



**CHARACTERISTICS OF PATIENTS WITH *PANIC DISORDERS* P THERE IS
HYPERTHYROIDISM ACCOMPANIED BY TONSIL HYPERTROPHY AND
THYROID EYE DISEASE WITH ECG PICTURE SICK DYSFUNCTION NODE**

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ABSTRACT

Background: Hyperthyroidism is an endocrine disorder with the second highest incidence rate after diabetes, and Graves' disease is the most common cause of hyperthyroidism. Objective: To determine the characteristics of patients with panic disorder in hyperthyroidism with an ECG picture of sick node dysfunction. Methods: This study is a Systematic Review using the Preferred Reporting Items for Systematic Reviews and Meta-analysis or com method. This method is carried out systematically following the correct stages or research protocols. The source was taken from the PubMed site, and the Google Scholar site with journals published in 2017-2022 and then filtered the results as many as 15,486. Results: Journal clustering was carried out and obtained the



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number of journals indexed in Scopus Q1 as many as 2 journals, Q2 as many as 2 journals, indexed Sinta S1 as many as 1 journal, so that there were 5 extracted journals. Conclusion: The majority of journals discuss age and lifestyle associated with the characteristics of panic disorder, as well as the factors of hyperthyroidism determined by age, and hyperthyroidism associated with panic disorder, ECG picture of sick node dysfunction.

Keywords: *Characteristics Patients, Hyperthyroid, Panic disorders, Sick Nodus Dysfunction, Hyperthyroidism.*

INTRODUCTION

Panic disorder can be defined as a fear, real or imagined, of an object, followed by a heightened psychiatric reaction. Other experts say that panic disorder is a form of unpleasant emotion characterized by worry, concern, and fear due to conflict, frustration, or pressure to do something beyond the limits of ability.^{1,2} Panic disorder has symptoms or signs that vary and are different in each person. The severity also varies from person to person. Some of the common symptoms include worry, malaise, irritability, uneasy tension, and restless sleep disturbances, such as difficulty falling asleep, frequent nightmares, and other physical complaints, such as muscle pain or shortness of breath.

The impact of panic disorder is related to the symptoms experienced. Panic disorder elicits physical and psychological responses. Physical responses include a faster heart rate, cold sweat, faster breathing, or shortness of breath. This condition will make the sufferer feel tired more quickly. Patients who experience changes in sleep patterns become difficult to sleep, often have nightmares, or become easily sleepy will also interfere with work productivity and ultimately result in physical disorders.^{3,4} If the anxiety condition lasts for a long period of time, the sufferer will feel increasingly depressed, feel uncomfortable in all situations. As a result, it can interfere with daily life and activities. Anxiety experienced by women with maternal status will also have an impact on their family members. Mothers with high levels of anxiety show a decrease in parenting warmth, responsibility, and sensitivity.⁵

Changes in thyroid function can cause changes in the liver. Impaired thyroid function can be seen by changes in thyroid levels and changes in Thyroid Stimulating Hormone (TSH) in the blood. Most of these disorders occur due to impaired synthesis of thyroid hormones. The thyroid gland produces thyroid hormones that control the body's metabolic rate. Hyperthyroidism indicates excessive activity of the thyroid gland in synthesizing thyroid hormones, thereby increasing tissue metabolism. Subclinical hyperthyroidism is a condition in which serum thyrotropin (TSH) levels are low (<0.5 mU/L) while free thyroxine (fT4) and free triiodothyronine (fT3) levels are within normal limits. Hyperthyroidism is a condition of decreased thyroid hormone secretion that causes a decrease in the body's metabolic rate.^{6,7}

Changes in thyroid function will lead to impaired cognitive function, behavior, as well as changes in mood and anxiety. Two-thirds of patients with thyroid disorders report that they experience psychiatric disorders. Some of the most common psychiatric disorders in people with thyroid disorders are anxiety, depression, phobias, obsessive-compulsive disorder and panic. The prevalence of anxiety disorders experienced by people with thyrotoxicosis is around 33-61%,

while in hypothyroid patients, the problems faced include depressive disorders or bipolar disorders.⁸

The thyroxine hormone produced by the thyroid gland maintains the rate of tissue metabolism for the normal functioning of cells and the whole body by stimulating O₂ consumption, protein synthesis, and transcription of other genes in the cell. Thyroxine hormone is not said to be essential for life, but its absence will cause deterioration and slow down the process of physical and mental growth.⁹ In addition, an excess of this hormone will cause the body to metabolize quickly, tremors, nervousness and excessive heat production. Hyperthyroidism is an endocrine disorder with the second highest incidence after diabetes, and Graves' disease is the most common cause of hyperthyroidism. About 60%-80% of hyperthyroidism cases are caused by Graves' disease, where women aged 20-50 years are more dominant than men.^{8,10} Therefore, the role of the ECG picture of sick sinus syndrome (SSS) in predicting the prognosis of serious diseases is still questionable. To address this issue, we conducted a systematic review to comprehensively evaluate the predictive role of the ECG picture of sick sinus syndrome (SSS) in the prognosis of grave diseases.

