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Risk Factors and Clinical Manifestations in Hyperthyroidism: A Systematic Review

Faktor Resiko dan Manifestasi Klinis Pada Hipertiroid: Tinjauan Sistematis

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ABSTRACT

Background: The recommended iodine intake for adult women is 150-300µg and for men <150µg, which functions in maintaining normal thyroid function. Hyperthyroid condition is characterized as increased synthesis or secretion of hormones by the thyroid gland. A family history of Graves' disease is the most frequently found risk factor, namely 60-80% worldwide. The prevalence of hyperthyroidism cases in Indonesia is around 6.8%
Objectives: Comprehensively identifying risk factors and clinical manifestations of hyperthyroidism in case studies.
Methods: This research was carried out with a systematic review using two databases, namely Pubmed and Scopus. The literature search strategy was carried out using *Convidence software* by including predetermined inclusion and exclusion criteria. There were 11 selected pieces of literature published from January 2016 to October 2022
Discussion: A total of 11 case studies showed that women dominated cases of hyperthyroidism with a ratio of 3:1. Through a systematic review conducted by researchers, it shows that Graves' disease is the leading risk factor and clinical manifestations such as swelling of the thyroid gland, difficulty breathing, progressive weight gain, tremors, and heart palpitations are often found.
Conclusion: Patients who are female and have a family history of Graves' disease are the most common risk factors found with clinical manifestations of swollen thyroid gland, difficulty breathing, progressive weight gain, tremors, and palpitations.

INTRODUCTION

Hyperthyroidism is a condition of increased production and secretion of thyroid hormone by the thyroid gland. This condition is characterized by increased T3 (triiodothyronine) and T4 (thyroxine) due to the immune system attacking the thyroid gland. The most significant risk factor is genetic, which is 80%, followed by environmental factors at 20% which comes from exposure to cigarette smoke and a person's stress level[1]. The body's need for iodine functions as a synthesis of thyroid hormone to help regulate cell metabolic activity. Iodine is also important for cell replication and is closely related to the development of fetal brain cells in the womb[2]. Consuming iodine is very important to support thyroid function, but excessive consumption can inhibit the formation of thyroid hormone, It can cause hypothyroidism or swelling of the thyroid gland[3].

The prevalence of hyperthyroidism cases in Indonesia is around 6.9%[4]. This percentage contrasts with the overall prevalence of hyperthyroidism in the United States at 1.2% and in Europe at 0.8%[5]. Specifically, the condition of hyperthyroidism based on age is more common in women. In general, to diagnose thyrotoxicosis and determine the cause, a thorough, careful and thorough history and physical examination is required, assisted by supporting examinations such as laboratory examination of levels of Thyroid Stimulating Hormone (TSHs), Free Thyroxine 4 (FT4), and sometimes tri-iodothyronine (T3) total[4,6].

In 1990, the salt iodization program was introduced, and it was widely recognized that iodization could reduce the prevalence of iodine deficiency in the population[7]. Mild cases can usually be treated with the best sources of iodine salt from dairy foods such as milk, egg yolks, and sea fish. On the other hand, some problems can be observed from a public health perspective that pregnant women, fetuses, neonates and infants are the groups most vulnerable to iodine problems because of the irreversible health risks that can cause brain damage and impaired intellectual

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development[5]. The recommended iodine intake for adult women is 150-300µg and for men <150µg to function in maintaining normal thyroid function, while in pregnant women, iodine intake increases along with the needs of the fetus[5]. Only 18% of pregnant women and 19% of breastfeeding women use iodine supplementation, according to data from The National Health and Nutrition Examination Survey (NHANES) 2011-20145. The World Health Organization (WHO) recommends 250 mcg of iodine daily for pregnant and breastfeeding women[8]. Therefore, the author aims to identify risk factors and clinical manifestations of hyperthyroidism comprehensively.

METHODS

This research was conducted with a systematic review using the PubMed and Scopus databases in the period 2016-2022 with the keywords "risk factor," "hyperthyroidism," "case reports," or "case study." This research literature refers to previously established inclusion and exclusion criteria. Several inclusion criteria in this study include: (i) research identifying risk factors for hyperthyroidism, (ii) research identifying clinical manifestations of hyperthyroidism, and (iii) literature consisting of case studies/case reports. Meanwhile, the exclusion criteria in this study, are (i) research involving participants with other comorbidities such as metabolic syndrome, diabetes, hypertension, cancer, and others; (ii) research conducted at the experimental animal or cellular level; and (iii) unpublished articles and duplicate articles. The literature search used Confidence software to facilitate article extraction. The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) diagram of the literature search strategy used in this study is presented in Figure 1.

