

## Assessment of thyroid dysfunction among different psychiatric disorders

<sup>1</sup>Dileep Singh Verma, <sup>2</sup>Bhagyashree Garasia, <sup>3</sup>Amrit Ku Gausai, <sup>4</sup>Suresh Gocher, <sup>5</sup>Sushil Kherada

<sup>1</sup>M.D, Assistant Professor, Department of Psychiatry, R.N.T. Medical College, Udaipur, Rajasthan, India

<sup>2</sup>M.D, Assistant Professor, Department of Psychiatry, Government Medical College, Dungarpur, Rajasthan, India

<sup>3</sup>M.D, Junior Specialist, Department of Psychiatry, Government Medical College, Dungarpur, Rajasthan, India

<sup>4</sup>M.D, Associate Professor, Department of Psychiatry, R.N.T. Medical College, Udaipur Rajasthan, India

<sup>5</sup>M.D, Senior Professor, Department of Psychiatry, R.N.T. Medical College, Udaipur, Rajasthan, India

### Corresponding Author:

Bhagyashree Garasia ([bhagyashree10garasia5@gmail.com](mailto:bhagyashree10garasia5@gmail.com))

### Abstract

Thyroid hormone abnormality is mutual in foremost psychiatric disorders. Thyroid hormones play critical function in the method of Neurogenesis and Neurodevelopment i.e., Myelination, dendrite proliferation and formation of synapses. There is link among thyroid axis and several experienced psychiatric disorders. Noteworthy results on cerebral thyroid characteristic are observed while there are even small variations in thyroid hormone levels, within the normal range. Alterations in mood, behaviour and cognition are resulting from this. Depression, psychosis and cognitive disorder are observed in the patients of hypothyroidism. Meanwhile, people with hyperthyroidism had been observed to have psychosis, aggression, anxiety as well as cognitive impairment. Memory impairment is related with Subclinical hypothyroidism.

The objective of this study was to analyse the socio-demographic profile with assessment and comparison the type of thyroid dysfunction among patients with major psychiatric disorders. This was a cross-Sectional Observational study on 166 patient samples. Assess serum thyroid stimulating hormone (TSH), T3 (triiodothyroxine), T4 (L-thyroxine), free unbound fractions of T3 and T4 (FT3 and FT4) with the COBAS e 411 ANALYSER at Kalpana path lab, R.M.R.S.M.B. govt. hospital, Udaipur for all recruited patients.

Result of our study is that thyroid dysfunction occurs significantly in patients with psychiatric disorders. Subclinical hypothyroidism was the most common abnormality observed in the study population. Thyroid dysfunctions were predominant in females. Most of the cases with thyroid dysfunction were from rural area and age group 41-50 years. In present study, 25% of total cases drug naïve for  $\geq 6$  months and 10.6% of total new cases had thyroid dysfunction. Most of the cases with thyroid dysfunction were related to F20-F29 block. Isolated increased FT4 level found in significant proportion of population. This is a useful finding as this calls for frequent monitoring of Thyroid function tests in all psychiatric patients on treatment, to

enable proper management.

**Keywords:** Hyperthyroidism, hypothyroidism, psychosis, schizophrenia

## Introduction

The thyroid gland is the biggest endocrine gland of body, weighing roughly 18-60 gms in adult <sup>[1]</sup>. Thyroid hormones play a crucial role for brain cells and their development and physiological functioning of the central nervous system (CNS) throughout life <sup>[2]</sup>. Thyroid cells are highly specialized to absorb and use iodine. Every other cell depends on the thyroid to manage its metabolism <sup>[3, 4]</sup>. Thyroid dysfunction is defined as the altered serum thyroid stimulation hormone (TSH) level with normal or altered thyroid hormones (free triiodothyronine fT3 and free thyroxine-fT4) <sup>[5]</sup>. Free T4 and Free T3 measure the particular active fraction of hormones that are entering our cells and controlling our health. The totals are the reservoirs of hormone that circulate in blood, bound on to transport proteins specially designed for the purpose. These release T4 and T3 into the free fractions as your tissues need them. Problem is that individuals are very variable with in the amount of transport of proteins they need, and thus the hormone reservoirs <sup>[6]</sup>. They can change by minimum of 2-fold from person to person, and in rare people even more than that. Measurements of Free T4 and Free T3 concentrations, therefore, correlate more reliably with clinical status than total T3 and total T4 levels. Thyroxine (T4) and triiodothyronine (T3) are produced by the thyroid gland after receiving stimulation from the thyroid-stimulating hormone (also called thyrotropin) which is synthesized and secreted by thyrotrope cells in the anterior pituitary gland. This is the hormone which regulates the endocrine function of the thyroid <sup>[7]</sup>.

