

AN OVERVIEW OF POSTPARTUM THYROIDITIS: PATHOGENESIS, DIAGNOSIS AND TREATMENT

I Gusti Lanang Rama Dwi Suputra^{1*}, Stephany Angelia²

¹Dokter magang, Departemen Ilmu Penyakit Dalam, RSUD Sanjiwani, Gianyar, Bali

²Dokter Umum, RSUD Tangguwisia, Singaraja, Bali

[*Email Korespondensi: Lramasuputra@gmail.com]

Abstract: An Overview of Postpartum Thyroiditis: Pathogenesis, Diagnosis and Treatment. *Postpartum thyroiditis is an autoimmune condition, the most common thyroid disease in pregnancy, and is often undiagnosed. Patients may suffer from this condition for an extended period of time, and its symptoms may have a devastating impact on their quality of life. This comprehensive review article provides an in-depth overview of postpartum thyroiditis, including its epidemiology, etiology, pathogenesis, diagnosis, prognosis, and treatment. The presence of postpartum thyroiditis is a reliable indicator of thyroid health in the future. Therefore, it is recommended that women with a history of this condition undergo routine testing, especially prior to conception.*

Keywords: Autoimmune, Postpartum Thyroiditis, Pregnancy

Abstrak: Gambaran Umum Tiroiditis Pascapersalinan: Patogenesis, Diagnosis dan Pengobatan. Tiroiditis postpartum adalah penyakit tiroid akibat kondisi autoimun yang paling umum terjadi pada kehamilan, dan seringkali tidak terdiagnosis. Pasien dapat menderita kondisi ini dalam jangka waktu yang lama, dan dapat berdampak buruk pada kualitas hidup pasien. Artikel ulasan komprehensif ini memberikan gambaran mendalam tentang tiroiditis postpartum, termasuk epidemiologi, etiologi, patogenesis, diagnosis, prognosis, dan pengobatannya. Tiroiditis postpartum merupakan indikator masalah gangguan fungsi tiroid dikemudian hari. Oleh karena itu, disarankan agar wanita dengan riwayat kondisi ini menjalani pemeriksaan rutin, terutama sebelum konsepsi selanjutnya.

Kata Kunci: Autoimun, Kehamilan, Tiroiditis Postpartum

INTRODUCTION

Postpartum thyroiditis is a destructive autoimmune thyroid disorder prevalent that manifests in the first postpartum year. It consists of transient hyperthyroidism, which affects 32% of patients, transient hypothyroidism, which affects 43%; and the classic form, which involves a sequence of transient hyperthyroidism, hypothyroidism, and recovery, which affects 25% of patients. (Naji Rad S & Deluxe L, 2022) Pregnant women without thyroid issues have this condition. Postpartum thyroiditis may cause thyroid dysfunction. Postpartum thyroiditis is linked with thyroid peroxidase (TPO) antibodies. Early-pregnancy thyroperoxidase (TPO) antibody positivity increases the risk of postpartum thyroiditis by 30% to 52%.

Following a miscarriage between 5 and 20 weeks, postpartum thyroiditis has been reported. Pregnancy's immunosuppression naturally lowers thyroid peroxidase (TPO) antibodies. A woman with a positive pregnancy test for TPO antibodies in all three trimesters has an 80% chance of postpartum thyroiditis. The Endocrine Society recommends high-risk postpartum thyroiditis screening. Women with postpartum thyroiditis, type 1 diabetes, or antithyroid peroxidase antibodies are at risk. High-risk women should have their serum TSH levels tested at three and six months postpartum. (Epp et al., 2021)

EPIDEMIOLOGY

The incidence of postpartum thyroiditis has been reported to vary from 1.1% to 16.7% in various studies,

with an average prevalence rate of 7.2%. Postpartum follow-up length and population iodine status affect rates. (Smith et al., 2017) Thailand has 1.1% incidence, whereas Brazil has 13.3%. Both regions consume less iodine. 19.1% and 20.0% of people with type 1 diabetes with a positive family history had postpartum thyroiditis. Postpartum thyroiditis recurrence in PPT patients is 42.4%. Prevalence triples in type 1 diabetics. In New York City, women with type 1 diabetes had 25% postpartum thyroiditis, compared to 8.8% overall. Since both are autoimmune conditions, type 1 diabetic women have a higher rate of postpartum thyroiditis. Additionally, type 1 diabetics have higher thyroid antibody rates. (Naji Rad S & Deluxe L, 2022)

