - 13).

The above results is in accordance with the studies of Sait Gonen et al.,[72] (2001), Rogers et al., (2001)[71], Constant et al., (2005)[12], Engum et al., (2002)[21] and Demet et al., (2003)[17], which concluded that hypothyroid patients had significantly higher incidence of anxiety disorders than euthyroid population.

HYPOTHESIS - 4

(Cognitive Impairment is more common in hypothyroid than euthyroid population).

Among 75 hypothyroid patients, 12 patients had cognitive impairment, accounting for 16% of study group. In contrary, none of the euthyroid population had cognitive impairment, (Table - 10). Thus result was statistically significant, with `p' value 0.001.

Among hypothyroid patients with cognitive impairment, all of them (12 patients) had moderate cognitive impairment and none had either mild or severe cognitive impairment, with statistical significance, with `p' value 0.001 (Table - 14).

The above results is in accordance with studies of Fylkesnes et al.,[26] (2000), Boillet et al., (1998)[8], Del Ser etr et al., (1990)[16], Srikanth and Nagaraja (2005)[76] and Patel et al., (2004)[63] which concluded that hypothyroidism is a significant cause of dementia.

HYPOTHESIS - 5

(Psychosis is more common in hypothyroid than euthyroid population).

Among 75 hypothyroid patients, only 2 patients had psychosis (with paranoid delusions and hallucinations), accounting for 2.7% of study group. In contrary, none of the euthyroid group had psychosis. Chi-square test revealed `p' value of 0.47, indicating `No statistical significance' (Table - 10).

The above result differs from earlier studies by McGaffee et al., (1981)[56]. Heinrich et al., (2002)[36], Heinrich et al., (2003)[37] and Aszalos et al., (2007) which emphasized that psychosis is highly significant among hypothyroid patients.

HYPOTHESIS - 6

(Psychiatric morbidity in hypothyroid patients does not depend on sociodemographic variables).

1. SEX

Among 38 hypothyroid patients with psychiatric morbidity, majority were females (86.8%), similar to non - psychiatric (83.8%), Chi-square test did not reveal any statistical significance. (`'p' value - 0.71) between the two groups (Table - 9).

2. AGE

Among 38 hypothyroid patients with psychiatric morbidity, most of the patients were above 50 years (49.5%), similar to non - psychiatric patients (94.6%) Chi - square test showed no clinical significance (`p' value - 0.59) between the two groups, (Table - 9).

3. RELIGION

Among 38 hypothyroid patients with psychiatric morbidity, most of the patients were Hindus (84.2%), similar to non - psychiatric patients (70.3%). Chi-square test showed no clinical significance (`'p' value - 0.19), between the two groups (Table - 9.)

4. MARITAL STATUS

Among 38 hypothyroid patients with psychiatric morbidity, most of the patients were married (84.2%), similar to non - psychiatric patients (89.2%). Chi-square test, showed no clinical significance (`p' value 0.53) between the two groups (Table - 9).

5. EDUCATION

Among 38 hypothyroid patients with psychiatric morbidity, most were Illiterates (47.4%), as opposed to non - psychiatric patients, in which majority of population studied upto 8th standard (45.9%). Between these two groups, there was no statistical significance, (`p' value - 0.08) (Table - 9).

6. OCCUPATION

Among 38 hypothyroid patients with psychiatric morbidity, majority of the patients were unemployed (57.9%), similar to non - psychiatric patients (48.6%). There was no statistical significance between these two groups, with a `p' value of 0.66, (Table - 9).

7. FAMILY SYSTEM

Family system was almost even in both groups of hypothyroid patients. There was no statistical significance between these two groups, with (`p' value 0.42) (Table - 9).

8. SOCIOECONOMIC STATUS

Among 38 hypothyroid patients with psychiatric morbidity, majority of the patients were from lower - soecioeconomic status (<Rs.1500 - 60.5%). Similarly, among 37 patients without psychiatric morbidity, majority of the patients were from lower socioeconomic status (<Rs.1500-62.2%) [Table 9].