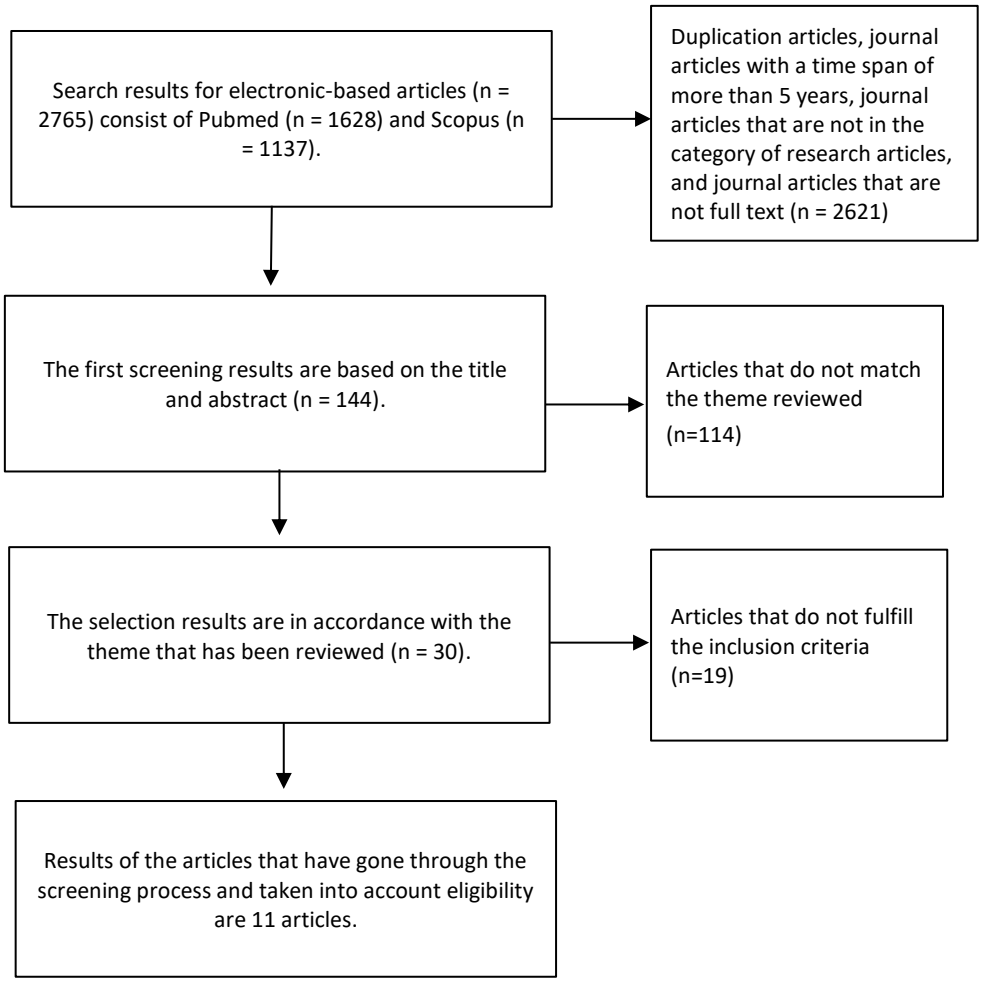

Figure 1. PRISMA flow diagram of the article selection process

DISCUSSION

Researchers obtained 11 works of literature with quite diverse respondent characteristics. One case was found in the adolescent age (15 years), while ten points were found in the adult age (>25 years). The results of the literature extraction presented in Table 1 showed that females are more dominant in experiencing cases of hyperthyroid disorders with a ratio of 3:1.