MATERIALS AND METHODS

Research Type and Design

This study is a Systematic Review using the Preferred Reporting Items for Systematic Reviews and Meta-analysis method or commonly called PRISMA, and this method is carried out systematically by following the correct stages or research protocols. Systematic review is one method that uses reviews, reviews, structured evaluations, classifications, and categorizations of evidence-based that have been produced previously.

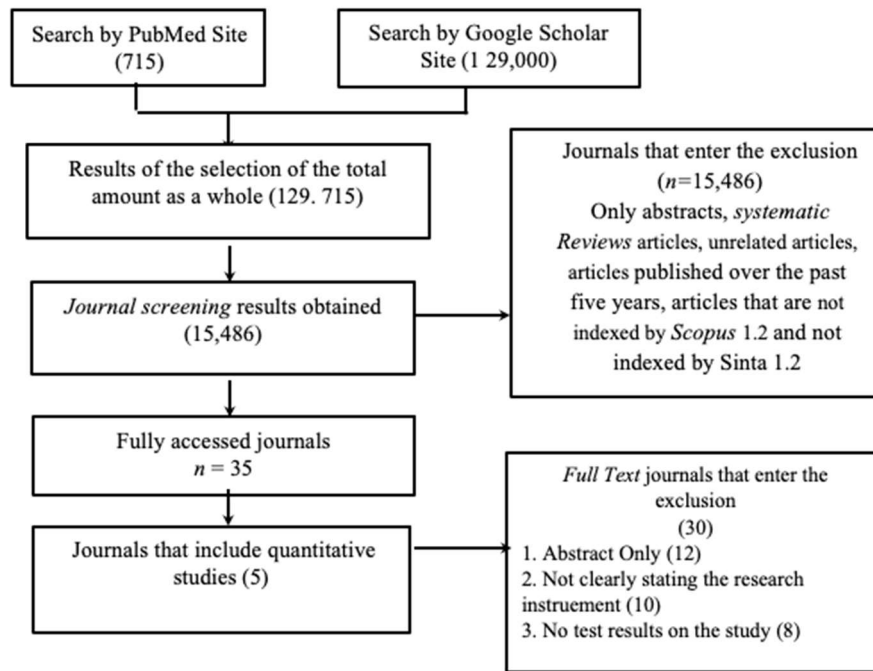


Figure 1. PRISMA diagram: Stages of *Systematic Review*

Data Collection Methods

1. Research Database Data Source

The data used to search the literature is through selection based on hyperthyroid criteria, which concern medical research and social health. Next, apply a literature review relating to panic and hyperthyroid disorders. Articles are searched by using PubMed and Google Scholar as databases. The search for articles relevant to this research topic was carried out using keywords: panic disorders, hyperthyroidism, sick nodus dysfunction, and hyperthyroidism with an ECG description of sick dysfunction nodes.

2. Publication time

The journals taken are journals published in 2017-2022

3. Inclusion and exclusion criteria

a. Inclusion criteria

- 1) Artikel research published in 2017-2022
- 2) The dependent variable in the research article is followed by *graves disease* with an ECG picture of sick sinus syndrome (SSS).
- 3) An independent variable in the research article is anxiety disorders
- 4) Articles indexed by Scopus 1.2 and Sinta 1.2

b. Exclusion criteria

- 1) Research articles with incomplete text
- 2) *Literature-based articles review /systematic review*
- 3) Not discussing dependent variables / unrelated articles

4) Articles with incomplete content

4. Publication Search Strategy

Publication searches on Pubmed and Google Scholar use selected keywords: cervical cancer, cervical cancer characteristics, and iron deficiency anemia.

RESULTS AND DISCUSSION

Research Results

Data information on cervical cancer as an independent variable analyzed is presented in the form of a table containing the title of the journal, year of publication, author of the destination in the journal, samples, and criteria, research instruments, between data or research methods and research results in the journal.