Hence, in terms of sociodemographic variables, there was no statistical significance between the two groups, among hypothyroid patients.

HYPOTHESIS - 7

(Psychiatric manitestations, common among clinical than subclinical hypothyroid patients).

Among 58 clinical hypothyroid patients in study group, 29 patients had psychiatric morbidity, accounting to 76.3% and 29 patients did not have any psychiatric disorder (78.4%).

Among 17 subclinical hypothyroid patients in study group, 9 patients had psychiatric morbidity, accounting for 23.7%, and 8 patients did not have any psychiatric disorder (21.6%).

Hence, there was no statistical significance between subtype of hypothyroidism and the incidence of psychiatric morbidity (χ^2 = 0.04 and `p' value `0.85') [Table 17].

Earlier studies by Baldini et al., (1997)[3], Haggarty et al., (1990)[30], Sait Gonen et al., (2001)[72] and Chureire et al., (2004), concluded that subclinical hypothyroidism patients are more prone for psychiatric morbidity. Gulseran et al,, (2006), concluded clinical hypothyroidism patients were vulnerable for psychiatric morbidity.

But, according to our study, these was no statistical significance between the subtype of hypothyroidism and psychiatric morbidity, which differs with earlier studies.

HYPOTHESIS - 8

(There is no significant correlation between severity of psychiatric manifestations in hypothyroid patients and varying thyroid profile).

Among 38 hypothyroid patients with psychiatric morbidity, 26 patients had free T_4 levels <0.6 ng/dl, accounting for 68.4%. Among 37 hypothyroid patients without psychiatric morbidity, 26 patients had free T_4 level <0.6 ng/dl, accounting for 70.3% (Table - 18). There was no statistical significance between varying free T_4 levels and psychiatric morbidity (`p' value - 0.58).

Earlier studies by Chureine et al., (2004)[11], emphasized the importance of thyroid screening tests and found statistical significance between varying Free T_4 levels and psychiatric morbidity, which varies with our study.

VARYING TSH LEVELS AND PSYCHIATRIC MORBIDITY

Among 38 hypothyroid patients with psychiatric morbidity, majority (28 patients - 73.7%) had TSH levels >10 µIU/ml. Among 37 hypothyroid patients without psychiatric morbidity, majority (29 patients -78.4%) had TSH levels >10 µIU/ml. There was no significant statistical difference between varying TSH levels of psychiatric morbidity (p value - 0.63) [Table –9].

Earlier studies by Weissel et al., (2003)[83], emphasized prevalence of psychiatric morbidity more in patients with TSH levels >10 µIU/ml, when compared to euthyroid population. Our study is not in accordance with earlier study.

HYPOTHESIS - 9

(The incidence of psychiatric morbidity increases with increasing symptom duration of hypothyroidism).

Among 38 hypothyroid patients with psychiatric morbidity, majority (23 patients - 60.5%) had symptoms for less than 6 months duration. Similarly, among 37 hypothyroid patients without psychiatric morbidity, majority (20 patients - 54.1%) had symptoms for less than 6 months duration. Applying chi-square test, `p' value was 0.74, indicating no statistical significance (Table 16).

Earlier studies by Heberfether et al., (1993)[26], concluded that patients with longer duration of hypothyroidism are more prone for psychiatric morbidity, which differs with our study.

SUMMARY

The present study is an attempt to find out the incidence of psychiatric morbidity and the significance of sociodemographic variable, varying thyroid profile, symptom duration, subtype in drug-naive hypothyroid patients.

The sample in this study consisted of 75 hypothyroid patients and 75 euthyroid patients from Endocrinology out-patient department of Stanley Medical Hospital, matched for age and sex, after obtaining informed consent.

There was no statistical significant difference between cases and controls, with regard to sociodemographic variables.

Among hypothyroid patients, there was no statistical significant difference between patients with and without psychiatric morbidity in sociodemographic variables.

The psychiatric morbidity in hypothyroid patients is significantly higher than euthyroid population.

The incidence of depression, cognitive impairment, and anxiety disorder are higher in hypothyroid patients. But the incidence of Psychosis is not statistically significant between cases and controls.

