ejpmr, 2020,7(8), 523-525

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

PREVALENCE OF THYROID DYSFUNCTION IN SCHIZOPHRENIA

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Article Received on 09/06/2020 **Article Revised on 29/06/2020** **Article Accepted on 19/07/2020**

ABSTRACT

Schizophrenia is a complex and pathological brain developmental disorder with multiple neurotransmitters abnormalities. The most commonly affected neurotransmitters are dopamine, serotonin, glutamate, and GABA. Thyroid hormone plays important role in brain development and also modulates all these neurotransmitters. Association between mental state and thyroid function has been long recognized since the earliest description of myxedema and thyrotoxicosis. But its role in psychotic disorder is often ignored and rarely assessed. This study was planned to study prevalence and type of thyroid dysfunction in schizophrenia. A present study is conducted on 100 patients newly diagnosed with schizophrenia using ICD-10 criteria from department of psychiatry. Serum Thyroid stimulating hormone (TSH), T3 (triiodothyroxine) and T4 (L-thyroxine) levels were estimated by radioimmunoassay technique. The data were analyzed using Chi-square (χ^2) test. Out of 100 patients 27 patients were found to have abnormal thyroid function test, from which 4 were hyperthyroidism and 23 were hypothyroidism. These finding suggests there is high prevalence of thyroid abnormality in patients suffering from schizophrenia. So patients with schizophrenia-spectrum disorders should be screened for abnormal thyroid hormonal status.

KEYWORDS: Schizophrenia, Thyroid Dysfunction, Hypothyroidism, and Hyperthyroidism.

INTRODUCTION

It has been found that psychiatric manifestations may be a prominent feature of hyperthyroidism and hypothyroidism.[1,2] A number of studies suggested that the episodes of hyperthyroidism.[3,4] or hypothyroidism may be precipitated by psychological stress. In addition, an integral relationship between the hypothalamic-pituitary-thyroid axis and affective psychiatric disorders have also been found.[5-7] It is well recognized that acute and chronic illness can produce profound alterations in thyroid function. In 1979, Cohen and Swigar[8] suggested that alterations in thyroid function are found in psychologically ill person. In 1998, Placidi et al. have also found higher rates of panic disorder, simple phobia, obsessive–compulsive disorder, major depressive disorder, bipolar disorder in thyroid patients than in the general population. Recently, Radhakrishnan R et al, in 2013 assessed thyroid status in schizophrenia-spectrum disorders.[9] This suggests co-occurrence of psychiatric and thyroid diseases, which may be the result of common biochemical abnormalities. Very few studies assessed Thyroid Hormone in patients suffering from schizophrenia. Thus the present study was designed to determine the prevalence of thyroid dysfunction in psychiatric patients with schizophrenia.

Schizophrenia as one of the most severe psychiatric disorders has the prevalence of 0.7 – 1.0%. It has Chronic and debilitating course, with many patients responding poorly to medication and suffering frequent and disrupting relapse. It usually presents with psychotic symptoms like delusions and hallucinations, thought disorder, and deficit features described as ‘‘negative’’ symptoms. Schizophrenia is a highly heritable disorder of complex genetic etiology.

Thyroid gland produce thyroxine (T4) and triiodothyronine (T3), which in turn are stimulated by Thyroid-stimulating hormone (also known as thyrotropin, TSH) which is synthesized and secreted by thyrotrope cells in the anterior pituitary gland. Production and secretion of TSH is stimulated by the hypothalamus, which produces thyrotropin-releasing hormone (TRH). Production of TSH is inhibited by somatostatin, which is also produced by the hypothalamus, and via a negative feedback loop by T3 and T4.[10]

MATERIAL AND METHODS

The present study was conducted in department of biochemistry in collaboration with Department of Psychiatry at Pt. B. D. Sharma, PGIMS, Rohtak with strict accordance to the protocol approved by the ethical

committee. A total of 100 schizophrenia patients were enrolled in the study, diagnosed by psychiatrist as per DSM V (confirmed by MINI-Plus). Newly diagnosed patients from 18 years to 55 years were included in the study; old cases of Schizophrenia, any chronic physical illness or patients on thyroid medication were excluded. As Neuroleptic medication has effect on deiodinases activities, N-glucuronidation of TH, and by consequence on TH levels. Haloperidol enhance type 2 deiodinase, Clozapine decreases type 2 but increases type 3 deiodinase activity in several brain regions. Other antipsychotics, such as clozapine, are piperazine-containing drugs that undergo N-glucuronidation. Given that the enzyme UDP-glucuronosyltransferase is responsible for the glucuronidation of TH, a competitive mechanism may be conducive to TH level changes.

