REVIEW ARTICLE

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Characteristics of Toxic and Non Toxic Diffuse Goiter Sufferers with Hyperparathyroidism and SND ECG Features

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ABSTRACT

Background: Goitre, the second most prevalent endocrine disorder after diabetes, is followed in incidence rate. The most common source of hyperthyroidism is Graves' Disease. Graves' disease is responsible for around 60% to 80% of hyperthyroidism cases, with women aged 20 to 50 being more predominant than men. This autoimmune disorder is characterized by the presence of TSI and TSAb, which are secreted into the thyroid gland and bind to its TSH receptor. As a result, it stimulates the thyroid gland to produce thyroxine hormone under the influence of the TSH receptor. Prolonged TSAb stimulation leads to hyperthyroidism and thyroid enlargement. Hyperthyroidism causes the heart rate to weaken, and an overview of the ECG pattern shows atrial fibrillation with a fast RR pattern. Know Characteristics of Toxic and Non-Toxic Diffuse Struma sufferers with Hyperparathyroidism and ECG picture of RVR Atrial Fibrillation.
Method: This study employs the PRISMA approach, which involves a systematic execution of research steps and adherence to proper research protocols. Data sources were collected from both the PubMed and Google Scholar websites, encompassing journals published between 2017 and 2022. Subsequently, a screening process was conducted, resulting in the retrieval of 15,486 outcomes.
Result: Journal clustering was conducted, resulting in the acquisition of the count of journals indexed by Scopus in the Q2 category and journals indexed by Sinta in the S1 category. A total of eight journals were retrieved.
Conclusion: Most journals discuss age and lifestyle issue characteristics of Toxic and Non-Toxic Diffuse Goiter Patients with Hyperparathyroidism and ECG Atrial Fibrillation RVR.
Key words: Goiter, atrial fibrillation, toxic, non-toxic

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INTRODUCTION

The body's metabolic rate is regulated by thyroid hormones generated by the thyroid gland. These hormones have a direct impact on neurotransmitter function. In typical situations, thyroid hormone impacts tissue metabolism, oxidative processes in tissues, growth, and the synthesis of proteins (1). Disorders related to thyroid function can be detected through alterations in thyroid levels and variations in Thyroid Stimulating Hormone (TSH) levels in the bloodstream. The majority of these conditions arise from disruptions in the synthesis of thyroid hormones. Hyperthyroidism signifies an overactive thyroid gland in the production of thyroid hormones, consequently elevating metabolism within the body's tissues (2,3).

Alterations in thyroid function can lead to disruptions in cognitive abilities, behavior, and alterations in mood and anxiety levels. Approximately two-thirds of individuals suffering from thyroid-related conditions are documented to exhibit psychiatric issues, such as anxiety, depression, phobias, obsessive-compulsive disorder, and panic. The occurrence rate of anxiety disorders among those with thyrotoxicosis falls within the range of 33-61%, while hypothyroid patients typically grapple with problems like depression or bipolar disorder (4).

The thyroxine hormone, produced by the thyroid gland, plays a crucial role in regulating tissue metabolic rates to support normal cell function and overall bodily health. This hormone stimulates oxygen (O_2) consumption, protein synthesis, and gene transcription within cells. Inadequate thyroxine levels can lead to delays in development and hinder physical and mental growth processes. Conversely, an excessive amount of this hormone can result in an increased metabolism, leading to symptoms such as tremors, nervousness, and excessive heat production. Hyperthyroidism is the second most common endocrine disorder, following only diabetes in prevalence. Graves' Disease is the primary cause of hyperthyroidism, accounting for approximately 60% to 80% of cases. This condition is more frequently observed in women aged 20 to 50 compared to men (4,6).

A medical condition called diffuse goiter is identified by the generation of thyroid-stimulating immunoglobulin (TSI) or thyroid stimulating antibody (TSAb). These substances are discharged within the thyroid gland and bind to the thyroid stimulating hormone (TSH) receptor situated within the thyroid gland. Consequently, this activation prompts the thyroid gland to operate, generating the thyroxine hormone as a result of TSH receptor stimulation. Sustained TSAb stimulation leads to hyperthyroidism and the enlargement of the thyroid gland, a condition referred to as thyromegaly. Virtually all individuals diagnosed with Graves' disease exhibit the typical symptoms associated with hyperthyroidism (7). Common signs that manifest in young patients encompass temperature intolerance, perspiration, exhaustion, shedding pounds, palpitations, and trembling. In contrast, elderly individuals may exhibit more ambiguous and less defined symptoms, like weariness or weight reduction, often accompanied by extrathyroidal indications, such as ophthalmopathy, dermopathy, and osteopathy (5,8).