Looking at the statistics of present study and correlating it with present literature and earlier studies, except for no significant statistical difference of psychosis, all other findings correlate with earlier studies.

Among hypothyroid patients, various parameters like symptom duration, varying thyroid profile and subtype of hypothyroidism, does not reveal any significant statistical difference between patients with and without psychiatric morbidity.

CONCLUSIONS

1. The incidence of Psychiatric morbidity in hypothyroid patients is significantly higher than euthyroid population.

2. The incidence of Depression, Anxiety Disorder and cognitive impairment is higher in hypothyroid patients than euthyroid population.

3. The incidence of psychosis is not significant in hypothyroid patients when compared to euthyroid population.

4. The incidence of psychiatric morbidity in hypothyroid patients does not depend on socio demographic variables.

5. The incidence of Psychiatric morbidity does not depend upon the sub type of hypothyroidism.

6. The incidence of Psychiatric morbidity does not differ with varying thyroid profile (Free T_4 and TSH) among hypothyroid patients.

7. The incidence of Psychiatric morbidity does not differ with varying symptom duration of hypothyroidism.

LIMITATIONS AND SUGGESTIONS

1. The study size of the sample is small. Hence the study cannot be generalised to population.

2. The study did not include diagnosis of Mental Retardation and Mania. Literature suggests a small percentage of hypothyroid population with these disorders.

3. Only Free T_4 and TSH were considered for thyroid profile. Inclusion of Free T_3, would have strengthened this study.

4. Cross-sectional nature of the study.

5. Treatment of psychiatric morbidity patients either with Psychotrophic drugs or Thyroxine replacement therapy (if symptoms are less severe or less than 1 month duration) and follow-up later would have made this study more informative.

6. Appropriate treatment and follow-up would have demonstrated reversible type of Dementia in Hypothyroid patients.

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ETHICAL COMMITTEE APPROVAL

/

MINUTES OF THE ETHICAL COMMITTEE MEETING HELD ON 17-5-2007 AT DEAN'S CHAMBER AT GOVERNMENT STANLEY HOSPITAL, CHENNAI-1

The Dean, Vice Principal, presided over the meeting

The Committee members were present to discuss the projects submitted by the applicants to do the project in the Stanley Medical College and Hospital.

The applicants and their guides (Senior Professors of this college) also present in the meeting.

The following projects were submitted for the approval of the Ethical Committee.

1.Dr.R.Surendran, HOD of Surgical Gastroenterology – "Multiple center, Open-label, Randomized Comparative Study of Tigecycline Vs Ceftriaxone Sodium plus Metronidazole for the Treatment of Hospitalized patients with complicated Intra-addominal infection – Sponsored by Wyeth Pharmaceuticals, Inc."

2.Dr.G.Rajkumar, MD Paediatrics Second year. – "Correlation between Clinical manifestations and sero positivity for HIV among children admitte in Stanley Medical College & Hospital."

3.Dr.G.Murugan, PG in Biochemistry – "Evaluation of trace element status in Hemodialysis patients"

4. Dr. Syed Ummar. I – "Psychiatric Sequelae in Drug – Naïve Hypothyroid patients"

5.D.G.Sasikala – MD Microbiology-PG – Isolation, Speciation of candida in vaginal candidiasis and antifungal susceptibility in relation to azole resistance.

6. Dr.Anand Bhimaray Janagond PG in Microbiology – "Study of opportunistic infections in HIV positive patients"

7.Dr.Mrs. David Agatha, First Year MD Microbiology PG – Study of aerobes and anaerobes in Otitis media, Diabetic foot lesions and Orodental Infections."

8.Dr.Mohamed Rafi – "Intervention study in Malnutrition among infants in Rural Commuity of Thiruvallur District t PHC Block level."

9.Dr.M.Sridhar, MD Psychiatry (Final Year) - "Quality of Sleep and Day time Sleepiness in Depression"

10.Dr. M.Priya Subhashini, PG in MD Psychiatry (Final year) – Evaluating the Risk Factors Associated with attempted suicide among individuals with alcohol dependence."

