



Study of the Consequences of Mothers' Hypothyroidism in Children: A Systematic Review

Marzieh Pazokian^{1*}, Farzane Khalandi¹

¹Faculty of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Corresponding Author: Farzaneh Khalandi, MSC in Critical Care Nursing, Faculty of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: farzykhalandi@gmail.com

Received April 21, 2019; Accepted July 28, 2019; Online Published September 22, 2019

Abstract

Introduction: Hypothyroidism is a common endocrine disorder that, occurs in 2% to 5% of pregnancies. During pregnancy, the body's demand for thyroid hormones increases, which affects the growth of the fetus. In case of inadequate and defective production of thyroid hormones, adverse effects on the development of the fetus will appear. Lack of symptoms of hypothyroidism during pregnancy causes late diagnosis, resulting in a lack of timely treatment and impaired fetal development. The purpose of this review is to investigate the effects of mothers' hypothyroidism on children.

Methods: This systematic review study was performed by searching the Google Scholar, PubMed, and Science Direct databases for the period between 2018 and 2008 by including the keywords for hypothyroidism, thyroid hormones, growth in the uterus. A number of papers related to the use of the Cochran seven-step model were obtained and analyzed for the final analysis.

Results: Thyroid hormones play a vital role in fetal development for ectopic life, through direct and indirect mechanisms that, act on the development of the fetus. Thyroid hormones help in the synthesis of surfactant and lung evolution, stimulation of secretion of catecholamine, increased beta-adrenergic receptors of the lung and stimulation: the activity of sodium and potassium pumps in the alveolar cell surface, the effect on the transmission of brain neurotransmitters and growth hormone, and nervous function.

Conclusions: Thyroid hormones play a key role in fetal development. Therefore, in women with hypothyroidism, especially when not treated, it affects the development of the fetus and increases the incidence of complications in neonates. So early diagnosis of hypothyroidism and adequate and timely treatment during pregnancy is cornerstone in preventing impaired growth and development of the fetus and the occurrence of defects in childhood.

Keywords: Hypothyroidism, Thyroid Hormones, Intrauterine Growth, Perinatal

Citation: Pazokian M, Khalandi F. Study of the consequences of mothers' hypothyroidism in children: A systematic review. Int J Med Rev. 2019;6(3):101-104. doi:10.29252/ijmr-060306.

Introduction

Hypothyroidism is a common endocrine disorder characterized by deficiency in the production of thyroid hormones and affects 2% to 5% of pregnancies.¹ Reduction and deficiency of iodine are the most preventable cause of hypothyroidism worldwide, and insufficient iodine, autoimmune thyroiditis are major causes of hypothyroidism.²

In pregnancy, the body's need and demand for thyroid hormone increases.² The treatment inadequacy for hypothyroidism has many adverse effects during pregnancy, such as abortion, preterm labor, and complete immobilization of the fetus, as well as autism and decreased IQ in the newborn.³ Thyroid hormones, through direct and indirect mechanisms, affect intrauterine fetal growth, including direct mechanisms; the effect on embryo metabolism through effects on the consumption of oxygen and glucose by the fetus. At the cellular and epithelial surface of the pulmonary alveoli, the oxidative metabolism and the activity of the pumps of sodium

and potassium are affected. One of the indirect mechanisms is the effect on fetal development through intervention in the endocrine system and secretion of the growth hormone.⁴ Evidence suggests that, the lack of treatment for women with hypothyroidism during pregnancy increases the risk of asthma in newborns, the transfer of mother's thyrotropin hormone by placenta to fetus is essential for the growth of organs. Therefore, the defect in the transfer of thyroid hormones to the fetus causes insufficient growth and development of vital organs in the neonate.⁵