ETIOLOGY

Postpartum thyroiditis is an autoimmune disorder that is linked to the existence of thyroid peroxidase (TPO) antibodies. Postpartum thyroiditis is destructive thyroiditis with lymphocytic infiltration. This condition may arise after childbirth. HLA-D and HLA-B haplotypes are linked to postpartum thyroiditis and Hashimoto thyroiditis. These findings highlight genetic predispositions to illness. Graves disease and Hashimoto thyroiditis are two autoimmune thyroid diseases related to TPO antibodies. The quantity of TPO antibodies in the thyroid gland determines lymphocyte infiltration. Antibody-dependent cell-mediated cytotoxicity is induced by TPO antibodies fixing complement. (Premawardhana & Lazarus, 2017)

PATHOGENESIS

Postpartum thyroiditis is strongly associated with thyroid autoimmunity during pregnancy, as shown by the presence of anti-thyroid peroxidase antibodies (TPO-Ab). Thyroid peroxidase is essential for thyroid hormone production by iodinating tyrosyl residues and linking them to generate T4 and T3. Major autoantigens are found on the thyrocyte's apical membrane-bound glycoprotein. All autoimmune thyroid diseases, including Hashimoto's,

Grave's, and postpartum, include TPO antibodies. Antibody titer indicates glandular lymphocytic invasion. (Keely, 2011) Unlike antithyroglobulin antibodies, these antibodies may induce antibody-dependent cell-mediated cytotoxicity. However, TPO-Ab is heterogeneous, recognizing various locations on the TPO molecule, activating complement differently, and destroying differently. TPO-Ab is strongly associated with postpartum thyroiditis, however, it is unclear whether it is a cause or a marker of thyroid cell disruption. (Argatska & Nonchev, 2014)

In postpartum thyroiditis, the inflammatory process is triggered by the emergence of TPO-Ab, activation of the complement cascade, raised IgG1 levels, lymphocyte abnormalities, increased NK cell activity, and certain HLA haplotypes. (Naji Rad S & Deluxe L, 2022) The inflammatory process activates thyroglobulin proteolysis in thyroid follicles. Hyperthyroidism results from the obliteration of thyroid follicles, which releases large amounts of thyroxine (T4) and triiodothyronine (T3) into the circulation. Hyperthyroidism is transient and lasts until all thyroglobulin stores are depleted from the blood, and the follicles have no more. Due to high T4/T3 levels, TSH secretion is downregulated, and new hormone generation is limited in hyperthyroidism. Inflammation must stop for thyroid hormone production to resume. (Epp et al., 2021)

DIAGNOSIS

Postpartum thyroiditis refers to the occurrence of painless thyroiditis in individuals during the postpartum period. Postpartum thyroiditis manifests within a timeframe of six months, with a typical onset period of two to four months following delivery. This condition's clinical course is indistinguishable from that of painless thyroiditis that occurs independently of pregnancy. The clinical progression of thyroid dysfunction resembles that of subacute thyroiditis, albeit lacking the presence of anterior neck pain or tenderness of the thyroid gland. Postpartum thyroiditis is observed

in 3 to 8 percent of all pregnancies.(Edlow & Norwitz, 2019) The typical progression consists of three stages: thyrotoxic, hypothyroid, and recovery. The thyrotoxic period takes one to three months after birth, followed by hypothyroidism three to six months later. After a year, normal thyroid function typically returns. The majority of individuals recover completely, while others develop hypothyroidism. Most patients diagnosed with postpartum thyroiditis exhibit either negligible or mild symptoms during the thyrotoxic phase, such as heat intolerance, palpitation, irritability, and fatigue. (Groer & Jevitt, 2014)

Postpartum thyroiditis in a hypothyroid state is primarily characterized by symptoms such as cold intolerance, constipation, dry skin, fatigue, impaired concentration, and paresthesia. According to a study, individuals diagnosed with postpartum thyroiditis and exhibiting positive thyroid peroxidase (TPO) antibodies experienced greater symptoms than those who tested negative for TPO antibodies.(Keely, 2011)