ICD-10 defines various psychiatric disorders- Schizophrenia, Schizoaffective disorder, Major depressive disorder, Bipolar disorder, Acute psychosis, Dissociate disorder, Panic disorder, Substance use disorder etc <sup>[8]</sup>. While the diagnosis of psychiatric disorders depends on various criteria, Thyroid function tests are currently accustomed assist the diagnosis, treatment and prognosis of assorted psychiatric conditions. This is often because both hypothyroidism and hyperthyroidism are found to be related to neuropsychiatric manifestations like psychosis, anxiety, depression and mood disorders <sup>[9, 10, 11]</sup>. Most psychiatric patients might not have overt thyroid dysfunction. If a thyroid abnormality is present, it is usually mild and may be considered as a risk factor for disorder instead of as a determinant <sup>[12]</sup>. This is an important factor in the treatment of psychiatric illnesses as studies show that TSH levels are directly linked with the severity of psychiatric co morbidity. This makes a case for screening, and has implication for prognosis and treatment response. Studies on the coexistence of thyroid dysfunction and major psychiatric disorders with in the Indian population are limited. Hence, this study going to be carried out to evaluate and compare the presence of thyroid dysfunction in psychiatric patients.

## Aims and Objectives

**Aims:** “Assessment of Thyroid dysfunction among Major Psychiatric disorders in Udaipur region”.

## Objectives

1. To study the socio-demographic profile of psychiatric patients.
2. To assess the type of thyroid dysfunction among patients with major psychiatric disorders.
3. To compare various thyroid dysfunction among major psychiatric disorders.

## Materials and Methods

A cross-Sectional observational study was conducted in Department of Psychiatry, M.B. Govt. Hospital, R.N.T. Medical College, Udaipur. All consecutive patients attending psychiatry department who were full-filling the inclusion and exclusion criteria were considered. Duration of study was from 20th September 2017 to 28th February 2018.

### Inclusion criteria

Patients aged 15 to 60 years of both the gender who presenting for first time in psychiatric outdoor of M.B. Government hospital, Udaipur (1st episode) without on treatment for thyroid disorder or if patient is a known case of psychiatric disorder but is drug naïve for 6 months for psychotropic drug/drugs. Patient/attendant should give informed consent and full-fill the ICD-10 criteria for psychiatric disorder.

### Exclusion criteria

Patient who presenting for first time in psychiatric outdoor of M.B. Government hospital, Udaipur (1st episode) with on treatment for thyroid disorder or on psychotropic drug/drugs or other drugs which affects thyroid functions. Patients suffering from any other neurological disorders or significant physical co-morbidity, a case of mental retardation or pregnancy. Patient is having history of significant substance abuse or dependence except tobacco and age less than 15 or more than 60 years should excluded.

### Instruments of study

- 1) **Consent form:** This form was in Hindi language & it was given, once the patient enrolled in the study.
- 2) **Screening Performa:** This included basic questions regarding the Patient's complains, history details (past, family, personal), history of questions related to the eligibility for determining the inclusion & exclusion criteria.
- 3) **Modified kuppuswamy scale:** For socio-demographic profile.
- 4) **ICD-10 (diagnostic criteria):** Used for finding of major psychiatric disorders including Schizophrenia, schizotypal and delusional disorders [F20-29], Mood/Affective disorders [F30-39], Neurotic, stress related and somatoform disorders [F40-48] and Behavioural syndromes associated with physiological disturbances and physical factors [F50-59] blocks.
- 5) **Thyroid function test assessment:** Thyroid function test was measured with the COBAS e 411 ANALYSER, which is an automated random-access, multichannel analyser for immunological assay (Roche Diagnostic Ltd). It is planned for both qualitative and quantitative in vitro determination of a wide range of analytes by use of electro-chemiluminescence technology.

Thyroid function test assessment [Estimation of T3, T4, TSH, FT3, FT4] was measured with the COBAS e 411 ANALYSER by use of electro-chemiluminescence technology at Kalpana path lab, R.M.R.S. M. B. govt. hospital, Udaipur and its biological ref. interval for T3 0.8-2.0 ng/ml, T4 5.1-14.1 µg/dl, FT3 2.3-4.2 pg/ml, FT4 0.89-1.79 ng/dl, TSH 0.27-4.2 µIU/ml, The study was conducted at the Department of Psychiatry, RNT Medical College, Udaipur a tertiary-care government teaching hospital in the state of Rajasthan. The centre has both outpatient and inpatient facilities and caters patients with a wide variety of psychiatric disorders. Patients seeking care at the hospital are either self-referred, or referred from other

hospitals or private practitioners.