11.Dr.N.Gowdhaman, PG in MD(Physiology) – Pulmonary function studies in women with Rheumatoid arthritis.

12.Dr.B.Adikesavan, PG in M.D.(Physiology) – Nerve conduction studies in Hypothyroid and Hyperthyroid patients.

13.Dr.P.Rajeshprabhu – DM Postgraduate – "Naturl history of cirrhosis with portal hypertension –Predictors of morbidity and mortality"

14.Dr.P.Rajeshprabhu – DM Postgraduate – "Doppler study as an indirect assessment of hepatic venous pressure gradient in assessing the severity of portal hypertension"

15.Dr. Anand/Dr.Gokul – DM Postgraduate – "Are Antisecretory Drugs A.Nutrient Supplement for the poor."

16.Dr.Aravindh. S. DM Postgraduate – "Autonomic Function Testing in Decompensated Liver Disease with Disproportionate Pedal Edema and in Non-Cirrhotic Portal Hypertension"

17.D.Aravindh. S. – DM Postgraduate – "Heart Rate Variability in Cirrhotics and Non Cirrhotics"

18.Navaneeth Chandru Kumar etc. – DM Postgraduate- "Hepatitis B vaccinationstatus among medical students of Stanley Medical College"

19.Dr.Elisha Benjamin J.B.Rajesh Prabhu –DM Postgraduate – "Studies on the expression pattern and mechanism of nuclear localization of Gas7 protein inhuman preneoplastic and neoplastic Gastric tissues."

20.Dr.Aparna Vijayasekaran etc. – DM Postgraduates – "GER Prevalance amongst Stanley Medical School and Hospital Personnel"

21.D.S.Chandra Mohan , DM Postgraduate – "Serprevalence of anti-filarial antibodies in cirrhotic patients – South Indian population"

22.Dr. S.Chandra Mohgan, DM Postgraduate – "Role of UGI Endoscopy and Laboratory Investigations in Functional Dyspepsia"

23.Dr.Selvasekaran , DM Postgraduate – "Pulmonary functions in liver cirrhosis"

24.Dr.Selvasekaran, DM Postgraduate – "Patency of Left Portal Vein in Extra Hepatic portal Vein Obstruction."

25.Dr.Parthasarathy.S., & Dr.Ssselvasekaran, DM Postgraduates – "Altered activation of MUCI/EGFR down stream signaling insquamous cell carcinoma and H.Pylori mediated Barrett's Adenocarcinoma sequence in Oesophagus."

The applicants are narrated their project aim and the way of the study conducted in the Stanley Medical College and Hospital, Chennai-1.

The Project submitted by the Prof. & HOD of Surgical Gastroenterology is also approved by the Committee. But the project involved with the sponsored company. Hence he is requested to get necessary permission from the Director of Medical Education, Chennai-10 for doing the project in the Government Stanley Hospital, Chennai-1.

The topic presented by Dr.B.Gayathri – "Value of High sensitivity C.Reactive protein in Diabetes mellitus " was approved after corrections.

Dr.S.Ramamanohaori, submitted the topic –"Health Education intervention study on OBESE Children in Britania Hr. Sec. School, Padi, Chennai-50" - for approval of the committee. But she is not represented in the Ethical Committee meeting on 17-5-2007.

After going through eight copies of protocol, patient information sheet, investigator brochure and informed consent, the ethics committee has approved of all the above, the study under the referenced protocol.

SIGNATURE OF THE ETHICAL COMMITTEE MEMBERS:

Dr.T.Raveendran, Dean

Dean
Stanley Medical College
Chennai-600 001
Tamil Nadu – India

Dr.A.Sundaram, Vice Principal,

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Dr.Mustaq Ahmed Khan

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Dr.P.Jayanthi

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V Jayant
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Gastroenterologist
Reg. No. 45456
GOVT. SM. H... CHENNAI

Nursing Superintendent

Advocate

ar.

ANNEXURES

CONSENT FORM

I was informed and explained of the purpose and nature of the study. I am willing to participate in this study. I hereby give my full consent for the study.

