JAMBI MEDICAL JOURNAL
Jurnal Kedokteran dan Kesehatan
Vol. 13 No 2 November 2025
DOI: 10.22437/jmj.v13i2.43494
Journal homepage: https://online-journal.unja.ac.id/kedokteran
p-Issn : 2339-269x
e-Issn : 2580-6874

Review Article

Literature Review: The Iceberg Phenomenon in Hyperthyroidism and Mental Disorders

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Article History:
Submit: April 2025
Accepted: Nov 2025

Keyword:

Review; Mental disorders; Hyperthyroidism; Prevalence; Treatment;

ABSTRACT

Background: Elevated thyroid hormone levels have a high prevalence this year. It has a long-term impact on the cognitive and productivity of sufferers, leading to a decrease in the quality of life of individuals and an increase in social and economic burden. Previous studies have shown a direct link between hyperthyroidism and mental disorders, but the impact on cognitive and emotional functioning still needs to be clarified. Early detection and management are the main challenges in preventing and treating this condition.

Methods : Our study was a literature review of medical journal for the last 10 years through NCBI, Google Scholar, Clinicalkey, Semantic Scholar, Sciencedirect, and Springer.

Discussion: Hyperthyroidism caused by dysregulation of the Hypothalamic-Pituitary-Thyroid axis that disrupts the balance of triiodothyronine and thyroxine hormones, leading to emotional and cognitive impairment. The brain and thyroid tissue are also affected by the FDPS, PPIL3, MMAB, and ALDH2 genes, which are characterized by significant expression in areas of brain function that are involved in cognitive, emotional, and social behaviour.

Conclusion: A multidisciplinary approach, including pharmacological therapy, cognitive therapy, and community education, is an important step in reducing the impact of hyperthyroidism on mental health as well as social and economic aspects.

INTRODUCTION

Hyperthyroidism is defined as the thyroid gland's excessive release and secretion of the thyroid hormones thyroxine (T4) and triiodothyronine (T3). This physiological process of the excessive thyroid gland causes changes in the basal metabolic system, body temperature control, energy balance as well as cardiac rhythm so that in different conditions, it can show common symptoms such as weight loss despite high appetite, tachycardia in sedentary conditions and even cause the effect of excessive anxiety. These features are shown through trembling hands, high fatigue, or uncomfortable effects on the body. The risk of anxiety due to thyroid function is associated with a personality that is sensitive to criticism and a tendency towards high outcome standards that trigger anxiety.[1] These

conditions result in abnormally high serum levels. Hyperthyroidism is a common thyroid disorder characterized by low levels of thyroid-stimulating hormone (TSH) and elevated levels of T4.[2] The most common type of hyperthyroidism is caused by thyroid hormone secretion, namely in Graves' disease.[3] There are three most common etiologies of this disorder, namely due to Graves' disease, toxic multinodular goitre (TMNG), and toxic adenoma (TA). Risk factors for this disorder are related to smoking lifestyle, iodine deficiency, iodine excess, selenium deficiency, use of certain drugs, and genetics.[2]

Globally, a cross-sectional study conducted in China reported a higher prevalence of hyperthyroidism and subclinical in areas with iodine sufficiency than in areas with iodine deficiency. A marked increase in hyperthyroidism occurred in the last decade. Similar to China. A large-scale cross-sectional study in India also reported a high incidence of hyperthyroidism at 10%.[4] Furthermore, based on a population repeat study conducted in Italy, in the Piedmont region, the overall prevalence of hyperthyroidism was 756 per 100,000 population and had an incidence of 81 cases per 100,000 people per year. This prevalence and incidence increases with age, with women having twice the rate of men. Regarding geographical distribution, the Hasthe region has an increasing incidence gradient from north to southwest.[5] In Indonesia, the prevalence of this case is 10% of 100 samples taken from individuals visiting health centres or hospitals in Padang City. Hyperthyroidism is most common in the adolescent group, with a percentage of 33%, and less common in the elderly, who only have a percentage of 6%.[6]

The majority of individuals with hyperthyroidism clinically experience functional barriers that have an impact on high levels of anxiety and depression. Even though patients with mental health symptoms have reached euthyroidism, they still experience a decrease in quality of life.[7] The signs and symptoms that most often characterize hyperthyroidism are feelings of nervousness and anxiety.[3] This is supported by research that shows a relationship between hyperthyroidism and anxiety. The condition of hyperthyroidism is associated with impaired focus or attention, impaired information processing, and more emotional sensitivity, which has a direct impact on cognition or behaviour. The relationship between hyperthyroidism and anxiety is complex; thyroid hormone (T3) plays an important role in brain function, including cognition, memory and neurogenesis. Thyroid hormones cross the blood-brain barrier through specialized proteins such as OATP1 and MCT8, whose mutations can trigger neurological disorders. Thyroid receptors (TR) regulate gene expression and are distributed in different brain areas. In addition to T3 and T4, metabolites such as T1AM affect neurotransmitters and potentially protect the brain.[8]