## Results

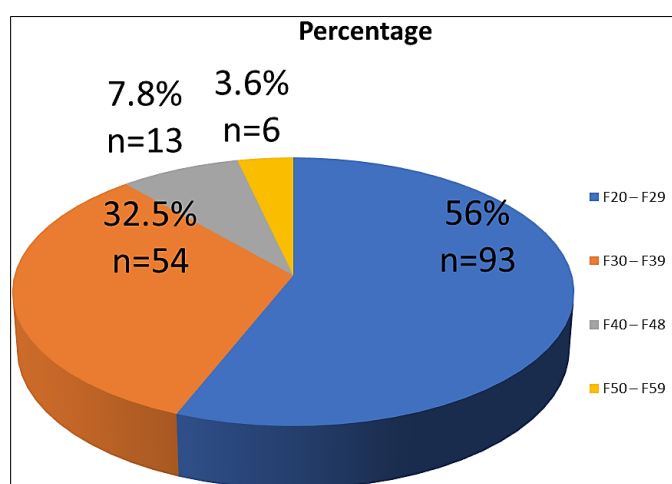
The present study constitutes 166 patients who met inclusion criteria and exclusion criteria. They were selected from the OPD of PSYCHIATRIC dept. of M.B.G. Hospital, attached to R.N.T. Medical College, Udaipur (Rajasthan).

In the Present Study, Majority of Study Population Were Males (101/166). In the study patient's age ranged from 15-60 yrs. and Majority of Cases (47 or 28.3%) were within 21-30 Years of Age. The mean age of participants was 30.09 with S.D 13.81. Most of the cases were related from Rural area in this study (114 or 68.7%), rest of the 52 (31.3%) were from Urban area. Most of the cases were new cases (142 or 85.5%). Cases with Drug naïve for  $\geq 6$  months were 24 (14.5%).

**Table 1:** Patient Profile

Variable	Value	Percentage	
Gender	Male	101	60.8
	Female	65	39.2
Age Group	15-20	19	11.4
	21-30	47	28.3
	31-40	38	22.9
	41-50	29	17.5
	51-60	33	19.8
Type of Residence	Rural	114	68.7
	Urban	52	31.3
Case wise type	New case	142	85.5
	Drug Naïve for $\geq 6$ months	24	14.5

In this study, majority of cases were related to Block F20-29 (93 or 56%) and 32.5% cases in F30-39, 7.8% in F40-48 and 3.6% in F50-59 Block.



**Fig 2:** ICD-10 Block wise distribution of cases

**Table 3:** Diagnosis wise distribution of thyroid dysfunction cases

Diagnosis	Hypothyroidism	Hyperthyroidism	Total	P value
Schizophrenia	6 (66.7%)	3 (33.3%)	9(100%)	0.587
ATPD	2 (100%)	0 (0%)	2(100%)	
Depressive episode	4 (100%)	0 (0%)	4(100%)	

BPAD	3 (100%)	0 (0%)	3(100%)
Manic episode	1 (100%)	0 (0%)	1 (100%)
Anxiety disorders	0 (0%)	0 (0%)	0 (0%)
Dissociative disorder	1 (100%)	0 (0%)	1 (100%)
Adjustment disorder	0 (0%)	0 (0%)	0 (0%)
OCD	0 (0%)	0 (0%)	0 (0%)
Other psychiatric disorders	1 (100%)	0 (0%)	1 (100%)
Total	18 (85.7%)	3 (14.3%)	21(100%)

Out of 21(100%) cases with thyroid dysfunction, 18 (85.7%) were case of Hypothyroidism and 3 (14.3%) were case of Hyperthyroidism. In Schizophrenic group, out of 9(100%) cases with thyroid dysfunction, 6 (66.7%) were case of Hypothyroidism and 3 (33.3%) were case of Hyperthyroidism. In ATPD group, total 2(100%) cases with thyroid dysfunction were case of Hypothyroidism. In Depressive group, total 4 (100%) cases with thyroid dysfunction were case of Hypothyroidism. In BPAD group, out of 3 (100%) cases with thyroid dysfunction were case of Hypothyroidism. In Manic group, total 1 (100%) case with thyroid dysfunction were case of Hypothyroidism. In Dissociative disorders total 1 (100%) cases with thyroid dysfunction were case of Hypothyroidism. In Anxiety disorders group, Adjustment disorder group, OCD group no case with thyroid dysfunction. In Other psychiatric disorders total 1 (100%) cases with thyroid dysfunction were case of Hypothyroidism. No significant difference was found in Thyroid Dysfunction groups among different major psychiatric disorders. (P value>0.05)