Signature of the Patient/Control

Name of the Patient/Control

PROFORMA

1. Name
2. Age (Years)
3. Sex (Male / Female)
4. Religion (Hindusism/Islam/Christianity/others)
5. Marital status (Married/Unmarried/Divorced/Seperated)
6. Educational status (Illetrate/Educated (details))
7. Occupation (Unemployed/ Manual labourer/ others)
8. Family type (Nuclear / Joint)
9. Per Capital Income
10. Symptom duration
11. Detailed present/past/personal/family/personality history
12. Physical examination
13. Mental status examination
14. Investigations values. (Free T4 levels/TSH levels/ Type of hypothyroidism)
15. HRSD
16. HARS
17. MMSE
18. BPRS
19. ICD-10 Diagnostic Criteria

ANNEXURE-2

HAMILTON PSYCHIATRIC RATING SCALE FOR DEPRESSION (HMA-D, HRSD)

INSTRUCTIONS: For each item, select the one "cue" which best characterizes the patient

1) Depressed Mood (sadness, hopeless, helpless, worthless)

0 = Absent
1 = These feeling states indicated only on questioning
2 = These feeling states spontaneously reported verbally
3 = Communicates feeling states nonverbally (i.e through facial expression, posture, voice, and tendency to weep)
4 = Patient reports virtually only these feeling states in his spontaneous verbal and nonverbal communication

2) Feeling of Guilt

0 = Absent
1 = Self-reproach, feels he has let people down
2 = Ideas of guilt or rumination over past errors or sinful deeds
3 = Present illness in a punishment. Delusions of guilt
4 = Hears accusatory or denunciatory voices and/or experiences threatening visual hallucinations

3) Suicide

0 = Absent
1 = Feels life is not worth living
2 = Wishes he were dead or any thoughts of possible death to self
3 = Suicide ideas or gesture
4 = Attempts at suicide (any serious attempt rates 4)

4) Insomnia Early

0 = No difficulty falling asleep
1 = Complains of occasional difficulty falling asleep (eg, more than 30 minutes)
2 = Complains of nightly difficulty falling asleep

5) Insomnia Middle

0 = No difficulty
1 = Patient complains of being restless and disturbed during the night
2 = Waking during the night-any getting out of bed rates 2 (except for purposes of voiding)

6) Insomnia Late

0 = No difficulty
1 = Waking in early hours of the morning but goes back to sleep
2 = Unable to fall asleep again if he gets out of bed

7) Work and Activities

0 = No difficulty
1 = Thoughts and feelings of incapacity, fatigue or weakness related to activities, work or hobbies
2 = Loss of interest in activity; hobbies or work-either directly reported by patient, or indirect in listlessness, indecision and vacillation (feels he has to push self to work or activities)
3 = Decrease in actual time spent in activities or decrease in productivity. In hospital, rate 3 if patient does not spend at least 3 hours daily in activities (hospital job or hobbies) exclusive of ward chores.
4 = Stopped working because of present illness. In hospital, rate 4 if patient engages in no activities except ward chores, or if patient fails to perform ward chores unassisted.

8) Retardation (slowness of thought and speech; impaired ability to concentrate; decreased motor activity)

0 = Normal speech and thought
1 = Slight retardation at interview
2 = Obvious retardation at interview
3 = Interview difficult
4 = Complete stupor

9) Agitation

0 = None
1 = Fidgetiness
2 = Playing with hands, hair, etc
3 = Moving about, can't sit still
4 = Hand wringing, nail biting, hair-pulling, biting of lips

10) Anxiety Psychic

0 = No difficulty
1 = Subjective tension and irritability
2 = Worrying about minor matters
3 = Apprehensive attitude apparent in face or speech
4 = Fears expressed without questioning

11) Anxiety Somatic

0 = Absent
1 = Mild
2 = Moderate
3 = Severe
4 = Incapacitating

Physiological concomitants of anxiety (eg, dry mouth, wind, indigestion, diarrhea, cramps, belching, palpitations, headaches, hyperventilation, sighing, urinary frequency, sweating)