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Table 1. Characteristics of selected research

Research	Sex (M/F)	Age (Old)	Thyroid Disorders	Risk Factors	Comorbidities	Clinical Symptoms	Laboratory Data			Treatments	Recovery Time
							TSH	Free T_3	Free T_4		
(Kulkarni et al.) 2021[9]	M	45	Toxic adenoma	Family history	Graves' Disease	• Thyroid Gland (+) • Hoarseness • Breathing Difficulties • Mild tachycardia	0.02 mIU/L	2.21 ng/mL	10.74 g/dL	**Pharmacological** Anti-thyroid medication 5% Lugol's iodine 8 drops (60 mg) Methimazole 10 mg Propranolol 20 mg Hydrocortisone 10 mg Surgery	8 Days
Asif et al., 2022[10]	M	37	Psychosis	Family History	Graves' Disease	• Thyroid Gland (+) • Mood Swings • Insomnia • Talking more • Acting paranoid • Hyperactive	(<0.01 uIU/mL) normal: (0.27-4.20 uIU/mL)	(9.27 pg/mL) normal: (1.80-4.60 pg/mL)	(3.4 ng/dL) normal:(0.9-1.8 ng/dL)	**Pharmacological** Anti-thyroid medication Methimazole 30mg Propranolol 80 mg Hydrocortisone 100mg	1 week
(Kazakou et al., 2018)[11]	F	33	Fetal Hyperthyroidism	Family History	Graves' disease in pregnant women	• Intrauterine growth retardation • Oligohydramnios • Increased heart rate (signs of heart failure) • Fetal tachycardia • Hydrops	1.7 U/ml normal: (1-3)	N/A	18.53 pmol/L Normal: (12-22)	**Pharmacological** Anti-thyroid medication Methimazole, Propranolol are given to newborns The infant died → severe infection and shortness of breath	30 + 3 weeks
(Overcash et al., 2016)[3]	F	27	Fetal Goiter	Consuming excessive iodine supplements during pregnancy	Hypothyroidism during pregnancy	• Infant neck hyperextension → due to the presence of • Polyhydramnios with amniotic fluid	2.73 IU/mL (normal : 0.4–3.6 IU/mL)	2.0 ng/mL (1.8–3.7 ng/mL) .	8.3 g/dL (normal: 7.5–10.3 g/dL)	**Pharmacological** Anti-thyroid medication Synthroid 75µg	-

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Research	Sex (M/F)	Age (Old)	Thyroid Disorders	Risk Factors	Comorbidities	Clinical Symptoms	Laboratory Data			Treatments	Recovery Time
							TSH	Free T_3	Free T_4		
(Pangaribuan & Santi Syafril, 2021)[12]	F	31	Postpartum Thyroiditis	Postnatal inflammation of the thyroid gland	Diabetes Mellitus Type 2 Dyslipidemia	• Thyroid Gland (+) grade 2 • Hoarseness • Feeling tired easily	75.41 mU/ml	0.53	0.46	**Pharmacological** Euthyrox 1x100 mcg, Lantus injection 10 IU SC Additional therapy of Simvastatin 1x 20 mg.	6 Days
Onwukwe., et al 2022[13]	F	44	Autoimmune Thyroid	Family history	Graves' Disease	• Progressive weight gain • Constipation • Cold intolerance	100 mIU/L (0.30-3.5)	1.4 pmol/L	3.2 pmol/L	**Pharmacological** Anti-thyroid medication Thyroxine 200mcg/hari	-
Punitha et al., 2019[14]	F	60	Papillary Thyroid Cancer	Thyroid carcinoma	Hypertension	• Thyroid gland (+) • Coughing • Shortness of breath • Odinophagia	N/A	N/A	N/A	**Pharmacological** Anti-cancer drugs → Vincristine, Cyclophosphamide, Doxorubicin Chemotherapy →corticosteroids	6 cycles
Tsai et al., 2022[15]	F	66	Thyroid dysfunction	-	Osteoporosis	• Progressive weight loss • Anxiety • Insomnia • Heat intolerance • Tremors • Heart palpitations	0.09 mIU/L (0.3-4.7)	400 pg/dL (222-383)	1.6 ng/dL (0.8-1.7)	Anti-thyroid medication	-