Five ml venous blood sample was taken from antecubital vein aseptically in plain vials from each subject after obtaining Written informed consents from the patients or their family members. Samples were used after serum separation. Serum was separated by centrifugation (2000rpm X 10 minutes) after clotting. Total T3, T4 and TSH levels were measured within one hour of sample collection.

TT3, TT4 Levels were measured by RIA technology.[11] While TSH levels were estimated by IRMA technology. TSH> 4.I μIU/ml with T4 < 6.09 μIU/ml was considered to represent clinically significant hypothyroidism, while TSH ≤ 0.02 μIU/ml was considered to indicate clinically significant hyperthyroidism.[12]

RESULTS

The thyroid status of 100 patients with schizophrenia was assessed. Out of which 42 were women and 58 were males. Among 42 women, 27 had Normal TSH levels, 11 had high TSH Levels (Hypothyroidism) and 2 were found to be Hyperthyroidism (Low TSH Levels). Out of 58 males, 42 were normal, 12 had Hypothyroidism and 2 had hypothyroidism. These finding suggested that there was not much gender difference but there is high prevalence of thyroid abnormality in patients suffering from schizophrenia. So patients with schizophrenia-spectrum disorders should be screened for abnormal thyroid hormonal status.

Table 1: Age and sex distribution of patients.

Age group	<30	30 - 45	45-55	Total
Women	35	6	1	42
Men	46	10	2	58
Total	81	16	3	100

Table 2: Prevalence of thyroid abnormality in patients suffering from schizophrenia.

Gender	TSH (Normal)	Abnormal TSH (Hypothyroidism)	Abnormal TSH (Hyperthyroidism)
Women	27	11(26.2)	2(4.76)
Men	42	12(20.69)	2(3.44)

DISCUSSION

We have found prevalence of thyroid dysfunction in schizophrenia patients. This follows up the work of Radhakrishnan et al. [2013] and study conducted in a hospital sample in South- East Asia which showed that 36.4 per cent of patients with schizophrenia had thyroid dysfunction.[13]

Thyroid hormones play an important role in neurodevelopment, specifically in neurogenesis, myelination, dendrite proliferation and formation of synapses. TH modulates crucial brain neurotransmitter systems including the dopaminergic, serotonergic, glutamatergic, and *δ*-amino- butyric acid (GABA) menergic networks.[14] All these neurotransmitters systems are involved in pathogenesis of schizophrenia and drugs acting on these neurotransmitters improve symptoms of schizophrenia. The interaction between the pituitary-thyroid axis and the neurotransmitters are strongly implicated in schizophrenia.

Thyroid hormones regulate the levels of dopamine receptors and the activity of tyrosine hydroxylase, the rate limiting enzyme of the cathecolaminergic pathway.[15-17] Dopamine inhibits TSH secretion, as treatment with dopamine blockers lead to increase in TSH level or to subclinical hypothyroidism, and that hypothyroidism can lead to increased dopamine receptor sensitivity. Strawn et al., 2004 established a link between serotonergic system and TH modulation. CSF levels of 5 – hydroxyindoleacetic acid (5-HIAA) and homovanillic acid, major metabolites of serotonin and dopamine and plasma concentrations of THs were measured, indicative of Monoamino interaction. Diminished 5HT activity in hypothyroidism was found.[18]

The role of T3 on glutamatergic system in Central nervous system (CNS) was studied by Mendes-de-Aguiar et al. T3 is capable of regulating extracellular glutamate levels by modulating the astrocytic glutamate transporters and, consequently, by promoting neuronal development and neuroprotection.[19] The role for the GABA-ergic system in the pathogenesis of schizophrenia derives mostly from neuropathologic studies. In schizophrenic patients there is upregulation of the postsynaptic GABA-A receptors and reduction of glutamic acid decarboxylase (GAD) 67 and reelin (a protein that colocalizes with GABAergic

interneurons).[20] TH effect GABAergic system at multiple levels, i.e circuit formation, synthesis and metabolism of GABA, GABA release and reuptake, and GABA receptors.[21]

Our study had few limitations. A sample size needs to be large along with controls that would provide 80% power to detect this association with 95% confidence. Cerebro spinal fluid (CSF) Thyroid Hormone Level could have been assessment as CSF TH level samples more likely represent TH brain homeostasis (study in an Alzheimer's disease population, which revealed rT3 level alterations in the CSF that were not reflected in the sera samples). Familial, Prenatal, Neonate, and Early Childhood Thyroid Status was not known. Diagnostic groups of our study were not homogenous; the women were less as compared to man in the schizophrenia group.

CONCLUSION

Despite these limitations, the prevalence of abnormal thyroid hormonal status was found in this patient population. This implicates that schizophrenia patients need to be regularly screened/treatment for abnormal thyroid hormonal status. The fine-tuning of these networks and their precise implication on disease etiology certainly warrants further investigation.

ACKNOWLEDGEMENT

We have no acknowledgements to make.

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