Postpartum thyroiditis is diagnosed based on clinical symptoms and thyroid function tests like TSH and free T4. Biochemically, postpartum thyroiditis and painless thyroiditis are similar. These include higher or upper limits of normal serum-free T4 and T3 levels and lowered blood TSH during hyperthyroidism. This phase may be overt or subclinical.(Gao et al., 2021) The blood T4 level may stay low for days to weeks before the serum TSH level rises in those transitioning from hyperthyroidism to hypothyroidism. TSH was suppressed during hyperthyroidism. Anti-thyroid peroxidase antibody levels are elevated in 60–85% of postpartum thyroiditis patients. Hypothyroid patients or those who have just become hypothyroid have the greatest levels of these antibodies. (Wong et al., 2018)

Certain patients may exhibit a marginal elevation in C-reactive protein and/or erythrocyte sedimentation rate. Healthcare providers responsible for caring for women following childbirth

must be cognizant of the potential for postpartum thyroid dysfunction, which may manifest in various symptoms during the postpartum phase.(Gao et al., 2021)

Histopathology of postpartum thyroiditis shows lymphocyte infiltration, germinal centers, and thyroid follicular collapse. Thyroid fine-needle aspiration reveals follicular cells, lymphocytes, and colloids. During recovery, follicles are more normal, but fibrosis and lymphocytic infiltration may still be visible.(Naji Rad S & Deluxe L, 2022)

TREATMENT

Treatment was needed for 40% of hypothyroid patients but not for thyrotoxicosis. Most people may progressively reduce its intensity over a year if treatment is needed. Several studies have shown that up to 20% of postpartum thyroiditis patients may require more intensive therapy. No prospective studies have examined the best time and approach for postpartum thyroiditis treatment. Treatment is based on the thyrotoxic state's transience. No studies have evaluated the effectiveness of treating the hyperthyroid phase of postpartum thyroiditis. (Keely, 2011) Nevertheless, subclinical hyperthyroidism impairs quality of life. Whenever necessary, the treatment of hyperthyroidism should be determined jointly by the patient and physician based on the severity of symptoms.

Postpartum thyroiditis symptoms are usually mild-mannered. Beta-blockers are commonly prescribed to alleviate symptoms such as palpitations, irritability, and anxiety. The negative consequences of beta-blockade are the morbidity linked to this treatment's administration. Propranolol is considered the preferred therapeutic option due to its capacity for convenient dose titration, resulting in the mitigation of symptoms such as palpitations, irritability, and nervousness. The duration of therapy typically spans less than three months and is subject to modification based on the levels of thyroid hormone and associated symptoms.(Samuels, 2012) According to the Food and Drug

Administration, using propranolol while breastfeeding is acceptable. The disadvantage of refusing treatment is that the woman will continue to exhibit symptoms. Thyrotoxic management is based on its transient nature. Since postpartum thyroiditis is destructive and does not boost thyroid hormone production, anti-thyroid medicines like methimazole and propylthiouracil have failed to cure it. (Epp et al., 2021)

After postpartum thyroiditis resolves, the serum TSH level should be tested in four to eight weeks (or if new symptoms occur) to screen for hypothyroidism. Treatment for hypothyroid postpartum thyroiditis is still a contentious topic. When to start therapy is unclear. Most doctors treat symptomatic postpartum hypothyroidism. (Alexander et al., 2017) However, treating asymptomatic women with high TSH levels is questionable. Therapy length is also debated. Hypothyroidism patients may wean L-T4 after 6–12 months or continue it till they have children. Treatment should be instituted for significant symptoms that develop in lactating or pregnant women. Postpartum thyroiditis patients with moderate hypothyroidism might seek levothyroxine (LT4) medication. (Keely, 2011) If medication is delayed, thyroid function should be assessed every four to eight weeks until euthyroid. Contraception should be recommended for women. Clinical studies have not determined the appropriate LT4 administration duration. Pregnant women or women that want to get pregnant should maintain euthyroidism. LT4 dosages should be progressively reduced 12 months after birth to determine the hypothyroid state's durability or transience in postpartum thyroiditis. Gradually reduce the dosage and check serum TSH levels every six to eight weeks. (Naji Rad S & Deluxe L, 2022)