The test used to confirm diffuse goiter, especially in Graves' disease, is the calculation of TSAb (9). The TSH-level test is the initial laboratory examination used for diagnosis. In case of discovering low TSH levels, it is advisable to conduct the following tests: Free Thyroxine (FT4) and Free Triiodothyronine (FT3). If there is a concurrent decrease in TSH alongside increased levels of Total Thyroxine (T4) and triiodothyronine (T3), hyperthyroidism can be conclusively diagnosed. Graves's disease can be determined by considering historical data, conducting a physical examination, and performing fundamental laboratory tests. The existence of orbitopathy, enlargement of the thyroid gland, with or without the presence of bruits, and pretibial myxedema all offer substantial evidence for establishing the diagnosis. Nevertheless, if the signs and symptoms do not align with the typical presentation, a comprehensive examination is still recommended (10,11).

Hyperthyroidism leads to significant cardiovascular complications, such as coronary artery disease, ventricular arrhythmias, atrial fibrillation, atrioventricular block, myocardial systolic dysfunction, pericardial effusion, diminished cardiac output, and elevated blood pressure (12). Severe sick sinus syndrome (SSS) necessitating pacemaker intervention is seldom induced by hypothyroidism. Earlier research has indicated that mental disorders can also be triggered by hyperthyroidism (13).

Hence, the validity of utilizing atrial fibrillation electrocardiograms (ECGs) with Rapid Ventricular Response (RVR) to forecast the outcomes of both toxic and non-toxic diffuse goiter remains uncertain. In order to tackle this matter, we conducted a systematic review aimed at thoroughly assessing the predictive significance of ECG characteristics pertaining to sick sinus syndrome in predicting goiter prognosis.

METHOD

This research offers a Systematic Review that was carried out using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) approach. This approach entails a rigorous and systematic execution of the research process, adhering to established protocols. The systematic review process is highly organized and methodical, comprising several sequential stages: 1) the compilation of Background and Objectives, 2) formulation of Research Queries, 3) literature exploration, 4) establishment of Selection Criteria, 5) practical screening, 6) Quality Checklist and Procedures assessment, 7) Data Extraction Strategy, and 8) Data Synthesis Strategy. Data sources were collected from PubMed and Google Scholar, focusing on journal publications spanning from 2017 to 2022. Subsequently, a thorough screening procedure was employed, yielding a total of 15,486 results (*fig. 1*).

The literature search involved the selection of data in accordance with struma criteria derived from the Wayne index, which pertains to medical research and social health. Subsequently, a literature review was conducted regarding SND and Graves' disease. Research articles were sought through the PubMed and Google Scholar databases, focusing on articles pertinent to this study using keywords such as toxic and non-toxic diffuse goiter, Graves' disease, SND, and