12) Somatic Symptoms - Gastrointestinal

0 = None
1 = Loss of appetite but eating without staff encouragement; heavy feelings in abdomen
2 = Difficulty eating without staff urging: requests or requires laxatives or medication for bowels or medication for GI symptoms

13) Somatic Symptoms-General

0 = None
1 = Heaviness in limbs, back, or head; backaches, headache, muscle aches; loss of energy and fatigability
2 = Any clear-cut symptom rates 2

14) Genital Symptoms (loss of libido, menstrual disturbance)

0 = Absent
1 = Mild
2 = Severe

15) Hypochondriasis

0 = Not present
1 = Self-absorption (bodily)
2 = Preoccupation with health
3 = Frequent complaints, requests for help, etc
4 = Hypochondriacal delusions

16) Loss of Weight (rate either A or B)

A. When rating by history:-
0 = No weight loss
1 = Probate weight loss associated with present illness
2 = Definite (according to patient) weight loss
3 = Not assessed

B. On weekly ratings by ward psychiatrist, when actual weight changes are measured:
0 = Less than 1 ib weight loss in week
1 = Greater than 1 ib weight loss in week
2 = Greater than 2 ib weight loss in week
3 = Not assessed

17) Insight

0 = Acknowledges being depressed and ill
1 = Acknowledges illness but attributes cause to bad food, climate, overwork, virus, need for rest, etc.
2 = Denies being ill at all

18) Diurnal Variation

A. Note whether symptoms are worse in morning or evening. If NO diurnal variation, mark none
0 = No variation
1 = Worse in AM
2 = Worse in PM

B. When present, mark the severity of the variation. Mark "None" if NO variation
0 = None
1 = Milk
2 = Severe

19) Depersonalization and Derealization (feelings of unreality, nihilistic ideas)

0 = Absent
1 = Mild
2 = Moderate
3 = Severe
4 = Incapacitating

20) Paranold Symptoms

0 = None
1 = Suspicious
2 = Ideas of reference
3 = Delusions of reference and persecution

21) Obsessional and Compulsive Symptoms

0 = Absent
1 = Mild
2 = Severe

ANNEXURE – 3

HAMILTON RATING SCALE FOR ANXIETY (HAM-A)

1) ANXIOUS MOOD

Worries, anticipation of the worst, fearful anticipation, irritability.

2) TENSION

Feelings of tension, fatigability, startle response, moved to tears easily, trembling, feelings of restlessness, inability to relax.

3) FEARS

Of dark, of strangers, of being left alone, of animals, of traffic, of crowds.

4) INSOMNIA

Difficulty in falling asleep, broken sleep, unsatisfying sleep and fatigue on waking, dreams, nightmares, night terrors.

5) INTELLECTUAL

Difficulty in concentration, poor memory

6) DEPRESSED MOOD

Loss of interest, lack of pleasure in hobbies, depression, early waking diurnal swing.

7) SOMATIC (Muscular)

Pains and aches, twitchings, stiffness, myoclonic jerks, grinding of teeth, unsteady voice, increased muscular tone.

8) SOMATIC (Sensory)

Tinnitus, blurring of vision, hot and cold flushes, feelings of weakness pricking sensation.

9) CARDIOVASCULAR SYMPTOMS

Tachycardia, palpitations, pain in chest, throbbing of vessels, fainting, feelings, sighing, dyspnea.

10) RESPIRATORY SYMPTOMS

Pressure or constriction in chest, choking feelings, sighing, dyspnea.

11) GASTROINTESTINAL SYMPTOMS

Difficulty in swallowing, wind, abdominal pain, burning sensations, abdominal fulness, nausea, vomiting, borborygmi, looseness of bowel, loss of weight, constipation.

12) GENITOURINARY SYMPTOMS

Frequency of micturition, urgency of micturition, amenorrhea, development of frigidity, premature ejaculation, loss of libido, impotence, menorrhagia.

13) AUTONOMIC SYMPTOMS

Dry mouth, flushing, pallor, tendency to sweat, giddiness, tension, headache, raising of hair.

