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COMPLICATIONS OF HYPOTHYROID IN PREGNANCY: A REVIEW

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Abstract

Hyperthyroidism that occurs in pregnancy is a hazardous condition for the mother and the fetus because hyperthyroidism in pregnancy varies, which is around 2-17 in 1000 births and constitutes 1%-3% of the total number of hyperthyroid cases. Hypothyroidism is an endocrine disorder in which the thyroid gland produces the hormone thyroxine in small amounts, causing the baby to experience mental retardation. Thyroxine hormone plays a role in metabolic processes and body systems. Hypothyroidism that occurs in pregnant women can cause complications that are dangerous for the mother and fetus. This review discusses complications that can occur in mothers and babies caused by hypothyroidism through several stages: formulating questions, sorting and eligibility of articles, selecting articles to be used, and evaluating articles. The article selection process uses the prism flow, and based on this flow, 14 articles were obtained that matched the research objectives. The selected articles were then reviewed, summarized, and assessed using JBI. Findings from various studies show the complications of hypothyroidism in pregnant women and infants, which can cause increased morbidity and mortality rates for mothers and infants. Therefore, it is crucial to recognize hypothyroidism in pregnant women and neonates in order to prevent pregnancy issues.

Keywords: Hypothyroid, Pregnancy, Complications.

INTRODUCTION

The American Thyroid Association recommends using population-defined trimester-specific reference intervals for thyroid function tests. Subclinical hypothyroidism was found in 4% in the first and second trimesters[1]

During pregnancy, there is an increase in body metabolism and increased secretion of hormones to meet the needs of the intrauterine fetus. Thyroid hormone levels rise, and symptoms can be mild, and people who have it may not even be aware they have it (subclinical hypothyroidism). Hormone levels of thyroxine (T4) and triiodothyronine (T3) are normal, but hormone levels of thyroid-stimulating hormone (TSH) are high. Thyroxine (T4) and triiodothyronine (T3) hormone levels drop, which can lead to symptoms and other problems. This is called overt hypothyroidism. The hormone TSH levels rise. Symptoms can be very bad. For example, myxedema is a continuation of hypothyroidism where thyroxine (T4) and triiodothyronine (T3) hormone levels are low and TSH hormone levels are very high, leading to loss of brain function, loss of awareness, and coma. Hypothyroidism can lead to heart diseases like high blood pressure and dyslipidemia, as well as problems with pregnancy, the brain, and the muscles [2], [3].

The American Thyroid Association's guidelines for managing thyroid disease in pregnancy have been revised to include recommendations on thyroid function tests,

iodine nutrition, thyroid autoantibodies, pregnancy complications, hypothyroidism, thyrotoxicosis, thyroid nodules, cancer, fetal and neonatal considerations, thyroid disease and lactation, and future research directions[4].

Pregnancy has a considerable effect on maternal thyroid function. Mild thyroid enlargement is considered a normal component of pregnancy. The increase in size reflects the physiologic changes induced by pregnancy. Various adverse consequences, which can affect both mother and fetus, are associated with thyroid hormone abnormalities and maternal thyroid autoimmunity. Pregnancy can lead to thyroid dysfunction, with hyperthyroidism being common. Hypothyroidism also has a negative effect on the nutritional quality of human milk [5], [6].

Abortion, preterm labor, preeclampsia, maternal postpartum thyroiditis, and decreased IQ in children are all sequelae of maternal thyroid dysfunction. During the first trimester of pregnancy, maternal serum Thyroid Stimulating Hormone (TSH) levels are significantly lower than pre-pregnancy levels as a result of cross-reactivity of human chorionic gonadotropin (hCG), secreted by the placenta to the TSH receptor on the thyroid gland. Thyroid autoantibody titers decrease throughout pregnancy as a result of the immune suppression inherent in pregnancy. As a result of the naturally occurring changes in thyroid hormone levels during pregnancy, all thyroid function tests in pregnant women should be interpreted differently to non-pregnant women. Causes include iodine deficiency, autoimmune thyroiditis, overtreatment, and combined maternal and fetal hypothyroidism. Imbalances in maternal thyroid hormone levels can affect the morbidity and mortality of the fetus and newborn [7].

Complications of pregnant women with hypothyroidism are high risks that can be dangerous for both mother and fetus[8]. Symptoms of hypothyroidism in pregnancy appear vague and are rarely recognized due to symptoms that are similar to pregnancy symptoms, such as fatigue, weight gain, sensitivity to cold temperatures, digestive problems such as constipation, insomnia, dry skin, forgetfulness, and difficulty concentrating.

