

Depression, Well-being and Hypothyroidism

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Abstract

Background: A connection between hypothyroidism and depression has been presumed for many years; however, the ground reality between such association has been difficult to outline with a lot of differing studies. With large cohort studies and in recent years, our understanding about this association has improved, but still the gray area remains much at large in comparison to what is crystal clear to us.

Objectives: Literature was reviewed regarding thyroid function and depression to assess if relationship between these two have been established or not.

Methods: PubMed was used as the database and the terms used to search literature were 'thyroid', 'mental health' and 'depression'. The key strategy was to review as many recent studies as we can and compare it to the ones which were conducted years ago. Sample size was also considered, and studies with a larger number of subjects were preferred. Results from these studies were compiled at one place and key common factors were looked for, linking hypothyroidism with depression.

Results: Despite large epidemiological studies, concrete relation between thyroid function and depression can't be established without thyroid dysfunction. The relation of the Hypothalamic-pituitary-thyroid function, the chief monoamines and the clinical subtypes of depression is intricate and does not directly establish a straight relationship. Subjects taking thyroxine have subordinate psychological well-being than subjects who are euthyroid. TSH cut of value for hypothyroid patients to be psychologically sound has been established to be 2.5 MIU/L.

Conclusion: After many years of research, still we remain in dark with respect to the relation between thyroid and depressive symptoms and it largely remains unclear. Hence, further studies will be required to build up strong evidence and connection between the two and to also state the pathophysiology behind it.

Keywords: Hypothyroidism; Depression; Thyroxine

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Introduction

Hypothyroidism has been linked to depression as there is overwhelming evidence that it triggers affective disease and psychic disorders. Patients with depression have a higher occurrence of hypothyroidism and patients those who are hypothyroid have a frequent incidence of depressive syndrome. Such observations were first noticed due to the similarity of the symptoms that both depression and Hypothyroidism exhibit. Also, then it was noticed that thyroid hormones were used in the treatment of clinical depression. In the year of 1949, a scientist named Asher described the connection between hypothyroidism and absurdity

in 14 clinical cases, and he called it 'myxedema madness' and exclusively stated that a melancholic state is demonstrable in Hypothyroidism that can easily be reverted with the use of thyroid hormones. A strong indicator came to light and it was that the aberrant abnormalities in the Hypothalamic-Pituitary-Thyroid axis of individuals suffering from depression [1].

Furthermore, it was scientifically established that thyroid hormone plays a significant and crucial role in the development and proper functioning of the brain. Thyroxine (T4) was the one mainly playing this key role. This hormone is necessary even during gestational period for the growth of fetal brain.

A study by Bathla concluded that psychiatric symptoms/disorders are common among people with hypothyroidism. His study was gender based and included both anxiety and depressive symptoms, the common being mood changes being the top among men and gastrointestinal somatic symptoms being the most in women [2].

Hypothyroidism also significantly alters the flow of blood and glucose utilization in the brain. Furthermore, patients with signs of depression may have structural aberrations of the hippocampus leading to defects in the memory function that it executes. Moreover, Thyroid peroxidase antibodies (TPO) have been linked to depressive states. Depression is variable and is prejudiced by vulnerability and the gradation, though not always, of thyroid catastrophe [3].

Importance of Thyroid Hormone

The standing of thyroid hormones on cerebral advancement and working are put forward by the dire neurological consequences of significant iodine deficiency, MCT8 mutations and untreated congenital hypothyroidism. Also with studies and progression in this matter we have come to realize the status of thyroid hormone transporters and iodothyronine deiodinases in carrying the hormones to specific locations where they need to exert their functions.

A Descriptive analytical comparative study conducted in Iran showed that the quality of life was somewhat similar in those people with or without hypothyroidism, but the mental health level significantly differed. Those with decreased levels of thyroid hormone through a questioner were found to be depressed and suffering from anxiety [4].

Thyro-stress

A study conducted by Sanjay Kalra et al. outlined the depressive symptoms associated with hypothyroidism. These symptoms were multifaceted and included social, psychological, financial and health related aspects. The word "thyro-stress" was proposed to explain these emotions, which may range from concern to terror, from anxiety to misery, or from lack of self-confidence to embarrassment. Although, many of these symptoms may be explained by uncontrolled hypothyroidism **itself**, they may also be attributed to unrecognized stress due to disease burden [5].