## Discussion

### Sociodemographic characteristics of patients

A total of 166 outpatients were recruited in the study out of which 60.8% (101) were males and 39.2% (65) were females. In the study patient's age ranged from 15-60 yrs. The mean age of participants was  $30.09 \pm 13.81$  S.D. These data were comparable with the study of Rajiv Radhakrishnan *et al.* [13]. Where male participants were more and mean age of the study subjects was  $37.46 \pm 13.56$  yr. Majority of Cases 47 (28.3%) were within 21-30 Years of Age and was comparable with the study of Dr. Pavan Kumar Sharma *et al.* [14]. In study 68.7% (114) cases were related from Rural area in this study, rest of the 52 (31.3%) were from Urban area. Most of the cases were new cases (142 or 85.5%). Cases Drug naïve for  $\geq 6$  months were 24 (14.5%).

In this study, majority of cases (56%) were related to Block F20-29, 32.5% cases in F30-39, 7.8% in F40-48 and 3.6% in F50-59 Block.

Schizophrenic 28.3% (47), ATPD 27.7% (46), Depressive episode 15.1% (25), BPAD 13.3% (22), Manic episode 4.2% (7), Anxiety disorder 2.4% (4), Dissociative disorder 1.8% (3), Adjustment disorder and OCD 0.6% (1), Other psychiatric disorders 6.0% (10), cases were included in the study. These data were comparable with the study of Rajiv Radhakrishnan *et al.* [13] and Krishna Bannad *et al.* [15].

In the study out of 166 patients 145 (87.3%) patients were euthyroid and 21 (12.7%) patients of the participants were with thyroid dysfunction among which 18 (10.9%) were of Hypothyroidism and 3 (1.8%) were of Hyperthyroidism. In participants having Hypothyroidism, 11 (61.1%) were female and 7 (38.9%) were male. Out of 3 (100%) participants having Hyperthyroidism, 1 (33.3%) were female and 2 (66.7%) were male.

In patients with thyroid dysfunction, 13 (61.9%) were of Subclinical Hypothyroidism, 5 (23.8%) were of Overt Hypothyroidism and 3 (14.3%) were of Overt Hyperthyroidism. In male participants with thyroid dysfunction, 6 (66.7%) were case of Subclinical Hypothyroidism, 1 (11.1%) were case of Overt Hypothyroidism and 2 (22.2%) were case of Overt Hyperthyroidism.

In female participants with thyroid dysfunction, 7 (58.3%) were case of Subclinical Hypothyroidism, 4 (33.3%) were case of Overt Hypothyroidism and 1 (8.3%) were case of Overt Hyperthyroidism. These data were comparable with the study of Dr. Dipti Bania *et al.* [16] where prevalence of hypothyroidism in the overall study population was 9.67%.

In cases with thyroid dysfunction, 11 (52.4%) cases were in F20-F29 block, 8 (38.0%) cases were in F30-F39 block, 1 (4.8%) case was in F40-F48 block and 1 (4.8%) case was in F50-F59 block. In F20-F29 block Out of total 11 (100%) cases with thyroid dysfunction, 6 (54.5%) were case of Subclinical Hypothyroidism, 2 (18.2%) were case of Overt Hypothyroidism and 3 (27.3%) were case of Overt Hyperthyroidism. In F30-F39 block Out of total 8(100%) cases with thyroid dysfunction, 5 (62.5%) were case of Subclinical Hypothyroidism and 3 (37.5%) were case of Overt Hypothyroidism. In F40-F48 block total 1(100%) cases with thyroid dysfunction were of Hypothyroidism. In F50-F59 block total 1(100%) cases with thyroid dysfunction were of Hypothyroidism. These data were contrary with the study of Upadhyay T *et al.* [17].

Evaluation of psychiatric co-morbidity among the subjects with thyroid disorder showed that; greater numbers of the subjects i.e., 48.3% (29) had neurotic, stress related and somatoform disorders (F40- F48) followed by 26.7% (16) of mood (affective) disorder (F30- F39). Others comorbidities were headache and lack or loss of sexual desire.