During birth, the onset of ventilation and gas exchange in the lung depend on structural and functional changes, including the production of surfactants and the removal of lung fluid.⁶ Thyroid hormones affect the synthesis of phospholipid membranes and surfactant protein components, and on the other hand, thyroid hormones play an important role in lung fluid reabsorption by stimulating the secretion of catecholamines and increasing the activity of sodium

and potassium pumps in cell membranes of alveoli.⁵ The presence of thyroid hormones depends on the evolution of the pituitary, hypothalamus, thyroid axis, and the transfer of thyroid hormones from mother to fetus. Thyroid hormones play a role in many physiological processes that are essential for the life of the fetus, therefore, deficiency in the thyroid hormones affects the growth of vital organs of the fetus and adapts to the extra uterine life of the fetal.⁴ Among the mechanisms influenced by thyroid hormones that are essential for the survival of the uterus, the role of thyroid hormones for the development of the lung² and role of growth hormone secretion and the development of the hippocampus can mentioned; therefore, Deficiency of thyroid hormones is effective in memory and neurological pathways and cause the risk of seizure and hyperactivity.^{7,8}

Therefore, mothers with hypothyroidism, especially when not treated, increase the risk of complications in children.² Given that, mothers have a low thyroid dysfunction in the world, and between 2% and 5% of pregnancies,¹ the association between asthma, hyperactivity, mental disorders, seizures in children with low mother's thyroid function is important. According to the studies, hypothyroidism may interfere with the development of vital organs and problems in pulmonary, neurological, mental and evolutionary systems in children. There are a lot of reviews about the effects of hypothyroidism in pregnant women, the aim of this study, is to investigate the effects of pregnancy hypothyroidism on the occurrence of complications and deficits in children. Due to the lack of studies in this area, and the importance of identification and timely treatment of hypothyroidism during pregnancy to reduce the incidence of complications in children. In this study, we decided to study the effects of mother's hypothyroidism on children.

The results of this review study aimed at encouraging the implementation of planning for early diagnosis of hypothyroidism during pregnancy, as well as adequate and timely therapeutic measures to prevent complications of hypothyroidism on the fetus and to reduce the incidence of defects in children are important.

Methods

The purpose of this systematic review is to investigate the effects of mothers' hypothyroidism on children with regard to keywords; hypothyroidism, thyroid hormones, intrauterine and perinatal growth during the period 2008 to 2018 using data banks including; PubMed information, Google Scholar and Science Direct sites. The search in databases and information sites was done in three steps, in the first stage of search, based on relevant keywords, regardless of entry and exit criteria, in the second stage, obtaining criteria was done in accordance with the purpose of the study and based on the keywords and time limitations, and in the third stage, the most relevant studies were analyzed.

Second step: This step involves searching for and identifying the articles that are most relevant to this study. At this stage, the search process conducted using the hypothyroidism keywords, thyroid hormones, perinatal intrauterine growth

and inclusion criteria, including 10-year articles and during the period 2008 to 2018, articles related to Hypothyroidism in pregnant women, and exclusion criteria including book studies and reports, articles related to hypothyroidism in non-pregnant women were exploited.

Stage Three: Analyzing and reviewing articles, this step involves collecting and studying relevant content. At this stage, the articles were re-examined. This method is used to write a summary of each article which can be applied to identify and discuss the strengths and weaknesses of each of the article.

In [Figure 1](#), electronic search results are shown systematically.

Results

The results of these studies indicate a key and important role of thyroid hormones in the development of the fetus. The lack of hypothyroidism in mothers during pregnancy to transfer sufficient thyroid hormones and embryo development is so important. According to the studies, thyroid hormones affect the development and growth of embryonic organs through direct and indirect mechanisms and it is necessary for embryo adaptation for ectopic life.