Health does not only refer to being physically healthy, characterized by the absence of disease. However, it encompasses physical, mental and social well-being. Mental health can be defined as a state in which individuals can work productively to overcome their problems, build social relationships, and be aware of their abilities.[9]

When an individual experiences disturbances in cognitive function, emotion regulation, and individual behaviour, it is a sign of mental health disorders.[10] Many factors, such as the social environment, lack of access to health services, lack of access to economic opportunities, lifestyle, and ongoing medical conditions, can influence the mental health of an individual.[11]

According to data from the World Health Organization, 1 in 8 people or 970 million people worldwide in 2019 reported experiencing mental disorders, with anxiety and depression being the most common disorders.[9] People with severe mental disorders have a 10-20 year shorter life expectancy. Based on the results of a survey

conducted in China on 32,552 respondents between July 22, 2013

Moreover, on March 5, 2015, this data shows that about 9.3% of the population experienced mental disorders in the past year, while 16.6% had experienced mental disorders at least once in their lives before the data search was conducted.[12] Then, according to research conducted in Bali, Indonesia, on 265 respondents between October 24 and November 22, 2022, it was found that 46.8% of adolescents experienced mental emotional disorders. In addition, it was found that 74% of adolescents experienced mild anxiety, 6.8% moderate anxiety, 7.9% severe anxiety, and 11.3% extreme anxiety. This prolonged anxiety can be a factor in more serious mental health disorders, such as depression.[13]

The interaction between hyperthyroidism and anxiety disorders reflects an association; clinical studies show that 31%-56% of patients with thyroid disorders experience depression or anxiety. One of the autoimmune disorders such as Graves' is related to the emergence of anxiety and depression due to the mistake of the thyroid gland in producing excess thyroid hormones or hyperthyroidism.[14] Based on another study conducted involving 1,894 female patients and 585 male patients diagnosed with hyperthyroidism, prevalence ratios were obtained; namely, individuals with hyperthyroidism had a 1.7 times higher risk of having ADHD than individuals without hyperthyroidism. In contrast, individuals with hyperthyroidism had a 4.9 times higher risk of having bipolar disorder than individuals without hyperthyroidism. Most surprisingly, patients with hyperthyroidism were almost 5 times more likely to experience suicidal tendencies than patients who were never diagnosed with hyperthyroidism. This reinforces the link between hyperthyroidism and various types of mental disorders.[15]

Studies conducted in the UK have found that hyperthyroidism has a social, economic and global impact. The social impact of hyperthyroidism affects social interactions in individuals with problems such as tremors, increased heart rate and accompanying emotional disturbances. The economic impact can be financially burdensome as the effects of this disorder require long-term treatment, including laboratory tests, antithyroid drugs, radioactive drugs, and even surgery. In terms of work productivity, hyperthyroidism results in chronic fatigue, sleep disturbances, and cognitive problems that can reduce work productivity levels.[4]

Based on the data from the studies obtained, the authors focused on the association of hyperthyroidism with the incidence of mental health disorders as well as the prevalence and impact of these events on a global scale.[16] This focus was raised by looking at data and clinical studies related to the relationship between these two variables. It is undeniable that anxiety disorders and hyperthyroidism are trending issues globally, as well as the social and economic impacts that they have on a global scale.[17]

Through this literature review, the authors aim to emphasize that hyperthyroidism has a relationship with the incidence of mental health disorders and can have an impact on a global scale. Based on the analysis of previous studies, this review is expected to increase public knowledge and awareness, especially among medical personnel, regarding the importance of early detection and optimal management of hyperthyroidism. This is expected to reduce the risk of anxiety disorders associated with hyperthyroidism and its global implications..

METHOD

This literature review was conducted to identify and analyze hyperthyroidism, mental disorders, risk factors, the relationship between hyperthyroidism and mental disorders, prevalence, global impact, and comprehensive management. This literature study utilized various sources, both national and international, that have been published within the last 10 years. The literature search process involved various systematic search

systems, such as NCBI, Google Scholar, Clinicalkey, Semantic Scholar, ScienceDirect and Springer, with the keywords: "hyperthyroidism," "mental disorder," "prevalence," "global impact," 'therapy,' "risk factors." Based on the selection process that has been carried out, a total of 26 kinds of literature were obtained.