Table 1. Journal Analysis

No	Researcher's Name	Analysis Data / Research Methods	Result
1	Rui Huang, Li Yan, Yuhua Lei Yuanhong Li (2021)	Analyze rare case reports	This is the first reported case of hypothyroidism with sick sinus syndrome requires a pacemaker and psychiatric disorders, and the symptoms can be corrected and inverted after thyroxine supplementation. This case highlights the importance of hypothyroidism screening when facing unexplained psychosis or sick sinus syndrome, in particular if combined. ³
2	M Tudoran, C Tudoran (2017)	Hyperthyroidism is usually associated with sinus tachycardia or supraventricular tachyarrhythmia, but rarely with dysfunction of sinus nodes or other conduction annoyance	Hyperthyroidism and SSS are a rare relationship, identified mostly in patients with Graves' disease, even in the subclinical stage, it poses therapeutic problems in the presence of concomitant tachyarrhythmia. Evolution good in most cases, after normalization of the thyroid hormones, rarely require implantation of a pacemaker. ¹¹

3	Fukaoa, Takamatsub Junta, Takeshi Arishimac, Mika Tanakad, Toshio Kawaie, Yasuki Okamotof, Akira Miyauchic, Akihisa Imagawa (20 20)	Systemic review studies	Mental disorders, depression and anxiety often converge with GD. Psychosocial factors include stress and disease awareness as well as Biological factors including the effects of thyroid hormones can affect the course of the disease. Psychosomatic approaches include antipsychotic drugs and psychotherapy based on bio-psycho-social medical model considered useful in GD patients with mental concomitant symptoms with hyperthyroidism. ¹
4.	T. Rago (2018)	Literature review analysis	AS patterns of autoimmune thyroid disease are defined. Signs of US malignancy in thyroid nodules are classified and scored in each nodule. We also propose a simplified risk stratification of nodules, based on the predictive value of each US sign, classified and scored according to the strength of the relationship with ferocity and the approximate reproducibility between different operators. ⁶
5.	M Agung Yudistira Permana (2020)	Case report analysis	<i>Graves' disease is a metabolic disease that is not uncommon, especially in women with the age of 20-50. Diagnosis enforcement can be done by examining the history of the disease, physical and laboratory examinations. Even with long treatment and continuous follow-up, the drugs that can currently be obtained are proven to produce good outcomes for patients.</i> ¹²

Discussion

In the study subjects with hyperthyroidism, the most common picture of heart rhythm disorders was atrial fibrillation rapid response of 6 people, sinus tachycardia 4 people, atrial fibrillation of normal response and RBBB of 3 people each, VES benigna of 2 people, as well as atrial flutter, SVES, and sinus tachycardia with RBBB of 1 person each. Thyroid hormones, particularly T3, are important regulators in the expression of cardiac genes. Some of these genes

are positively regulated and negatively regulated. An increase in T3 binding to TRs will induce positively regulated genes and suppress negatively regulated genes. The regulated genes include:

- Alpha myosin heavy chain that can increase myocardium contractility
- Ion channels Na^+ -K + ATPase and voltage-gated potassium ATPase which regulate the electrochemical response of the myocardium. Changes in the electrochemical function of the myocardium can result in increased systolic depolarization and diastolic repolarization resulting in a decrease in the duration of the action potential (Action Potential Duration). This can lead to an increase in Left Ventricular Mass (LVM). It also affects mothers with a history of hyperthyroidism and treatment with PTU (Propiltiouracil) which causes the fetus to have SND since birth.

Research on hypothyroid, hyperthyroid, and groups of people with normal TSH showed that primary hyperthyroid sufferers had the most severe anxiety levels compared to other groups. Other studies have suggested that people with subclinical hyperthyroidism and subclinical hypothyroidism have higher anxiety scores compared to euthyroid subjects. This opinion differs from the results of other studies that state that there is no relationship between thyroid abnormalities and mental disorders, neither depression nor panic disorder.

The relationship between tonsil hypertrophy in hyperthyroid patients and panic disorder is due to the thyrotoxicosis of hyperthyroid patients, hormones T3 and T4 which in abnormal circumstances cause tonsillitis infection accompanied by tonsil hypertrophy of the tonsils after thyroidectomy in hyperthyroid patients. This is one of the complications that occurs in hyperthyroid patients who are treated. With a history of panic disorder. An increase in electrochemical substances in the brain affects the production process of T3 and T4 hormones in hyperthyroid patients which can cause symptoms, one of which is thyroid eye disease. Patients who are not surgically performed can occur tonsil hypertrophy due to hyperplasia of the diffuse thyroid follicle to affect the kriptе in the tonsils so that it occurs enlargement of the tonsil gland itself. The influence of the pregnancy history of mothers with a history of hyperthyroidism and treatment with thyroid therapy also affects the occurrence of hyperthyroidism in children later with the risk of significant hypertrophic tonsils due to the influence of the mRNA chain affecting the child.