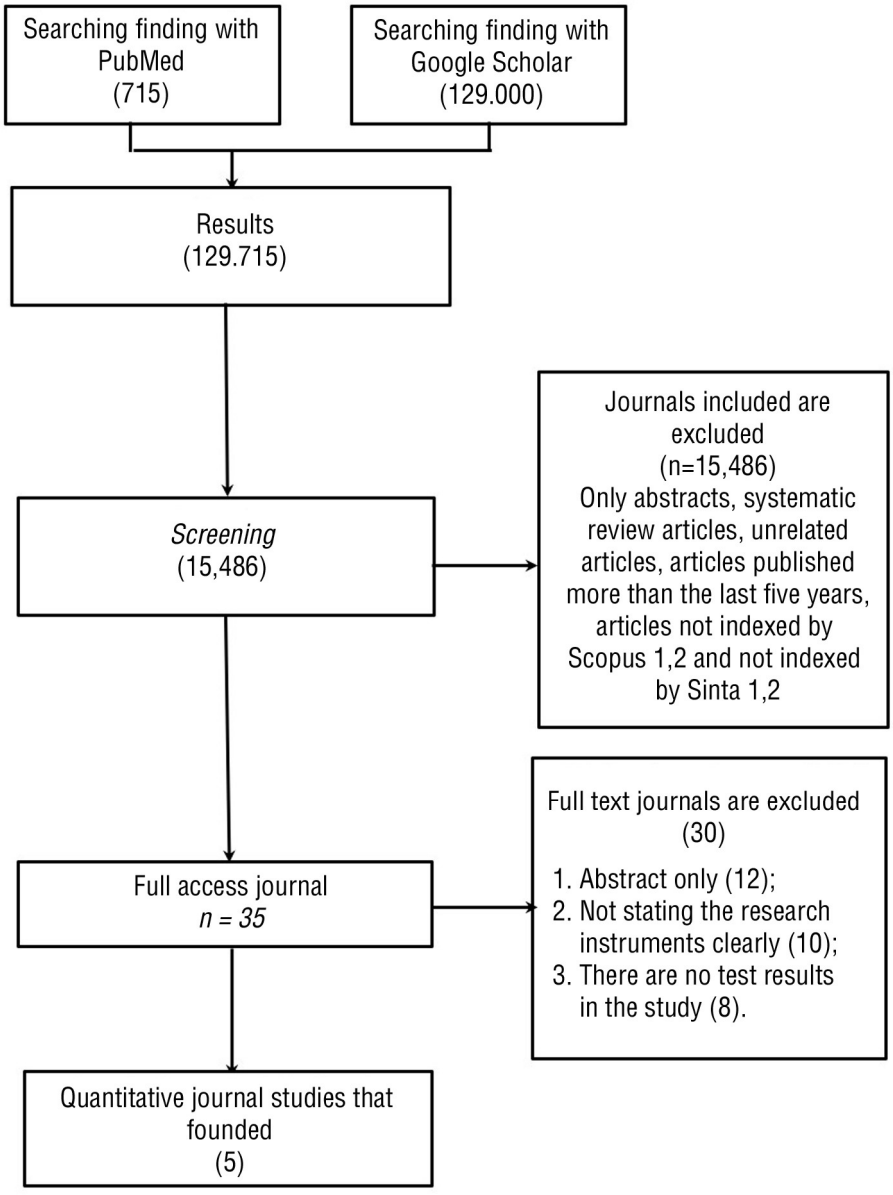

Figure 1 - PRISMA Diagram: stages systematic review

Graves' disease with the SND ECG. The chosen journals were those published between 2017 and 2022.

RESULTS

Clustering of journals was conducted, resulting in the acquisition of the number of journals included in Scopus Q2 and S1 journals listed in Sinta. Eight journals pertaining to the attributes of patients suffering from toxic and non-toxic diffuse goiter with ECG SND were identified. These journals were subsequently sifted through and compiled into a table to facilitate the elucidation of their contents. The selection of these journals was contingent upon their titles and abstracts, and they were subsequently evaluated against the inclusion criteria. Information extracted from the research encompassed the research title, author's name, publication year, research location, sample size, methodology, and findings (*table 1*).

DISCUSSION

Characteristics of Toxic and Non-Toxic Diffuse Struma Sufferers With an ECG SND Picture based on age and existing risk factors.

In individuals with hyperthyroidism as the research subjects, the predominant heart rhythm irregularities observed were as follows: fast-response atrial fibrillation was detected in six individuals, sinus tachycardia in four individuals, while normal-response atrial fibrillation and right bundle branch block (RBBB) were each found in three individuals. Two individuals exhibited benign ventricular ectopic beats (VES), and one person each experienced atrial flutter, supraventricular ectopic beats (SVES), and sinus tachycardia with RBBB.

Thyroid hormones, particularly T3, play a vital role in governing the expression of cardiac genes. These genes experience both positive and negative regulation (14). Increasing T3 that binds to TRs will induce positively regulated genes and suppress negatively regulated genes (15). These regulated genes include: Elevating T3 levels that interact with TRs will stimulate genes under positive regulation and inhibit genes under negative regulation (15). These affected genes encompass:

1. Alpha myosin heavy chain, known for its ability to enhance myocardial contractility (16);
2. The myocardium's electrochemical response is regulated by ion channels such as Na+-K+ ATPase and voltage-gated potassium ATPase (17). Alterations in the electrochemical performance of the myocardium have the potential to elevate systolic depolarization and diastolic repolarization, leading to a reduction in action potential duration. Such changes may lead to an augmentation in the Left Ventricular Mass (LVM) (18).