Some of the symptoms of hyperthyroidism are common in normal pregnancy, including increased heart rate, heat intolerance, and fatigue. Other symptoms more closely related to hyperthyroidism that most often occur are rapid and irregular heartbeat, mild tremors, unexplained weight loss or failure to gain normal pregnancy weight gain and severe nausea and vomiting associated with hyperemesis gravidarum [9], [10]. Poor control of thyrotoxicosis is associated with abortion, pregnancy-induced hypertension, prematurity, low birth weight, intrauterine growth restriction, stillbirth, thyroid storm, and maternal congestive heart failure [11].

The purpose of this review is to determine the complications that can occur in pregnant women with hypothyroidism and babies born to hypothyroid mothers.

RESEARCH METHODS

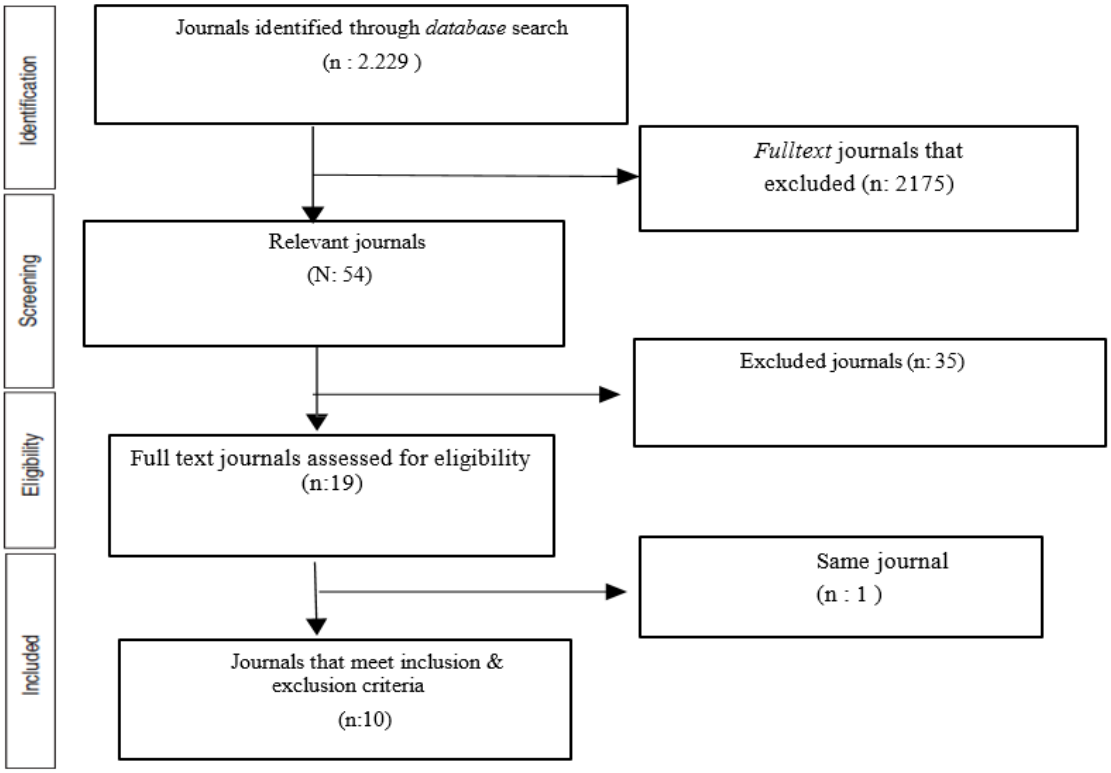

Figure 1: PRISMA Flow Diagram Results

This journal uses the systematic review stage. Organized using PICO (*problem intervention*, *comparison,* and *outcome*) rules, namely: "How does hypothyroid affect pregnancy? What are the complications that can occur in pregnant women with hypothyroidism and babies born to hypothyroid mothers?". Then, search for data sources in Science Direct, DOAJ, Pubmed, and Google Scholar using the keywords pregnant women, hypothyroid, and complications. After searching the data with these keywords, 2,229 articles were obtained: 918 articles from Pubmed, 803 articles from Google Scholar, and 508 from Science Direct. From these articles, screening is carried out by selecting articles relevant to the article's theme by reading the research abstract, and then 54 suitable articles are produced. The inclusion criteria are articles published in 2019-2024 with a research design using cohort. We read the contents of the 19 articles, and 10 articles that fit the inclusion criteria were obtained. Document selection was used the PRISMA (*Preferred Reporting Items for Systematic Reviews and Meta-Analyses*) flow and *JBI Levels of Evidence.*

RESULTS

Hypothyroidism is a relatively common disease in pregnancy. Between 2.2% and 2.5% of women have been found to have serum TSH levels of 6 mU/L or greater at 15 to 18 weeks gestation. The American Thyroid Association has defined overt hypothyroidism as normal serum FT4 with serum TSH more significant than 10 mIU/L, but this is not a standard definition. The prevalence of gestational hypothyroidism is 2- 5%, but the prevalence of subclinical hypothyroidism (3-5%) is much higher than overt hypothyroidism.