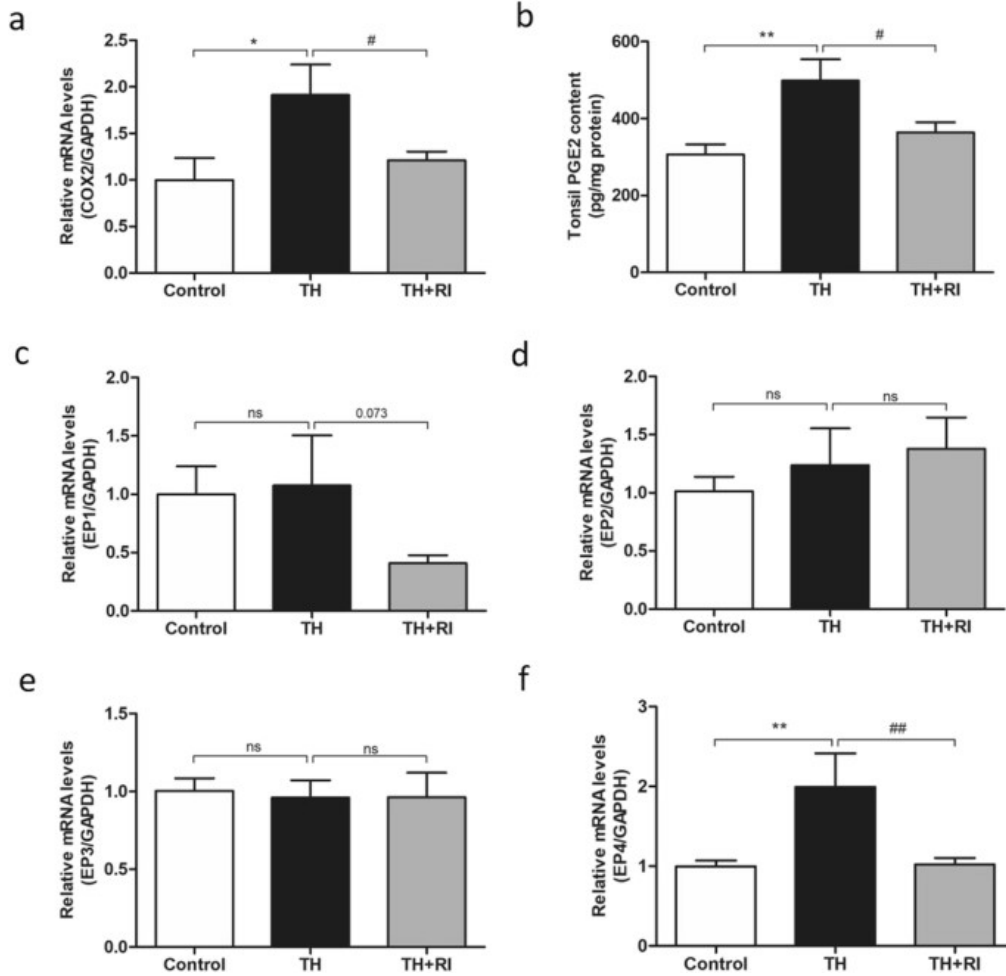


Figure 2. Molecular Graph of the occurrence of Tonsil Hypertrophy with the influence of mRNA in hyperthyroid patients

The relationship between panic disorder and thyroid function has been discussed in several studies. Gonen et al. stated that people with subclinical hypothyroidism and subclinical hyperthyroidism had higher anxiety scores than in euthyroid subjects. The results of Gonen's study are similar to this study, namely the anxiety score of people with thyroid disorders is higher than that of euthyroidism. Another study whose results were almost the same stated that people with hypothyroid overt and hyperthyroid overt more severely felt the symptoms of anxiety and depression. Research on hyperthyroid sufferers also showed that the hyperthyroid group had higher anxiety and depression scores than the euthyroid group