Research involving hypothyroidism, hyperthyroidism, and individuals with normal TSH levels has indicated that individuals with primary hyperthyroidism experience the highest degree of anxiety when compared to the other groups (19). Other research indicates that individuals with subclinical hyperthyroidism and subclinical hypothyroidism exhibit elevated levels of anxiety in contrast to euthyroid individuals (20). This viewpoint contrasts with the findings of other research, which assert that there is no correlation between thyroid disorders and mental health issues such as depression and anxiety (21).

Several studies have examined the connection between anxiety and thyroid function. In one particular study, it was discovered that individuals with subclinical hypothyroidism and subclinical hyperthyroidism exhibited elevated anxiety scores compared to those who had normal thyroid function (22). The results of this study are similar to this study. Namely, the anxiety score of people with thyroid disorders is higher than those with euthyroid. Another study with almost the same results stated that the symptoms of anxiety and depression were felt more severely by people with overt hypothyroidism and overt hyperthyroidism (23). Research on sufferers of hyperthyroidism also showed that the hyperthyroid sufferer group had higher anxiety and depression scores than the euthyroid group.

Research limitations & medical implications

In this research, the researcher encountered certain limitations. These limitations were identified as follows:

1. It was discovered that the researcher faced difficulties in regularly accessing full-text journals, leading to prolonged search efforts.
2. The researcher required additional time to gather relevant journals related to the research problem for appropriate referencing.
3. More time was needed by the author to comprehensively analyze and understand the journal contents and to compile journals or books relevant to the research problem for suitable reference sources.
4. The availability of journals pertaining to research variables concerning the characteristics of Graves' disease with an ECG SND picture was limited.
5. Researchers were able to find, at the very least, one journal that provided in-depth results on the

Table 1 - Journal analysis

No	Journal Title and Researcher Name	Objective	Population/ Sample	Instrument	Data Analysis / Research Methods	Results	Journal Clustering
1	Hyperthyroidism and Sick Sinus Syndrome, a Rare but Challenging Association: A Study of Three Cases M Tudoran, C Tudoran (2017)	This study looked at case reports aged 48 years, 63 years and 66 years	A female patient aged 48, 63, and 66 years was admitted to the emergency department by him relatives.	Analyzing case reports on three cases	Hyperthyroidism is typically linked to sinus tachycardia or supraventricular tachyarrhythmias, with infrequent occurrences of sinus node or conduction dysfunction disruption.	Hyperthyroidism and SSS rarely occur together, primarily found in individuals with Graves' disease, even during subclinical phases, which can lead to challenges in treatment when concurrent tachyarrhythmias are present. It generally improves in the majority of cases following the restoration of thyroid hormone levels and seldom necessitates the implantation of a pacemaker.	Q2
2	Graves' disease and mental disorders Atsushi Fukaoa, Junta Takamatsub, Takeshi Arishimac, Mika Tanakad, Toshio Kawaie, Yasuki Okamotof, Akira Miyauchic, Akihisa Imagawa (2020)	This study is to see whether graves disease and mental disorder are related to each other	Conduct a literature review of articles from 1985-2014	Analyzing journals on Pubmed, and Elsevier	Systemic review studies	Mental disorders, such as depression and anxiety, frequently occur alongside Gender Dysphoria (GD). Additionally, psychosocial elements encompass stress and an awareness of the condition, while biological elements, such as the impact of thyroid hormones, can affect the progression of the illness. Approaches involving both psychology and the body, like the use of antipsychotic medications and psychotherapy rooted in a bio-psycho-social framework, are considered viable treatments. Medical models are regarded as beneficial for individuals experiencing concurrent symptoms of mental health disorders and hyperthyroidism in the context of GD.	Q2
3	Digital Interventions for Generalized Anxiety Disorder (GAD): Systematic Review and Network Meta-Analysis Pedro Saramago (2021)	Generalized anxiety disorder is the most common mental health condition based on weekly prevalence. Digital interventions have been used as an alternative or as a supplement to conventional therapy to improven access, patient choice, and clinical results. Little is known about their comparative effectiveness for generalization anxiety disorders.	We included 21 randomized controlled trials with a total of 2350 participants of the general anxiety disorder population noneintervention.	We performed a systematic review and random network meta-analysis controlled trials comparing digital interventions with medication, non-digital interventions, non-therapeutic controls, and	The results obtained from the analysis of covariance and the ranking based on the cumulative rating curve indicated that antidepressant medication and group therapy had a greater likelihood of being considered the most effective interventions compared to digital interventions. It should be noted that supported digital interventions are not inherently superior to unsupported ones (pure self-help).	Because of the extensive confidence intervals, the outcomes of the network meta-analysis raise uncertainty regarding whether digital interventions are superior to no intervention or non-therapeutic active controls, or if they offer added advantages compared to standard therapy. Future research should involve comparisons between digital interventions and one-on-one therapy, as well as between digital interventions and non-digital self-help manuals. Additionally, including antidepressant medications as a treatment comparison and assessing their impact changes will be necessary.	Q2
4	Graves' disease and mental disorders Atsushi Fukao (2020)	Mental disorders are closely associated with thyroid disease. Due to its regulatory effect on serotonin andnoradrenaline, T3 has been closely linked to depression and anxiety	Literature review data study from 1998-2017	Literature review	Analysis of literature review	Mental disorders, such as depression and anxiety, frequently accompany Gender Dysphoria (GD). Psychosocial elements, such as stress and awareness of the condition, also play a role. Biological factors, including the impact of thyroid hormones, can affect the progression of GD. The psychosomatic approach incorporates the use of antipsychotic medications and psychotherapy grounded in a bio-psycho-social framework. Medical models are deemed beneficial for individuals experiencing simultaneous mental GD symptoms and hyperthyroidism.	Q2