Discussion

The purpose of this study is to systematically review the effects of mothers' hypothyroidism on children. According to studies, thyroid hormones play a significant role in many physiological processes, although these processes are small but crucial for the reconciliation of fetal ectopic life. Thyroid hormones are affected by two mechanisms that involve the direct mechanism of oxygen and glucose consumption by the fetus and the mechanism that indirectly affects the endocrine system.⁴ Physiological changes in pregnancy accompanied by some symptoms such as fatigue, anxiety, constipation, muscle cramps and weight gain are similar to those of hypothyroidism, which makes it difficult to diagnose hypothyroidism during pregnancy.⁹

Complications of hypothyroidism in mothers: Based on studies about hypothyroidism with pregnancy complications there are different symptoms such as; abortion, anemia in pregnancy, pregnancy-related hypertension, preeclampsia, early postpartum pains and postpartum hemorrhage, Gestational diabetes, as well as complications in infants born to mothers with hypothyroidism, preterm infant birth, low birth weight, intrauterine fetal death, and respiratory distress in newborns.¹⁰

The role of thyroid hormones in the development and growth of the fetus: Thyroid hormones play an essential role in the development and growth of the fetus and the ability of the fetal ectopic life. Thyroid hormones stimulate fetal development during the second half of pregnancy through anabolic mechanisms and affect the metabolism, growth factors and endocrine system.⁴

Thyroid hormones connect to brain receptors in the first three months before the activation of the embryonic thyroid hormones for growth, so the key to evolving in the first three

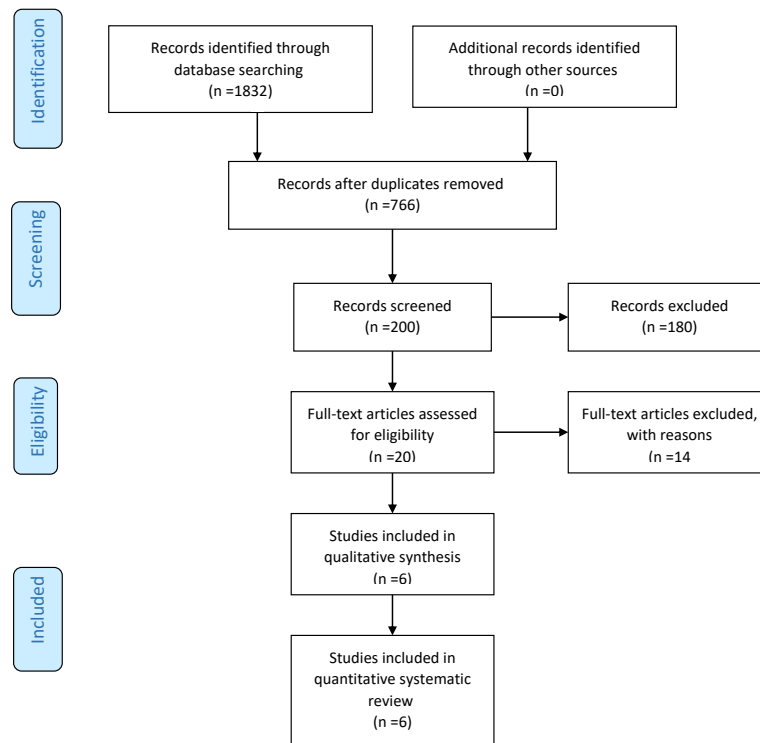


Figure 1. The Flow Chart of the Study.

months and the development of neurons. The results of the studies indicate that mothers' hypothyroidism and failure to supply the thyroid hormones can increase neurological disorders, including seizures in neonates.¹¹

The inadequacy of thyroid hormones transmitted from mothers with hypothyroidism leads to lack of complete growth and reduction volume of the hippocampus, which significantly reduces memory and effect on mental function.¹²

The development of the embryonic lung requires proper growth and proper functioning of the thyroid hormones, which is transmitted through the placenta to the fetus. In mothers with hypothyroidism, the process of transmission is difficult due to insufficient thyroid hormone, hence lung evolution is impaired.² Thyroid hormones plays a key role in the development of the fetus, through various mechanisms of lung development and fetal fitness for the development of ectopic pregnancy.¹³

The results of studies on the effect of thyroid function in

pregnant mothers and neonates are summarized in Table 1.