In Schizophrenic group, most patients were Euthyroid, followed by Hypothyroidism and then Hyperthyroidism. In ATPD group, mostly were Euthyroid followed by case of Hypothyroidism. In Depressive group the pattern was found to be similar that of ATPD group. In BPAD group, manic group and Dissociative disorders, most patients were Euthyroid and rest were Hypothyroid. In Anxiety disorders group, Adjustment disorder group OCD group all were Euthyroid. In Other psychiatric disorders almost, all were Euthyroid and rest were the case of Hypothyroidism.

No significant difference was found in Thyroid Dysfunction groups among different major psychiatric disorders. (P value>0.05) These data were comparable with the study of Rajiv Radhakrishnan *et al.* [13] Where Hypothyroidism was observed 37 of 147 (25.17%) patients with schizophrenia-spectrum disorders (schizophrenia = 25/108, schizoaffective disorder = 6/17, acute psychosis = 6/22).

Of the 185 patients with mood spectrum disorders 40 (21.62%) (bipolar disorder = 28/122, major depressive disorder =12/63) had hypothyroidism. Three subjects with schizophrenia and two with major depressive disorder had clinically significant hypothyroidism.

Hyperthyroidism was seen in six of 147 patients (4.08%) with schizophrenia-spectrum disorders (schizophrenia = 4/108, schizoaffective disorder = 1/17, acute psychosis = 1/22). Three of 185 patients (1.62%) with mood spectrum disorders (bipolar disorder= 3/122, major depressive disorder=0/63).

Overall, abnormal thyroid hormonal status was seen in 43 of 147 (29.3%) patients with schizophrenia-spectrum disorders (schizophrenia = 29/108, schizoaffective disorder = 7/17, acute psychosis = 7/22) and in 23.24 percent (43/185) of mood spectrum disorders patients (bipolar disorder = 31/122, major depressive disorder=12/63), 0.58 percent with dissociative disorder, 0.29 percent with panic disorder, 1.17 percent with other anxiety and substance use disorders.

In this study abnormal thyroid hormonal status was observed in 29.3 percent patients with schizophrenia-spectrum disorders (including schizophrenia, schizoaffective disorder, acute psychosis) in study. This was comparable with that reported in a similar study in a hospital sample in South East Asia which showed that 36.4 per cent of patients with schizophrenia had thyroid dysfunction [18]. Poyraz *et al.* [19] found that in a sample of 74 consecutive subjects with schizophrenia, 11 (14.86%) were serum positive for autoimmune thyroiditis which is comparable to our data. Thyroid dysfunction in bipolar disorder seen in that study was (25.41%) which was lower than that shown by Bartalena *et al.* [20] (32%) and higher than that

of Cassidy *et al.* [21] (11.51%). The high rate of thyroid dysfunction in schizophrenia-spectrum disorders makes a case for screening, and has implications for cognition and treatment response. Thyroid hormones have been directly implicated in working memory performance in schizophrenia [22].

In current study thyroid dysfunction was diagnosed on the basis of deviated serum TSH level. But important finding was 16 (9.6% of total participants) cases had only FT4 increased. P Saravanan *et al.* [23] strengthens this finding and concluded that free T4 concentrations may predispose to psychological morbidity even within the reference range in treated hypothyroid patients.

## Conclusion

Thyroid dysfunction occurs significantly in patients with psychiatric disorders. Subclinical hypothyroidism was the most common abnormality observed in the study population. Thyroid dysfunctions were preponderant in females. And most of the cases with thyroid dysfunction were from rural area and age group 41-50 years. In present study 25% of total cases drug naïve for  $\geq 6$  months and 10.6% of total new cases had thyroid dysfunction. Most of the cases with thyroid dysfunction were related to F20-F29 block. In this study higher prevalence of thyroid dysfunctions in patients with schizophrenia and mood disorders. Isolated increased FT4 level found in significant proportion of population. This is a useful finding as this calls for frequent monitoring of Thyroid function tests in all psychiatric patients on treatment, to enable proper management. Screening of thyroid parameters is warranted in this population in view of increasing prevalence of the study population.

## Limitations

1. Sample size was small. So further studies with larger sample size are needed.
2. This study was a hospital-based study; it may not represent the whole population.
3. Thyroid antibodies were not measured.