Table 1 - Journal analysis (continuation)

No	Journal Title and Researcher Name	Objective	Population/ Sample	Instrument	Data Analysis / Research Methods	Results	Journal Clustering
5	The Role of Cytotoxic T-lymphocyte-associated Protein 4 (CTLA-4) Gene, Thyroid Stimulating Hormone Receptor (TSHR) Gene and Regulatory T-cells as Risk Factors for Relapse in Patients with Graves Disease Fatima Eliana (2017)	Graves' disease (GD) is a condition commonly found in thyrotoxicosis. The management of GD begins with administration of antithyroid drugs, although the patient needs time time to achieve recovery or remission.	Compared 72 subjects with relapse and 72 subjects without relapse at 12 months after discontinuation of antithyroid treatment	Case control study	Genetic polymorphism analysis was conducted through PCR-RFLP. The quantification of Regulatory T cells was performed using flow cytometry analysis and ELISA for TRAb measurement. Logistic regression was employed due to the categorical nature of the dependent variable.	Genetic polymorphism at nucleotide 49 in codon 17 in exon 1 of the CTLA-4 gene, the SNP rs2268458 in intron 1 of the TSHR gene, combined with the levels of Regulatory T cells and TRAb, constitute risk factors for relapse in patients with Graves' disease.	S1
6	Long Term Antithyroid Drug Treatment: Systematic Review and Meta Analysis Azizi (2017)	Some studies have reported inconsistent findings regarding advantages and disadvantages long-term treatment with antithyroid drugs (ATD). A systematic review and meta-analysis was carried out to clarify various aspects of long-term treatment with ATD	Medline and the Cochrane Library for trials published between 1950 and May 2016 were searched systematic.	Literature review	Studies that included data on the extended treatment of TB for more than 24 months were incorporated. A summary was generated using a random effect model to calculate pooled prevalence estimates, odds ratios, and weighted mean differences.	Among the 587 related articles uncovered, six satisfied the inclusion criteria. Prolonged OAT therapy resulted in a remission rate of 57% [with a confidence interval (CI) ranging from 45% to 68%], with a higher rate observed in adults compared to non-adults (61% vs. 53%). The complication rate stood at 19.1% [CI 9.6–30.9%], of which only 1.5% constituted major complications. Each year of treatment saw an annual remission rate of 16% [CI 10–27%], which was more pronounced in adults versus non-adults (19% vs. 14%). Nonetheless, it's worth noting that this doesn't represent a true linear correlation, although a positive relationship between time and remission rates can be inferred. Meta-regression analysis unveiled that smoking had a notably adverse impact on remission rates. In conclusion, Long-term OAT treatment demonstrates efficacy and safety, particularly in adults, suggesting its consideration as an alternative therapy for Graves' disease.	Q2
7	Sick sinus syndrome and hyperthyroidism: A rare phenomenon Nitesh Kumar, Diwakar Verma, Kapil Gupta, Madhu Kiran, Prakarti Yadav, Shatrughan Pareek (2021)	This study is to look at case reports that are 70 years old	A 70 year old female patient was brought in to the emergency department by him relatives. He have a history of that feeling dizziness and light headedness. He is a known case of diabetes mellitus, hyperthyroidism, hypertension, and atrium fibrillation with controlled ventricular rate.	Analyzing case reports	Analyzing rare case reports	Hyperthyroidism and SSS are uncommon occurrences, particularly in individuals diagnosed with Graves' disease. SSS/SA/AV node block can be rectified through the treatment of hyperthyroidism to restore euthyroidism, potentially obviating the requirement for a pacemaker. This instance underscores the identification of SSS in hyperthyroidism, subsequent to the pacemaker implantation. Achieving control over hyperthyroidism eventually led to the restoration of a regular rhythm and the eventual removal of the pacemaker.	Q2