14) BEHAVIOUR AT INTERVIEW

Fidgeting, restlessness or pacing, tremor of hands, furrowed brow, sighing or rapid respiration, facial pallor, swallowing etc.

ANNEXURE - 4

MINI MENTAL SCALE (MMSE)

Score	Item

5 ( ) **TIME ORIENTATION**

Ask:

What is the year .....(1) Season .....(1)

month of the year .....(1) date .....(1)

day of the week .....(1)?

5 ( ) **PLACE ORIENTATION**

Ask:

Where are we now? What is the state .....(1) city .....(1)

party of the city .....(1) building .....(1)

floor of the building.....(1)?

3 ( ) **REGISTRATION OF THREE WORDS**

Say: Listen carefully. I am going to say three words. You say them back after I stop. Ready? Here they are... PONY (wait 1 second). QUARTER (wait 1 second). ORANGE (wait one second). What were those words?

..... (1)

..... (1)

..... (1)

Give one point for each correct answer, then repeat them until the patient learns all three

5 ( ) **SERIAL 7s AS A TEST OF ATTENTION AND CALCULATION**

Ask: Subtract 7 from 100 and continue to subtract 7 from each subsequent remainder until I tell you to stop. What is 100 take away 7?..... (1)

Say:

Keep going ..... (1) ..... (1)

..... (1) ..... (1)

3 ( ) **RECALL OF THREE WORDS**

Ask:

What were those three words I asked you to remember?

Give one point for each correct answer ..... (1)

..... (1) ..... (1)

2 ( ) **NAMING**

Ask:

What is this? (show pencil).....(1) What is this? (show watch) ..... (1)

1 ( ) **REPETITION**

Say:

Now I am going to ask you to repeat what I say, Ready? No its, ands, or buts

Now you say that ..... (1)

3 ( ) **COMPREHENSION**

Say:

Listen carefully because I am going to ask you to do something: Take this paper in your left hand (1), fold it in half (1), and put it on the floor (1)

1 ( ) **READING**

Say

Please read the following and do what it says, but do not say it aloud (1)

Close your eyes

1 ( ) **WRITING**

Say:

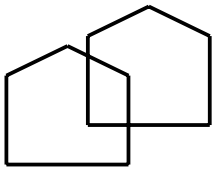
Please write a sentence. If patient does not respond, say: Write about the weather (1)

.....

.....

1 ( ) **DRAWING**

Say: Please copy this design



ANNEXURE-5

THE BRIEF PSYCHIATRIC RATING SCALE (BPRS)

This form consists of 18-symptom constructs, each to be rated on a 7-point scale of severity, ranging from "not present" to "extremely severe". It a specific symptom is not rated, make "o" = Not Assessed. Enter the score for the description which best describes the patient's condition.

0 = not assessed
1 = not present
2 = very mild
3 = mild
4 = moderate
5 = moderately severe
6 = severe
7 = extremely severe

1 **Somatic Concern:** Degree of concern over present bodily health. Rate the degree to which physical health is perceived as a problem by the patient, whether complaints have a realistic basis or not.

2. **Anxiety:** Worry, fear, or over concern for present or future. Rate solely on the basis of verbal report of patient's own subjective experiences. Do not infer anxiety from physical signs or from neurotic defense mechanisms

3. **Emotional Withdrawal:** Deficiency in relating to the interviewer and to the interviewer situation. Rate only the degree to which the patient gives the impression of failing to be in emotional contact with other people in the interview situation

4. **Conceptual Disorganisation:** Degree to which the thought processes are confused, disconnected, or disorganized. Rate on the basis of integration of the verbal products of the patient; do not rate on the basis of patient's subjective impression of his own level of functioning.

5. **Guilt Feelings**: Overcome or remorse for past behavior. Rate on the basis of the patient's subjective experiences of guilt as evidenced by verbal report with appropriate affect; do not infer guilt feelings from depression, anxiety, or neurotic defenses.

6. **Tension**: Physical and motor manifestations of tension, nervousness, and heightened activation level. Tension should be rated solely on the basis of physical signs and motor behaviour and not on the basis of subjective experiences of tension reported nby the patient.