CONCLUSION

After a series of processes passed, based on the results of research in the indexed journals *Scopus* and *Sinta* regarding *systematic review* of the characteristics of people living with panic disorder in hyperthyroid with tonsil hypertrophy accompanied by thyroid eye disease has a picture ECG Sick Nodus Dysfunction, it can be concluded that the majority of journals discuss age, sex-related to factors risiko the occurrence of hyperthyroidism. From the sub-chapters obtained, it can be

concluded that the factor risiko *hyperthyroid* is determined based on age, gender, and lifestyle. As well as hyperthyroid associated with panic disorder, and ECG picture Sick Nodus Dysfunction.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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REFERENCES

1. Fukao, A., Takamatsu, J., Arishima, T., Tanaka, M., Kawai, T., Okamoto, Y., Miyauchi, A. and Imagawa, A., 2020. Graves' disease and mental disorders. *Journal of clinical & translational endocrinology*, 19, p.100207. <https://doi.org/10.1016/j.jcte.2019.100207>
2. Aizawa Y, Fujisawa T, Katsumata Y, Kohsaka S, Kunitomi A, Ohno S, Sonoda K, Hayashi H, Hojo R, Fukamizu S, Nagase S. Sex-Dependent Phenotypic Variability of an SCN5A Mutation: Brugada Syndrome and Sick Sinus Syndrome. *Journal of the American Heart Association*. 2018 Sep 18;7(18):e009387. <https://doi.org/10.1161/JAHA.118.009387>
3. Huang, R., Yan, L., Lei, Y. and Li, Y., 2021. Hypothyroidism and complicated sick sinus syndrome and acute severe psychiatric disorder: A case report. *International Medical Case Reports Journal*, pp.171-176. <https://www.tandfonline.com/doi/full/10.2147/IMCRJ.S296071>
4. Subekti I, Pramono LA. Current diagnosis and management of Graves' disease. *Acta Med Indones*. 2018 Apr 1;50(2):177-82. <https://core.ac.uk/download/pdf/268043162.pdf>
5. Saramago P, Gega L, Marshall D, Nikolaidis GF, Jankovic D, Melton H, Dawson S, Churchill R, Bojke L. Digital interventions for generalized anxiety disorder (GAD): systematic review

- and network meta-analysis. *Frontiers in psychiatry*. 2021 Dec 6;12:726222. doi: 10.3389/fpsyt.2021.726222
6. Rago T, Cantisani V, Ianni F, Chiovato L, Garberoglio R, Durante C, Frasoldati A, Spiezia S, Farina R, Vallone G, Pontecorvi A. Thyroid ultrasonography reporting: consensus of Italian Thyroid Association (AIT), Italian Society of Endocrinology (SIE), Italian Society of Ultrasonography in Medicine and Biology (SIUMB) and Ultrasound Chapter of Italian Society of Medical Radiology (SIRM). *Journal of endocrinological investigation*. 2018 Dec;41:1435-43. <https://link.springer.com/article/10.1007/s40618-018-0935-8>
 7. Kotwal A, Stan M. Thyrotropin receptor antibodies—An overview. *Ophthalmic Plastic & Reconstructive Surgery*. 2018 Jul 1;34(4S):S20-7. DOI: 10.1097/IOP.0000000000001052
 8. Struja, T., Fehlberg, H., Kutz, A., Guebelin, L., Degen, C., Mueller, B., & Schuetz, P. (2017). Can we predict relapse in Graves' disease? Results from a systematic review and meta-analysis. *European journal of endocrinology*, 176(1), 87-97. <https://doi.org/10.1530/EJE-16-0725>
 9. Liu J, Fu J, Xu Y, Wang G. Antithyroid drug therapy for Graves' disease and implications for recurrence. *International journal of endocrinology*. 2017 Apr 25;2017. <https://doi.org/10.1155/2017/3813540>
 10. Srikandi PR. Hipertiroidismee Graves Disease: Case Report. *Jurnal Kedokteran Raflesia*. 2020 Nov 2;6(1):30-5. <https://ejournal.unib.ac.id/index.php/jukeraflasia>
 11. Tudoran M, Tudoran C. (2017). Hyperthyroidism and sick sinus syndrome, a rare but challenging association: A study of three cases. *Niger J Clin Pract*,20:1046-8. <https://www.ajol.info/index.php/njcp/article/view/161110>
 12. Permana MA, Adhy WP, Mappapa NK, Patola IA. Graves Disease dengan Gangguan Irama Jantung. *Medical Profession Journal of Lampung*. 2020 Sep 19;10(2):292-6. <https://doi.org/10.53089/medula.v10i2.69>