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Research	Sex (M/F)	Age (Old)	Thyroid Disorders	Risk Factors	Comorbidities	Clinical Symptoms	Laboratory Data			Treatments	Recovery Time
							TSH	Free T_3	Free T_4		
Dey Parijat., 2020[16]	M	48	Graves orbitopathy	Family history	Graves' Disease	• Pain in the eye area • Conjunctival hyperemia • Eyelid swelling • Reduced visual acuity (6/18) • Reduced colour vision	<0.01 mUL	21.6 pmol/L	35 pmol/L	**Pharmalogical** Anti-thyroid medication (1 mg Methylprednisolone)	3 days of treatment Decompression surgery
Subramonian., et al 2021[17]	F	15	Thyroid Dysfunction	-	Myalgias Hypertension	• Fatigue • Heat Intolerance • Mumbling • Myalgias • Heart Rate 148x/min and irregular • Blood Pressure 138/72mmHg	0.01 mU/L	>30.8 pmol/L	75.4 pmol/L	**Pharmacological** Anti-thyroid medication → methimazole 0.5mg/kg/day & bisoprolol 2.5mg 1x/day Synchronized cardioversion	4 months
Borrego., et al 2016[18]	F	53	Anxiety disorders	Endocrine system disorders	Thyroid dysfunction	• Heart palpitations • Trembling • Shortness of breath • Nausea • Psychiatric disorders	<0.005 mU/L	21 pmol/L	4 pmol/L	**Pharmacological** Anti-thyroid medication	-

Notes: M = Male; F = Female; TSH = thyroid-stimulating hormone; T3 = L-triiodothyronine; T4 = thyroxine; N/A = not available
Normal Values: TSH, 0.35-5.5 µU/mL; Free T3, 222–383 pg/dL; Free T4, 0.9-1.8ng/dL

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Risk Factors for Hyperthyroid Conditions

Hyperthyroidism refers to a condition when the body produces too affects many thyroid hormones so that the thyroid gland is too active in working, affecting metabolism in the body[19]. Several conditions that can affect excess hormone production include Graves' disease, excessive consumption of iodine supplements, inflammation of the thyroid gland after childbirth, and endocrine system disorders[3,10,12]. Through the systematic review above, researchers also identified several factors that increase the chance of hyperthyroidism. A family history of Graves' disease is the most dominant risk factor for the appearance of hyperthyroidism in patients as they get older[20]. Graves' disease is an autoimmune condition that occurs due to loss of immunotolerance, causing thyrotropin receptor antibodies (TRAb) to form, bind to, and stimulate thyroid-stimulating hormone (TSH) receptors. This condition will massively increase the synthesis and secretion of thyroid hormones[6]. Researchers also found cases with a maternal history of excessive iodine supplementation[3]. Although iodine consumption is significant to support thyroid function, excessive consumption can stimulate thyroid hormone production resulting in hyperthyroidism or swelling of the thyroid gland[2]. Excess consumption of iodine supplements in special conditions can result in the appearance of goiter in the fetus in the womb. During pregnancy, iodine crosses the placenta through active transport and iodine toxicity occurs when consumption is >1.1mg/day[21]. This can happen because the immature fetus cannot degrade intracellular iodine, so it will develop a hyperthyroid condition[22]. The recommendation for pregnant women is 200µg/day[21].

Women have a 3-10x higher risk of thyroid dysfunction compared to men[23]; right out of eleven cases found were dominated by female patients. According to endocrinologists, the thyroid gland synthesizes thyroid hormones used for complex metabolic processes, such as sexual activity, the nervous system, muscles, and skeleton. However, women are more vulnerable and very sensitive to hormonal changes, so excess iodine often causes more significant complications in women than men. The particular condition of hyperthyroidism is also found in postpartum pregnant women[6], characterized by elevated serum triiodothyronine T3 and/or thyroxin T4 and sometimes undetectable serum TSH[20].

Manifestations

Manifestations in hyperthyroidism adjust to the type of thyroid disorder that occurs. Special conditions in pregnant women with hyperthyroidism show fetal clinical symptoms such as intrauterine growth retardation, oligohydramnios, increased pulse rate (signs of heart failure), and fetal tachycardia[11]. Fetal hyperthyroidism occurs when excessive TSH antibody receptors cross the placenta. These antibodies stimulate adenylate cyclase in fetal thyrocytes, resulting in hyperthyroidism[24,25]. In this case, checking the TSH antibody receptor during 20-24 weeks of gestation is important. If the level exceeds the normal limit by three times, close monitoring should be done[24].