7. **Mannerisms and Posturing:** Unusual and unnatural motor behavior, the type of motor behavior which causes certain mental patients to stand out in a crowd of normal people. Rate only abnormality of movements, do not rate simple heightened motor activity here.

8. **Grandiosity:** Exaggerated self-opinion, conviction of unusual ability of powers. Rate only on the basis of patient's statements about himself or self in relation to others, not on the basis of his demeanor in the interview situation.

9. **Depressive Mood**: Despondency in mood, sadness, Rate only degree of despondency; do not rate on the basis of interferences concerning depression based upon general retardation and somatic complaints.

10. **Hostility**: Animosity, contempt, belligerence, disdain for other people outside the interview situation. Rate solely on the basis of the verbal report of feelings and actions of the patient toward others; do not infer hostility from neurotic defenses, anxiety, nor somatic complaints. Rate attitude toward interviewer under "uncooperativeness".

11. **Suspiciousness:** Belief, delusional or otherwise, that others have now or have had in the past, malicious or discriminatory intent toward the patient. On the basis of verbal report, rate only those suspicions which are currently held whether they concern past or present circumstances.

12. **Hallucinatory Behavior:** Perceptions without normal external stimulus correspondence. Rate only those experiences which are reported to have occurred which the last week and which are described as distinctly different from the thought and imagery processes of normal people

13. **Motor Retardation**: Reduction in energy level evidenced by slowed movements. Rate on the basis of observed behaviour of the patient only; do not rate on the basis of patient's subjective impression of own energy level.

14. **Uncooperativeness**: Evidence of resistance, unfriendliness, resentment, and lack of readiness to cooperate with interviewer. Rate only on the basis of the patient's attitude and responses to the interviewer, and interview situation; do not rate on the basis of reported resentment or uncooperativeness outside the interview situation

15. **Unusual Thought Content**: Unusual, odd, strange, or bizarre thought content. Rate here the degree of unusualness, not the degree of disorganization of thought processes.

16. **Blunted Affect**: Reduced emotional tone, apparent lack of normal feeling or involvement.

17. **Excitement:** Heightened emotional tone, agitation, increased reactivity.

18. **Disorientation:** Conclusion or lack of proper association for person, place, or time.

ABBREVIATIONS

ICD	-	International Classification of Diseases
HRSD, HAMD	-	Hamilton Rating Scale for Depression
HARS, HAMA	-	Hamilton Rating Scale for Anxiety
MMSE	-	The Mini Mental State Examination
BPRS	-	Brief Psychiatric Rating Scale.
T_3	-	Tri Iodo Thyronine
T_4	-	Thyroxine
TSH	-	Thyroid Stimulating Hormone

KEY TO MASTER CHART

A	Serial number	
B	Group	1 Case
		2 Control
C	Sex	1 Male
		2 Female
D	Age	1 18-30yrs 2)31-50yrs.3)51-65yrs.4)>65yrs.
E	Religion	1 Hinduism
		2 Islam
		3 Christianity
		4 Others
F	Marital status	1 Married
		2 Unmarried
		3 Married&Divorced
		4 Married&Seperated
G	Education	0 Illeterate
		1 upto8th std
		2 8th-12th std
		3 Higher studies
H	Occupation	0 Unemployed
		1 Manual labourer
		2 Others
I	Family type	1 Nuclear
		2 Joint
J	Income	1 <1500
		2 1500-5000
		3 >5000
K	Symptom Duration	0 Asymptomatic
		1 <6m
		2 6m-1yr
		3 >1yr
L	Free T4 level(ng/ml)	1 <0.6
		2 0.6-0.8
		3 0.8-2
M	TSH level(micro IU/ml)	1 0.39-6.16
		2 6.16-10
		3 >10
N	Thyroid subtype	1 Clinical hypothyroidism
		2 Subclinical Hypothyroidism
		3 Euthyroid
	0 Psychiatric sequelae	0 No Psychiatric disorder
		1 Depression
		2 Anxiety Disorder
		3 Cognitive Impairment
		4 Psychosis