RESULT AND DISCUSSION

One study was conducted at the Thyroid Clinic of Jinnah Postgraduate Medical Center and Department of Atomic Energy in Karachi, Pakistan. The sample used in this study was conducted on 200 patients, with 100 individuals having normal thyroid levels and 100 individuals with hyperthyroidism.[18] The study showed that 84% of patients with hyperthyroidism had depression, and 58% had anxiety. Through the Hamilton Depression Rating Scale (HDRS) measurement instrument comparing the severity of depression in patients with hyperthyroidism and euthyroidism, it was found that hyperthyroidism patients experienced depressed mood by 87% compared to euthyroid conditions, which were only 40%.[19] Then weight loss was 68% in hyperthyroidism compared to euthyroid conditions 20%, somatic anxiety 80% while euthyroid 49%, and loss of interest in work and activities in the hyperthyroidism group 72% compared to euthyroid conditions 38%.[20] Then, the Hamilton Anxiety Rating Scale (HARS) measurement instrument compares anxiety levels by looking at symptoms such as somatic sensory, insomnia, cardiovascular symptoms, and depressed mood. It was found that patients with hyperthyroidism experienced sensory somatic symptoms as much as 60% compared to the euthyroid group, which was only 22%.[21] Then, continued in insomnia showed that 59% of hyperthyroidism patients experienced insomnia and the euthyroid group was only 45%, cardiovascular symptoms in the hyperthyroidism group were 78% and in the euthyroidism group were 33%, and depressed mood in the hyperthyroidism group was 75% and in the euthyroidism group was 44%.[22]

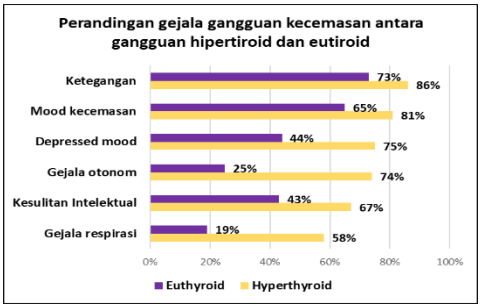

Figure 1. Comparison between hyperthyroidism and euthyroidism using the Hamilton Depression Rating Scale instrument

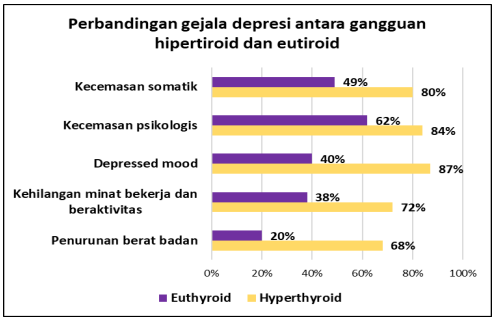

Figure 2. Comparison between hyperthyroidism and euthyroidism using the Hamilton Anxiety Rating Scale instrument

This study is in line with the results of another study conducted at the Endocrine and Diabetes Center, New Cross Hospital, Wolverhampton; in patients with hyperthyroidism, around 40.5% of patients experienced moderate to severe anxiety when first diagnosed. Hyperthyroidism is associated with significant Generalized Anxiety Disorder (GAD-7). Patients with anxiety and depression due to hyperthyroidism experience reduced social and occupational functioning. This condition can lead to lost work days, decreased work effectiveness, and reduced productivity in younger patients. The association of hyperthyroidism with anxiety and depressive disorders has long been recognized.[7] Furthermore, a registry-based study in Denmark found that the income of individuals with hyperthyroidism was lower than that of individuals with non-hyperthyroidism. The condition is associated with severe work disability, with data on an increased risk of receiving a disability pension as high as 88% and a significant reduction in work income.[23]

Interventions for the management of hyperthyroidism come in a variety of ways. Treatment with appropriate endocrinologic care through surgical procedures and the use of antithyroid (ATD) or radioactive iodine therapy (RAI) are effective options for reducing psychiatric disorders. It is proven that the endocrinological treatment reduces agoraphobia and panic disorders.[24] There is another treatment for hyperthyroidism patients. This treatment is called cognitive behavioural therapy (CBT), a psychotherapy that helps a person identify and change thought patterns that negatively impact one's emotions and behaviour. The benefits of CBT are effective in a short period and have a lasting positive impact across a range of mental health disorders, including obsessive-compulsive disorder. However, further research is still needed to examine the longevity of the effects of this therapy.[25]

There is another holistic treatment option for hyperthyroidism. This method is patient-centred management (PCM), which includes education and communication, symptom management, treatment options, shared decision-making, monitoring and follow-up, treatment side effects, psychological support, and lifestyle and nutritional modifications.[26]

CONCLUSION

Hyperthyroidism correlates with mental health disorders, especially depressive disorders and anxiety disorders; this is shown by the high prevalence of mental disorders in hyperthyroid patients. In a recent study, four gene expressions were associated with the thyroid axis and brain structure, but further research is needed to see the specific relationship with hyperthyroidism. Excessive imbalance of thyroid hormones (T3 and T4) can also affect cognitive function, emotional regulation, and social behaviour. This condition will lead to a decrease in quality of life and thus social and economic impact.

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