Table 1 - Journal analysis (continuation)

No	Journal Title and Researcher Name	Objective	Population/ Sample	Instrument	Data Analysis / Research Methods	Results	Journal Clustering
8	An Adolescent Patient with Sick Sinus Syndrome Complicated by Hypothyroidism Carrying a Case Report of the SCN5A A Variant Hiroaki Yamane, Mitsuru Seki, Takahiro Ikeda, Ayumi Matsumoto, Sadahiro Furui, Tomoyuki Sato, Kazuhiro Muramatsu, Toshihiro Tajima, Takanori Yamagata (2022)	This study is to see case report that is 13 years old	An old girlA 13 year old was referred to our hospital for bradycardia, as revealed by the school's electrocardiography (ECG) screening. There were no ECG abnormalities been observed during school screening 3 previous year. He has had no episodes of syncope, he reported noticing facial and lower leg edema as well as quickly tired over the past 2 years. An analysis its growth curve is also revealingIt's true that he experienced a growth slowdown during this 2 year period. No family history of arrhythmia, sudden death, or congenital heart disease	Analyzing case reports	Analyzing case reports	In this report, we've outlined the instances of a 13-year-old girl diagnosed with SSS who possesses the SCN5A variant and has additionally experienced the onset of hypothyroidism. The current case underscores the significance of genetic analysis, particularly for the SCN5A variant, among individuals dealing with hypothyroidism complicated by SSS or cardiac conduction disorders.	Q2

characteristics of Graves' disease with an ECG SND picture.

The study's findings suggest a connection between Graves' disease and the occurrence of an ECG picture of Sick Sinus Syndrome (SSS). Based on these study results, it is anticipated that healthcare professionals will gain a better understanding of the characteristics of individuals with anxiety disorders in Graves' disease who exhibit an ECG picture of Sick Sinus Syndrome (SSS).

CONCLUSION

After going through a sequence of procedures and considering research outcomes from Scopus and Sinta indexed journals that focus on the characteristics of systematic reviews in patients with diffuse toxic and non-toxic goiter displaying an ECG pattern of SND, we can draw the conclusion that the majority of these journals address the correlation between age and gender as risk factors for Graves' disease.

From the subsections examined, it is evident that the risk factors for Graves' disease are established based on age, gender, and lifestyle. Additionally, Graves' disease is linked to anxiety disorders and the presence of an SND ECG pattern.

Authors' contributions

The author acknowledges exclusive accountability for the subsequent tasks: conceptualization and design of the study, gathering of data, analysis and result interpretation, as well as the preparation of the manuscript. The final manuscript was reviewed and endorsed by all authors.

Conflicts of interest

The authors confirm that there are no conflicts of interest involving any financial organizations in relation to the content discussed in the manuscript.

REFERENCE

1. Slee A, Nazareth I, Bondaronek P, Liu Y, Cheng Z, Freemantle N. Pharmacological treatments for generalized anxiety disorder: a systematic review and network meta-analysis. Lancet. 2019;393(10173): 768-777.
2. Rago T, Cantisani V, Ianni F, Chiovato L, Garberoglio R, Durante C, et al. Reporting of thyroid ultrasound: consensus of the Italian Thyroid Association (AIT), Italian Society of Endocrinology (SIE), Italian Society of Ultrasonography in Medicine and Biology (SIUMB) and Ultrasound Chapter of the Italian Society of Medical Radiology (SIRM). J Endocrinol Invest. 2018;41(12):1435-1443.
3. Kotwal A, Stan M. Thyrotropin receptor antibodies - a review. Ophthalmic Plast Reconstr Surg. 2018;34(4S Suppl 1):S20-S27.
4. Struja T, Tehlberg H, Kutz A, Guebelin L, Degen C, Mueller B, et al. Can we predict Graves' disease recurrence? Results from systematic review