Complications that may arise during pregnancy include gestational diabetes, preterm rupture of membranes, hypertension, preeclampsia, and exacerbation of preexisting preeclampsia. Preeclampsia is additionally linked to placental abruption and eclampsia. Maternal complications during pregnancy have a direct impact on the developing fetus and the subsequent newborn. Elevating the likelihood of fetal growth problems, Intra Uterine Fetal Death (IUFD), raising the probability of abortion, early delivery, low birth weight (LBW), and heightening the chance of congenital hypothyroidism, which impacts the growth and development of children (Table 1).

Table 1: Journal Review Results of Hypothyroid Complications in Pregnancy

Author and year	Destination	Methods	Sample	Research results
Turunen S, Vääräsmäki M, Männistö T, Hartikainen AL, Lahesmaa Korpinen AM, Gissler M SE. Year 2022[12]	studying the relationship between maternal hypothyroidism and pregnancy complications And perinatal complications.	Cohort retrospect	All births between 2004 and 2013 (n = 16,364) to mothers in Finland	Hypothyroidism Maternal hypothyroidism is associated. with several complications pregnancy and perinatal complications, including diabetes mellitus gestational, hypertension gestational, severe preeclampsia, labor by cesarean section, premature birth, congenital anomalies major, and admission to intensive care unit neonatal intensive care unit
Sharin P. Barse, Vaishali R. Korde, Jaya S. Barla in 2020[13]	to assess the prevalence of thyroid dysfunction during pregnancy and its impact on the mother and fetus.	Prospective cohort	698 women pregnant with pregnancy Single in obstetrics and gynecology, MIMER Medical College, and Hospital Rural Bhausaheb Sardesai Talegaon.	There is a high prevalence thyroid dysfunction during pregnancy. Therefore, early diagnosis and prevention of consequences thyroid dysfunction during pregnancy is very important.
Patricia Lemieux,1Jennifer M. Yamamoto, Kara A et al. in 2021[14]	to investigate: (1) frequency and distribution of thyrotropin testing (TSH) testing and adjustment of levothyroxine dose adjustment based on gestational age gestational age,	A retrospective cohort study	All pregnant women who were detected hypothyroid period October 2014 and September 2017	TSH less than 0.10 mIU/L during pregnancy increases chance of labor preterm compared with pregnancy control pregnancies (odds ratio customized, 2,14 [95% confidence

	(2) the magnitude of Increase levothyroxine based on the etiology of hypothyroidism. etiology, and (3) the relationship between over-treatment and under treatment during pregnancy with poor pregnancy outcome poor pregnancy outcome in women who using thyroid replacement before pregnancy			interval 95% confidence interval 1,51-2,78]). TSH ≥10.00 mIU/L during pregnancy not associated with poor pregnancy or poor neonatal outcomes in the analysis multivariate
Mahadik K, Choudhary P, Roy PK. The year 2020. Kiran Z, Sheikh A, Humayun KN, Islam N. Year 2021.[9]	evaluating the mother and fetus in pregnant women with thyroid abnormalities (hypothyroid) Study the incidence of hypothyroidism before pregnancy and during Pregnancy and the complications.	Prospective cohort Cohort retrospective	198 pregnant women in the third trimester with Hypothyroid. 660 pregnant women who gave birth to live babies in Hospital Aga University Khan University Hospital. Data collected on women pregnant women with Hypothyroidism who diagnosed before pregnancy and during pregnancy during the years 2008-2016	Results. The results obtained in babies born are babies born with LBW. 31.6%, admitted to NICU 42.1%, and Low APGAR score 21.1%. The results obtained show that the risk of anemia increases in pregnant women with hypothyroidism.
Kiran Z, Sheikh A, Humayun KN, Islam N. Year 2021.[15]	evaluating the mother and fetus in pregnant women with thyroid abnormalities (hypothyroid) Study the incidence of hypothyroidism before pregnancy and during	Prospective cohort Cohort retrospective	198 pregnant women third trimester with Hypothyroid. 660 pregnant women who gave birth to live babies in Hospital Aga University Khan University Hospital. Data collected on	Neonatal jaundice is the result of neonatal outcome (37.6%). Almost 15% required hospitalization in the intensive care unit. The most common clinically significant congenital anomaly was cardiovascular abnormalities,