Ten kinds of literature were found involving adult patients aged >25 years with quite diverse thyroid disorders such as toxic adenoma, psychosis, autoimmune thyroid, and thyroid papillary cancer. Clinical manifestations, as in Table 1, generally show clinical symptoms such as swelling of the thyroid gland, difficulty breathing, progressive weight gain, tremors, and palpitations[9,13,14]. Researchers also found manifestations that appear in visual disturbances, namely pain in the eye area, conjunctival hyperemia, swollen eyelids, reduced visual acuity (6/18), and reduced color vision; this condition is related to thyroid eye disease[16].

Assessment

Diagnosis in hyperthyroid patients is carried out by conducting examinations related to clinical manifestations. Laboratory examinations performed to establish the diagnosis of hyperthyroidism are examinations of Free Thyroxine 4 (FT4), tri-iodothyronine (T3), and Thyroid Stimulating Hormone (TSHs) levels. In neonatal hyperthyroidism, diagnosis is made by looking at the history of autoimmune disease in the mother, anti-thyroid medications taken during pregnancy, premature birth, intrauterine growth restriction, microcephaly, narrow sutures, increased body temperature, irritable, very restless, hyperactive, tachypnea (breathing very quickly) hyper-reflection, tachycardia (heart rate >160x/min), arrhythmia (heart rhythm disturbance), enlarged heart ventricles, heart failure, and hypertension[20]. Researchers found cases of congenital hyperthyroidism that were detected through ultrasound examination and recognized clinical manifestations in the fetus, namely extension of the neck with a mass around the neck so that the infant's head was looked up accompanied by fetal tachycardia[11].

Elevated free T4 levels do not always correlate with the thyroid gland's size. Enlargement of the thyroid gland in Graves' disease is generally evenly distributed and palpably tender. In thyroid tumors, the lump is palpated hard, even without thyroid function abnormalities. Goiter gland is palpable consistency, nodular, painful, murmur, and bruit. Patients with symmetrical thyroid enlargement are accompanied by eye abnormalities. Eye abnormalities or orbitopathy are symptoms that often occur in graves' disease[16]. Laboratory examination is done by recognizing the presence of increased FT4 and FT3 levels, decreased TSH levels, and positive TRAb. In cases with suspicion of Toxic Adenoma, radiologic examination is needed to confirm the diagnosis[11].

Researchers found cases of hyperthyroidism experienced by pre-elderly and elderly groups with clinical manifestations such as progressive weight loss, insomnia, heat sensitivity, anxiety disorders, tremors, shortness of breath, hypertension, and odinophagia[14,15]. In one case, thyroid dysfunction was found to be accompanied by osteoporosis[15].

Treatments

Treatment for hyperthyroid conditions is adjusted to the cause of the problem. Age, physical condition, and severity of the patient's condition should be considered. According to the American Thyroid Association Guidelines, hyperthyroid states with Graves' disease should choose safe and effective treatments for

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patients[26]. In some developed countries such as America. Japan. And some countries in Europe, , health professionals are more inclined to use the treatment of anti-thyroid medications[27]. Previous studies have also shown that all three treatment methods (anti-thyroid medications, radioactive iodine, and surgery) show good results on the long-term quality of life of patients[28]. In some cases, anti-thyroid medication is most commonly given in patients with toxic adenoma, psychosis, fetal hyperthyroidism, fetal goiter, autoimmune, thyroid eye disease, and anxiety disorders[2,9,10,13,16,18]. Anti-thyroid medications that are widely used in the findings of the cases discussed are methimazole with varying doses of 0.5mg to 30mg/kg/day. While beta-blocker medications are propranolol and bisoprolol, the dose given is adjusted to the patient's condition. The recommended dose of beta-blocker medications is propranolol 10-40mg with a frequency of 3-4x a day, and this prescription is recommended for pregnant and lactating women. As for atenolol 25-100mg adjusted to a frequency of 1-2x a day, but not recommended for use in pregnant women[20]. Based on the findings above, anti-thyroid medications are widely used because in addition to adjusting to other conditions and comorbidities, these drugs have minimal side effects compared to other hyperthyroid therapies such as radioactive iodine or surgerypembedahan[20].