PROGNOSIS

Postpartum thyroiditis has variable clinical manifestations. Postpartum thyroiditis affects 30% of patients one year after delivery. Within 12 to 18

months after the commencement of symptoms, the thyroid function returns to normal in most cases of postpartum thyroiditis. Nonetheless, certain cases do not recuperate from the hypothyroid phase and develop permanent hypothyroidism. (Naji Rad S & Deluxe L, 2022)

CONCLUSIONS

Postpartum thyroiditis (PPT) is an autoimmune disorder that leads to thyroid gland dysfunction. Women without pre-existing thyroid issues usually get it during the first year following the delivery. Postpartum thyroiditis has the potential to result in either temporary or enduring thyroid dysfunction. This article comprehensively reviews postpartum thyroiditis's epidemiology, etiology, pathogenesis, diagnosis, treatment, and prognosis. Postpartum thyroiditis strongly predicts future thyroid health, thus women with a history should be tested routinely, particularly before pregnancy.

REFERENCES

- Alexander, E. K., Pearce, E. N., Brent, G. A., Brown, R. S., Chen, H., Dosiou, C., Grobman, W. A., Laurberg, P., Lazarus, J. H., Mandel, S. J., Peeters, R. P., & Sullivan, S. (2017). 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease during Pregnancy and the Postpartum. *Thyroid*, 27(3), 315–389. <https://doi.org/10.1089/thy.2016.0457>
- Argatska, A., & Nonchev, B. (2014). Postpartum Thyroiditis. *Folia Medica*, 56, 145–151. <https://doi.org/10.2478/folmed-2014-0021>
- Edlow, A. G., & Norwitz, E. R. (2019). Endocrine Diseases of Pregnancy. In *Yen and Jaffe's Reproductive Endocrinology* (pp. 662–708.e17). Elsevier. <https://doi.org/10.1016/B978-0-323-47912-7.00027-5>

- Epp, R., Malcolm, J., Jolin-Dahel, K., Clermont, M., & Keely, E. (2021). Postpartum thyroiditis. *BMJ*, n495. <https://doi.org/10.1136/bmj.n495>
- Gao, X., Wang, X., Han, Y., Wang, H., Li, J., Hou, Y., Yang, Y., Wang, H., Teng, W., & Shan, Z. (2021). Postpartum Thyroid Dysfunction in Women With Known and Newly Diagnosed Hypothyroidism in Early Pregnancy. *Frontiers in Endocrinology*, 12. <https://doi.org/10.3389/fendo.2021.746329>
- Groer, M., & Jevitt, C. (2014). Symptoms and Signs Associated with Postpartum Thyroiditis. *Journal of Thyroid Research*, 2014, 1–6. <https://doi.org/10.1155/2014/531969>
- Keely, E. J. (2011). Postpartum thyroiditis: an autoimmune thyroid disorder which predicts future thyroid health. *Obstetric Medicine*, 4(1), 7–11. <https://doi.org/10.1258/om.2010.100041>
- Naji Rad S, & Deluxe L. (2022). Postpartum Thyroiditis. In *In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. PMID: 32491578.*
- Premawardhana, L. D. K. E., & Lazarus, J. H. (2017). Postpartum Thyroid Dysfunction. In *Encyclopedia of Endocrine Diseases* (pp. 746–751). Elsevier. <https://doi.org/10.1016/B978-0-12-801238-3.04192-1>
- Samuels, M. H. (2012). Subacute, Silent, and Postpartum Thyroiditis. *Medical Clinics of North America*, 96(2), 223–233. <https://doi.org/10.1016/j.mcna.2012.01.003>
- Smith, A., Eccles-Smith, J., D’Emden, M., & Lust, K. (2017). Thyroid disorders in pregnancy and postpartum. *Australian Prescriber*, 40(6), 214–219. <https://doi.org/10.18773/austprescr.2017.075>
- Wong, K. K., Gandhi, A., Rubello, D., Gross, M. D., & Jaffe, C. (2018). Challenging Diagnosis of Postpartum Thyroiditis and Co-Existing Thyroid Nodule. *AACE Clinical Case Reports*, 4(1), 30–34. <https://doi.org/10.4158/EP171755.CR>