	pregnancy and the complications.		women pregnant women with hypothyroidism who diagnosed before pregnancy and during pregnancy during the years 2008-2016	while Mongolian spot was the most frequent congenital condition most frequently reported.There is statistically significant association between low birth weight and congenital anomalies
Marín Urueña SI, Infante López ME, Samaniego Fernández CM, Montejo Vicente MM, Escribano García C, Izquierdo Caballero R, Mulero Collantes I CCS. Year 2020[16]	Analyzing the incidence of of congenital hypothyroidism in newborns born of mothers with hypothyroidism	Prospective cohort	70 newborns of women with autoimmune thyroid disease (Hypothyroid).	Screening of newborns of hypothyroid mothers showed a high number of laboratory controls with poor diagnostic results (congenital hypothyroidism).
Zeba N, Chithra Arumgamuthu Kanagamuthu, Jayaraj P. Year 2022[17]	assessing hypothyroidism during pregnancy and its effects on the mother and fetus evaluate pregnancy that are based on exposure to maternal hypothyroidism and thyroid autoimmunity	Cohort retrospective Cohort Retrospectiv e	160 pregnant women with hypothyroidism in Department of Obstetrics and Gynecology Dhanalakshmi Srinivasan Medical College and Hospital, Tamil Nadu during 1 year, February 2019 to January 2020. A total of 14,744 pregnancies from North Denmark Region Pregnancy Cohort (2011-2015)	Results. results obtained significant between hypothyroidism in pregnancy and preterm labor preterm labor, as well as the significant to impaired fetal growth intra uteri, weight body weight low birth weight, and fetal distress
Louise Knøsgaard, Stig Andersen,Annebir the Bo Hansen Peter Vestergaard, Stine Linding Andersen year 2022[18]	assessing hypothyroidism during pregnancy and its effects on the mother and fetus evaluate pregnancy that are based on exposure to maternal	Cohort retrospective Cohort Retrospectiv e	160 pregnant women with hypothyroidism in Department of Obstetrics and Gynecology Dhanalakshmi Srinivasan Medical College and Hospital, Tamil Nadu	A high frequency of poor pregnancy outcomes is seen in pregnancies exposed to maternal TSH above 10 mIU/L, whereas no association with thyroid autoantibodies is

	hypothyroidism and thyroid autoimmunity		during 1 year, February 2019 to January 2020. A total of 14,744 pregnancies from North Denmark Region Pregnancy Cohort (2011-2015)	seen. with thyroid autoantibodies are seen.
Caroline Minassian, Lowri A. Allen et al. in 2023[19]	determine the course of action during pregnancy, and assess impact of treatment strategies before conception on the status of maternal thyroid status.	Prospective cohort Hyperthyroidism and subsequent pregnancies Next (January 2000 to December 2017).	women aged 15- 45 years old with clinical diagnosis	Pregnancy with definitive treatment previously more may have thyroid status suboptimal compared to pregnancies that initiated during treatment with antithyroid drugs A gradual decrease gradual decrease in use of treatment definitive treatment before pregnancy from 2000 to 2017
Luisi S, Giorgi M, Riggi S, Messina G SF. Year 2020[20]	evaluating the impact of hypothyroidism on the course of pregnancy and neonatal outcome	Prospective cohort	60 pregnant women with hypothyroidism	the risk of abortion is 8.7 times higher found in hypothyroid women, delayed fetal growth, increased risk of premature rupture of membranes (PROM), and a higher risk of developing hypertension and gestational diabetes

DISCUSSION

Hyperthyroidism is a disorder that occurs because the thyroid gland produces more thyroid hormones than the body needs. The study indicates that subclinical hypothyroidism is prevalent in low-risk pregnant women, and it is recommended that all these women be screened for thyroid dysfunction to reduce maternal and neonatal morbidity[21]. Hyperthyroidism in pregnancy is due to the intense stimulation of the thyroid gland by hCG and is usually limited to the first 12-16 weeks of pregnancy[22]. During pregnancy, hypothyroidism can lead to several complications, such as an increased risk of preeclampsia. A study at KIMS hospital found that 48 out of 700 pregnant women had thyroid disorders, with a 6.8% prevalence. Hypothyroidism was more common in the 21-30 year age group. The study recommends routine screening, early diagnosis, and prompt treatment for favorable maternal and fetal outcomes[23].