It is important to consider case findings in pregnant women with fetal hyperthyroidism or fetal goiter[3,11]. Hyperthyroidism occurs in 1-5% of neonates born to mothers with a history of Graves' disease[18]. Treatment with anti-thyroid medications such as methimazole or carbimazole is able to cross the placenta, which aims to maintain normal maternal and fetal thyroid function. However, if there are indications of hypothyroidism in the fetus, the dose should be reduced[24]. Fetal examination (heart rate, thyroid dopplet, bone maturation) as well as maternal anti-thyroid medication dosage should be considered by doctors and endocrinologists to achieve a balance between hypothyroidism and hyperthyroidism in the fetus[25,29]. Early diagnosis and treatment are essential to prevent permanent endocrine system disruption and early infant death.

CONCLUSIONS

Hyperthyroid refers to a condition when the body produces too much thyroid hormone, resulting in an overactive thyroid gland, and this condition will affect metabolism in the body. Hyperthyroidism is characterized by clinical symptoms such as swelling of the thyroid gland, difficulty breathing, progressive weight gain, tremors, and palpitations. Patients who are female and have a family history of Graves' disease are the most common risk factors. Recommendations are expected for future researchers to be able to focus research on graves' disease in terms of molecular to organic levels, so that more comprehensive findings are obtained.

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REFERENCES

1. Ferraninda, F., Kusumajaya, H. & Ardiansyah, A. Faktor-Faktor Yang Berhubungan Dengan Penyakit Hipertiroid Pada Pasien Poliklinik Penyakit Dalam Di UPTD RSUD Dr. (HC) Ir. Soekarno Provinsi Bangka Belitung Tahun 2022. *J. Ilmu Kesehat. Bhakti Husada Heal. Sci. J.* **14**, (2023).
2. Hernández, M. del C. V., Wilson, K. L., Combet, E. & Wardlaw, J. M. Brain Findings Associated with Iodine Deficiency Identified by Magnetic Resonance Methods: A Systematic Review. *Open J. Radiol.* **03**, (2013).
3. Overcash, R. T., Marc-Aurele, K. L., Hull, A. D. & Ramos, G. A. Maternal iodine exposure: A case of fetal goiter and neonatal hearing loss. *Pediatrics* **137**, (2016).
4. Kusrini, I. & Kumorowulan, S. Nilai Diagnostik Indeks Wayne Dan Indeks Newcastle Untuk Penapisan KASUS HIPERTIROID. *Balai Penelit. dan Pengemb. GAKI, KEMENKES RI* (2010).
5. Gupta, P. M. *et al.* Use of iodine-containing dietary supplements remains low among women of reproductive age in the United States: NHANES 2011–2014. *Nutrients* **10**, (2018).
6. De Leo, S., Lee, S. Y. & Braverman, L. E. Hyperthyroidism. *The Lancet* vol. 388 906–918 at https://doi.org/10.1016/S0140-6736(16)00278-6 (2016).
7. Delange, F. The disorders induced by iodine deficiency. *Thyroid* vol. 4 at https://doi.org/10.1089/thy.1994.4.107 (1994).
8. Young, M., Wolfheim, C., Marsh, D. R. & Hammamy, D. World health organization/United Nations children's fund joint statement on integrated community case management: An equity-focused strategy to improve access to essential treatment services for children. *Am. J. Trop. Med. Hyg.* **87**, (2012).
9. Kulkarni, S., Murchite, S., Parab, S., Tiwari, V. & Rajagopal, A. Pre-operative use of Lugol's iodine in a case with toxic adenomatous goiter. *Int. Surg. J.* **8**, (2021).
10. Asif, H., Nwachukwu, I., Khan, A., Rodriguez, G. & Bahtiyar, G. Hyperthyroidism Presenting With Mania and Psychosis: A Case Report. *Cureus* (2022) doi:10.7759/cureus.22322.
11. Kazakou, P. *et al.* Fetal hyperthyroidism associated with maternal thyroid autoantibodies: A case report. *Case Reports Women's Heal.* **20**, (2018).
12. Pangaribuan, J. P. & Santi Syafril. Postpartum Thyroiditis: A Case Report. *J. Endocrinol. Trop. Med. Infect. Dis.* **3**, (2021).