TSH (Thyroid Stimulating Hormone)

The levels in plasma of Thyroid Stimulating Hormone (TSH) are the most endorsed test to assess the thyroid function. The normal range varies in the general population, and for most of the laboratories it falls between 0.35 and 5.50 mIU/L.

Some studies with depressed patients found a reduced basal serum level of TSH, but within the normal variation range. However, one study conducted by Talaeia A et al. included participants that were in total 174 hypothyroid patients. Study basis was Beck depression test where a score of less than 10 was considered healthy and a score of more than 10 was well-thought-out to be depressed. In accordance to Roc curve analysis, the optimal cut- off value of TSH was 2.5 MIU/L with high sensitivity. The optimum TSH cut- off in light of severe depression was 4 MIU/L [6].

A most likely theory for the upsurge in serum TSH in depressive states branches from the observations that the plasma levels of this hormone is also prejudiced by somatostatin. Somatostatin inhibits the release of TSH by the hypophysis. Some studies also mentioned that there is reduction in somatostatin levels in the Cerebrospinal fluid of depressed subjects, and this may be the responsible factor for the increase of serum TSH in clinical depression.

TRH (Thyroid Releasing Hormone)

One of a study by Banki et al. ascertained the brain Thyrotropin releasing hormone levels in depressed and maniac individuals and compared it to a control group who were psychologically sound and well. It was found out that there is a three-fold increase in the TRH levels in depressed individuals in comparison to the controls. Another study demonstrated high levels of TRH in the cerebrospinal fluids of depressed patients [7,8].

This long-lasting stimulation of TRH in the hypophysis could possibly be the cause for the TSH serum variations found in depressed patients. Another study established that the recurrent administration of TRH causes a dampened response to the TRH challenge test, that which happens in depressive states too [9,10].

Autoimmunity

Numerous studies have examined whether the presence of autoimmunity with thyroid hormone levels well within the reference range is linked to depression. It has been established that stressful proceedings can intensify or trigger episodes of autoimmune diseases. Also, there appears to be a strong link between thyroid autoimmunity and postpartum depression. Two studies have shown an association between thyroid autoimmunity and depression. Pop et al. demonstrated an association between Thyroid Peroxidase (TPO) antibody levels to be >100 mU/l and depression. Another study by Kirim et al. showed a strong connection in 201 subjects with TPO or TG antibody and depression. In contrast to the above-mentioned studies, there was another study by Fjaellegaard K concluded that elevated anti-TPO levels cannot be used as an over-all marker of poor well-being or depression. All of the three studies have a small sample size and have high chances of selection bias. A large sample size, unselected cohorts with thyroid antibody assessment are essential for the resolution of this issue [3,11].

Another study by Krysiak demonstrated that thyroid autoimmunity has a strong impact on the sexual function and depressive states of young women. Tools like Female sexual function index (FSFI) and Beck depression inventory (BDI) were used. Those females particularly who had autoimmune hypothyroidism were the most sexually dysfunctional and suffered from anxiety [12].

Conclusion

Thyroid hormones play an important part in mood and behavior, and cognition is an established fact. Thus, the association between psychological disorders and thyroid status is a foremost area of concern. Although, something that appears to be in wealth in literature, the relationship between hypothyroidism and depression is not clearly defined [13,14].

There is a general agreement that minor alterations, even if it's within the standard range, of the thyroid hormone levels amidst depressed individuals have significant effects on the functioning of the brain and its activity, and that can be an important aspect in the understanding of the biological basis of depression.

Thyroid autoimmunity seems to be a strong factor in the questionable relationship of hypothyroidism and depression. Many authentic studies with larger sample sizes have documented the fact that both are linked to each other. TSH levels in association to depression and TRH relation with depression has also been

established, but, more studies need to be carried out on this area to accept it as concrete evidence.

Many other studies are either years old or have very few participants involved. Hence, a lot of facts cannot be based on them and also, it keeps us from reaching to clear cut results. Newer studies on a larger scale with a bigger sample size can be helpful in this regard. After reviewing several studies, one can sense a strong sense of connection between hypothyroidism and depressive states but nothing tangible can be established and documented.

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