TSH levels are higher in preeclamptic women, but TT4, TT3, and FT3 are lower[24]. A study in India reveals that 13.3% of pregnant women have subclinical hypothyroidism, highlighting the need for routine antenatal screening and larger-scale research to address this public health issue[25]. During pregnancy, there is an increase in thyroid demand and iodine uptake. Estrogen hormone increases serum thyroxine-binding globulin (TBG), α-hCG, released by the placenta during pregnancy, identical to TSH, which has weak thyrotropic activity. The exact mechanism of hypothyroidism in preeclamptic women has not been found. However, according to various theories, the mechanism in preeclampsia is related to decreased plasma protein concentration and increased endothelin levels. High estrogen circulation can alter thyroid function. The decrease in thyroid function may be due to anti-angiogenic factors in preeclampsia that reduce nitric oxide production. This can decrease thyroid circulatory flow, which can lead to hypothyroidism. The results showed that subclinical hypothyroidism (SCH) was almost twice as likely to cause preeclampsia[26]**.**

Subclinical hypothyroidism in pregnancy is a risk factor for premature rupture of membranes. Another study found that hypothyroid mothers have an increased risk for spontaneous abortion, intrauterine growth restriction (IUGR), and low birth weight (LBW). Hypothyroidism is important in smooth muscle contraction in the renal system and systemic arteries, causing increased peripheral vascular resistance, diastolic blood pressure, and decreased tissue perfusion. Thyroxine hormones also play a role in the process of differentiation, development, and implantation of the placenta, if thyroxine levels are deficient, it can affect the placenta, the risk that may occur placental abruption, preterm labor, and intrauterine growth disorders, hypothyroidism in pregnancy in addition to causing complications in the mother can also be dangerous for the baby. Hypothyroid pregnancy, with various risks and complications in pregnancy as described earlier, can cause congenital hypothyroidism which can cause disability in the child. Disorders of the placenta can cause uteroplacental flow from mother to fetus during pregnancy to be disrupted, can result in fetal hypoxia intrauterine growth disorders, and, if not treated immediately, can cause fetal death in the womb (IUFD). The risk of babies born prematurely with LBW is high, born with asphyxia and respiratory distress syndrome. Research suggests APGAR scores are often lower in babies born to mothers with hypothyroidism. APGAR score depends on adequate uteroplacental circulation and oxygenation during fetal gestation[27].

Untreated hyperthyroidism is often associated with the incidence of pregnancy complications, including miscarriage, hypertensive disorders, preterm labor, low birth weight, and maternal emergencies such as thyrotoxic crisis and maternal congestive heart failure[28]. There is a wide range of management for hyperthyroidism in pregnancy. Antithyroid medication is the treatment of choice in controlling hyperthyroid symptoms during pregnancy. Another treatment modality that can be used is surgery, but if there are side effects with antithyroid medication, then surgery should be considered[16]**.**

The impact of pregnancy on maternal thyroid physiology is considerable. A study conducted at ESI Hospital found that subclinical thyroid dysfunction during pregnancy has adverse effects on both mother and fetus, emphasizing the importance of routine antenatal thyroid screening[29]. Changes in the structure and function of the gland sometimes cause difficulty in diagnosing thyroid disorders. *Thyroid-binding globulin* (TBG) concentration in maternal serum increases equivalent to the level of total thyroid

hormone and bound thyroid hormone. Serum TSH in early pregnancy decreases due to thyroid stimulation[17]**.**

CONCLUSION

Various complications may occur in pregnancy and babies born due to hypothyroidism during pregnancy. Complications that occur can cause death in the mother and fetus. During pregnancy, thyroid hormones have an important role in maternal and fetal metabolism, play a role in the cardiovascular system, and regulate blood pressure, so pregnant women with hypothyroidism are at risk of increased blood pressure, which can become gestational hypertension and preeclampsia, which can adversely affect the condition of the mother and fetus. Thyroid hormones also play a role in the early development of the placenta and its implantation process, so they can affect its function during pregnancy. If the placenta, which distributes all nutrients from the mother to the fetus, is disrupted, fetal growth and development will also be disrupted. This can increase maternal and infant morbidity and mortality rates (MMR and IMR).

Suggestion

Given the impact that hyperthyroidism in pregnancy can have, severe treatment needs to be taken. The low incidence rate globally and the lack of prevalence information in Indonesia make hyperthyroidism in pregnancy underestimated. A thorough examination of the history of the disease and pregnancy, as well as a physical examination and sonographic examination, is important to be carried out to confirm the diagnosis.

Early detection needs to be done in pregnant women so that pregnant women can be given appropriate therapy during pregnancy to minimize complications that may occur, as well as early detection in newborns by screening for congenital hypothyroidism.

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