## References

1. Cummings CW, *et al.* Thyroid anatomy. In: Cummings CW, editor. Otolaryngology-head and neck surgery. 3rd ed. Mosby: St. Louis, 1998, 2445-9.
2. Williams PL, Bannister LH, *et al.* Gray's anatomy. 38th ed. New York: Churchill Livingstone, 1995, 1891-6.
3. Springer International Publishing Switzerland Imam SK, Ahmad SI (eds.), Thyroid Disorders: Basic Science and Clinical Practice, 2016, 4. DOI 10.1007/978-3-319-25871-3\_1.
4. <https://www.endocrineweb.com/endocrinology/overview-thyroid>
5. Peter PAS eds. Epidemiology of Thyroid dysfunction hypothyroidism and hyperthyroidism. Thyroid International. 2009;2:1-16.
6. Williams GR. Neurodevelopmental and neurophysiological actions of thyroid Hormone. J Neuroendocrinol. 2008;20:784-94.
7. The role of your thyroid in psychiatric illness, Charles Meusburger, Article Source: <http://EzineArticles.com/5506756>
8. Sapini Y, Rokiah P, Nor Zuraida Z. Thyroid disorders and psychiatric morbidities, review paper, MJP Online, Early MJP 02-08-09.
9. Bauer M, Goetz T, Glenn T, Whybrow PC. The thyroid-brain interaction in thyroid disorders and mood disorders. J Neuroendocrinol and hyperthyroidism may increase the risk of developing bipolar disorders. 2008;20:1101-1114.

10. CD-ICD-10-CM-International Classification of Diseases, Tenth Revision, Clinical Modification. www.cdc.gov.)
11. Trzepacz PT, McCue M, Klein I, Levey GS, Greenhouse J. A psychiatric and neuropsychological study of patients with untreated Graves' disease. *Gen Hosp Psychiatry*. 1988;10:49-55.
12. Robertas B, Arthur J, Prange Jr. Thyroid Disease and Mental Disorders: Cause and Effect or Only co morbidity? *Curr Opin Psychiatry*. 2010;23(4):366-68.
13. Rajiv Radhakrishnan, Sam Calvin, *et al*. Thyroid dysfunction in major psychiatric disorders in a hospital-based sample. *Indian J Med Res*. 2013 Dec;138:888-893.
14. Dr Pavan Kumar Sharma, *et al*, Study on Thyroid Dysfunction in Patients Attending Rama Medical Collage Hospital & Research Centre, Kanpur (Uttar Pradesh)-A Hospital Based Study. *JMSCR*. 2015;3(10):7750-7756.
15. Krishna Bannad, Prashanth YM. A Study of Thyroid Dysfunction among Patients with Major Psychiatric Disorders at a Tertiary Care Centre in Mangalore. *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)* e-ISSN: 2279-0853, p-ISSN: 2279-0861. 2016 Jun;15(6):115-118. Ver. XIV, www.iosrjournals.org
16. Dr. Dipti Bania, *et al*, A Study on Prevalence of Thyroid Function Disorders Amongst The Population of Barpeta District, Assam, *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 16(2), 47-50. e-ISSN: 2279-0853, p-ISSN: 2279-0861.
17. Thapa DK, Upadhyaya TL, *et al*. The study of Psychiatric Disorders in patients with Thyroid Disorder at the tertiary care centre in Western Region of Nepal. *J Psychiatrists' Association of Nepal*, 2013, 2(2).
18. Sim K, Chong SA, Chan YH, Lum WM. Thyroid dysfunction in chronic schizophrenia within a state psychiatric hospital. *Ann Acad. Med Singapore*. 2002;31:641-4.
19. Poyraz BC, Aksoy C, Balcioglu I. Increased incidence of autoimmune thyroiditis in patients with antipsychotic-induced hyperprolactinemia. *Eur Neuropsychopharmacology*. 2008;18:667-72.
20. Bartalena L, Pellegrini L, Meschi M, Antonangeli L, Bogazzi F, Dell'Osso L, *et al*. Evaluation of thyroid function in patients with rapid-cycling and non-rapid-cycling bipolar disorder. *Psychiatry Res*. 1990;34:13-7.
21. Cassidy F, Ahearn EP, Carroll BJ. Thyroid function in mixed and pure manic episodes. *Bipolar Disord*. 2002;4:393-7.
22. Zoeller RT, Rovet J. Timing of thyroid hormone action in the developing brain: clinical observations and experimental findings. *J Neuroendocrinol*. 2004;16:809-18.
23. Saravanan P, *et al*. Psychological wellbeing correlates with free T4 but not free T3 levels in patients on 'adequate' thyroid hormone replacement, *Endocrine Abstracts*. 2006;11:781.