and meta-analysis. Eur J Endocrinol. 2017;176(1):87-97.
5. Liu J, Fu J, Xu Y, Wang G. Antithyroid drug therapy for Graves' disease and implications for recurrence. Int J Endocrinol. 2017:2017:3813540.
6. Srikandi NMPR, Suwidnya IW. Hyperthyroidism Graves disease: case report. Rafflesia Medical J. 2020;6:30-35.
7. Widjaja, DK & Setiawan, AA Description of Heart Rhythm Disorders Caused by Hyperthyroidism. Diponegoro Medical Journal 6, (2017).
8. Pokhrel B, Bhusal K. Graves Disease. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023.
9. Dakkak, W. & Doukky, R. Sick Sinus Syndrome. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023.
10. Aung ET, Zammitt NN, Dover AR, Strachan MWJ, Seckl JR, Gibb FW. Predicting outcomes and complications after radioiodine therapy in Graves' thyrotoxicosis. Clin Endocrinol (Oxf). 2019;90(1):192-199. Epub 2018 Oct 25.
11. Alkorashy M, Al-Ghamdi B, Tulbah SA, Al-Numair NS, Alhadeq F, Takroni SA, et al. A novel homozygous variant of SCN5A detected in sick sinus syndrome. Pacing Clin Electrophysiol. 2021;44(2):380-384. Epub 2020 Oct 1.
12. Eliana F, Soewondo P, Asmarinah A, Harahap A, Djauzi S, Prihartono J, et al. The Role of Cytotoxic T-lymphocyte-associated Protein 4 (CTLA-4) Gene, Thyroid Stimulating Hormone Receptor (TSHR) Gene and Regulatory T-cells as Risk Factors for Relapse in Patients with Graves Disease. Acta Med Indones. 2017;49(3):195-204.
13. Huang R, Yan L, Lei Y, Li Y. Hypothyroidism and Complicated Sick Sinus Syndrome and Severe Acute Psychiatric Disorders: Case Report. Int Med Case Rep J. 2021:14:171-176.
14. Azizi F, Malboosbaf R. Long-term antithyroid drug treatment: a systematic review and meta-analysis. Thyroid. 2017;27(10):1223-1231.
15. Yamane H, Seki M, Ikeda T, Matsumoto A, Furui S, Sato T. An Adolescent Patient with Sick Sinus Syndrome Complicated by Hypothyroidism Carrying a Case Report of the SCN5A A Variant. Int Heart J. 2022;63(3):627-632.
16. Tudoran M, Tudoran C. Hyperthyroidism and sick sinus syndrome, a rare but challenging association: A study of three cases. Niger J Clin Pract. 2017;20(8):1046-1048.
17. Saramago P, Gega L, Marshall D, Nikolaidis GF, Jankovic D, Melton H, et al. Digital Interventions for Generalized Anxiety Disorder (GAD): A Systematic Review and Network Meta-Analysis. Front Psychiatry. 2021:12:726222.
18. Subekti I, Pramono LA. Current Diagnosis and Management of Graves' Disease. Acta Med Indones. 2018;50(2):177-182.
19. De Regibus V, Rordorf R, Giorgianni C, Canclini C, Vicentini A, Taravelli E, et al. Autosomal recessive atrial disease presenting with sick sinus syndrome (SSS), right atrial fibrosis, and biatrial dilatation: The clinical impact of a genetic diagnosis. Int J Cardiol. 2016: 208:67-9.
20. Mallick R, Asban A, Chung S, Hur J, Lindeman B, Chen H. To admit or not to admit? Experience with outpatient thyroidectomy for Graves' disease in a high-volume tertiary care center. Am J Surg. 2018; 216(5):985-989.
21. Hussain YS, Hookham JC, Allahabadia A, Balasubramanian SP. Epidemiology, management and outcomes of Graves' disease - real life data. Endocrine. 2017;56(3):568-578.
22. Juwita DA, Suhatri & Hestia R. Evaluation of Antithyroid Drug Use in Hyperthyroid Patients at Dr. M. Djamil Padang, Indonesia. Journal of Pharmaceutical & Clinical Sciences. 2018;5:49-54.
23. Fukao A, Takamatsu J, Arishima T, Tanaka M, Kawai T, Okamoto Y, et al. Graves' disease and mental disorders. J Clin Transl Endocrinol. 2019:19:100207.