How to cite: *Anidha, Y., Ayu, W. C., Sari, N. M. W., & Nadhiroh, S. R. (2023) Risk Factors and Clinical Manifestations in Hyperthyroidism: A Systematic Review: Faktor Resiko dan Manifestasi Klinis Pada Hipertiroid: Tinjauan Sistematis. Amerta Nutrition, 7(2SP), 344–351.*

13. Onwukwe, C. H., Nwalozie, J. C., Kalu, O. K. & Chikezie, N. I. Autoimmune thyroid disease: Case reports of two siblings. *J. Clin. Sci. Res.* **12**, (2023).
14. Punitha, S., Jeyamani, V. P., Sindhu, S., Bhuvaneshwari, P. & Arshath, A. Papillary thyroid cancer patient with hyperthyroidism-a case study. *Int. J. Res. Pharm. Sci.* **10**, (2019).
15. Tsai, K. & Leung, A. M. Subclinical Hyperthyroidism: Case Report and Review of the Literature. in *A Case-Based Guide to Clinical Endocrinology, Third Edition* (2022). doi:10.1007/978-3-030-84367-0_7.
16. DeY, P. Thyroid Eye Disease: A Case Report, Review of Current Literature and Usefulness of Joint Specialist Clinics. *J. Thyroid Disord. Ther.* **9**, (2020).
17. Subramonian, D., Wu, Y. J., Amed, S. & Sanatani, S. Hyperthyroidism With Atrial Fibrillation in Children: A Case Report and Review of the Literature. *Frontiers in Endocrinology* vol. 12 at https://doi.org/10.3389/fendo.2021.689497 (2021).
18. Benavente López, S. *et al.* Hyperthyroidism and Psychotic Symptoms: a Case Report. *Eur. Psychiatry* **33**, (2016).
19. Doubleday, A. R. & Sippel, R. S. Hyperthyroidism. *Gland Surgery* vol. 9 124–135 at https://doi.org/10.21037/gs.2019.11.01 (2020).
20. Ross, D. S. *et al.* 2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis. *Thyroid* **26**, (2016).
21. Leung, A. M. & Braverman, L. E. Consequences of excess iodine. *Nature Reviews Endocrinology* vol. 10 at https://doi.org/10.1038/nrendo.2013.251 (2014).
22. WOLFF, J. & CHAIKOFF, I. L. Plasma inorganic iodide, a chemical regulator of normal thyroid function. *Endocrinology* **42**, (1948).
23. Wafa, B., Faten, H., Mouna, E., Fatma, M. & Mohamed, A. Hyperthyroidism and hepatic dysfunction: Report of 17 cases. *JGH Open* **4**, (2020).
24. Léger, J. & Carel, J. C. Diagnosis and management of hyperthyroidism from prenatal life to adolescence. *Best Practice and Research: Clinical Endocrinology and Metabolism* vol. 32 at https://doi.org/10.1016/j.beem.2018.03.014 (2018).
25. Banigé, M. *et al.* Study of the factors leading to fetal and neonatal dysthyroidism in children of patients with graves disease. *J. Endocr. Soc.* **1**, (2017).
26. Klein, I., Becker, D. V. & Levey, G. S. Treatment of hyperthyroid disease. *Annals of Internal Medicine* vol. 121 at https://doi.org/10.7326/0003-4819-121-4-199408150-00010 (1994).
27. Wartofsky, L. *et al.* Differences and similarities in the diagnosis and treatment of Graves' disease in Europe, Japan, and the United States. *Thyroid* **1**, (1991).
28. Abraham-Nordling, M. *et al.* Graves' disease: A long-term quality-of-life follow up of patients randomized to treatment with antithyroid drugs, radioiodine, or surgery. *Thyroid* **15**, (2005).
29. Hume, R. *et al.* Human fetal and cord serum thyroid hormones: Developmental trends and interrelationships. *J. Clin. Endocrinol. Metab.* **89**, (2004).

How to cite: *Anidha, Y., Ayu, W. C., Sari, N. M. W., & Nadhiroh, S. R. (2023) Risk Factors and Clinical Manifestations in Hyperthyroidism: A Systematic Review: Faktor Resiko dan Manifestasi Klinis Pada Hipertiroid: Tinjauan Sistematis. Amerta Nutrition, 7(2SP), 344–351.*