Thyroid hormones are essential for the development of vital organs, including lung, therefore in hypothyroidism disorders in pregnant women, sufficient amounts of thyroid hormones are not transmitted to the fetus through of the placenta. Furthermore, in the autoimmune thyroiditis anti-hormone antibody passes through of the placenta and affects the β -adrenergic receptors of the lung and the membrane of the epithelial cells of the alveolus, so asthma occurs in infants born to mothers with hypothyroidism.²

In the last three decades, childhood asthma is one of the major problems in the world. This increase in the incidence of asthma causes changes in the environment and lifestyle.

According to a study of atopy and asthma in pregnant mothers, transfer of immunoglobulin from placenta to fetus, is one of the major causes of the development of lung and causes asthma in newborns.¹⁴⁻¹⁶

Solution for Problem: According to the studies, testing

Table 1. Hypothyroidism Effects on Neonates Born of Mothers With Hypothyroidism

First Author	Published Year	Location of Study	Results
Liu et al ²	2017	Denmark	The lack of treatment for hypothyroidism in pregnant women increases the risk of asthma during childhood.
Nazpour et al ⁹	2014	Iran	Hypothyroidism has adverse effects on pregnancy outcomes.
Forhead and Fowden ⁵	2014	Britain	Thyroid hormones stimulate fetal growth during the second half of pregnancy through anabolic mechanisms on embryo metabolism and effect on growth factors and endocrine system.
Andersen et al ³	2014	Denmark	Thyroid hormone disorders in pregnant mothers increase risk of hyperactivity and autism in children.
Andersen et al ⁷	2013	Denmark	Thyroid hormone disorders in pregnant mothers affect the development of neuronal pathways and the lack of timely treatment of hypothyroidism in pregnant women increases the risk of seizures in childbirth infants.
Liu et al ¹⁷	2014	China	Hypothyroidism is associated with increased risk of abortion
Willoughby et al ⁸	2014	Canada	The inadequate transfer of thyroid hormone from mothers with hypothyroidism causes the hippocampus to not evolve and reduce its volume and affect the memory of the child.

to determine the level of thyroid hormones to detect hypothyroidism in the perinatal period and the replacement of levothyroxine in the first trimester of pregnancy is one of the therapeutic strategies to prevent complications of hypothyroid on the embryo.^{17,18}

Conclusions

Considering the important role of thyroid hormones in embryonic development and the growth of vital organs of the fetus moreover, due to the hidden concomitant symptoms of thyroid gland during pregnancy, as well as late detection and inadequate treatment of hypothyroidism lead to impairment development of vital organs of the embryo and increases the risk of fetal malformation. So early detection and timely treatment along with use adequate drug interventions can prevent incidence of complications.

Authors' Contributions

All authors contributed equally to this study.

Conflict of Interest Disclosures

The authors declare they have no conflicts of interest.

References

- Lazarus JH. Thyroid function in pregnancy. *Br Med Bull.* 2011;97:137-148. doi:10.1093/bmb/ldq039.
- Liu X, Andersen SL, Olsen J, et al. Maternal hypothyroidism in the perinatal period and childhood asthma in the offspring. *Allergy.* 2018;73(4):932-939. doi:10.1111/all.13365.
- Andersen SL, Laurberg P, Wu CS, Olsen J. Attention deficit hyperactivity disorder and autism spectrum disorder in children born to mothers with thyroid dysfunction: a Danish nationwide cohort study. *BJOG.* 2014;121(11):1365-1374. doi:10.1111/1471-0528.12681.
- Shields BM, Knight BA, Hill A, Hattersley AT, Vaidya B. Fetal thyroid hormone level at birth is associated with fetal growth. *J Clin Endocrinol Metab.* 2011;96(6):E934-938. doi:10.1210/jc.2010-2814.
- Forhead AJ, Fowden AL. Thyroid hormones in fetal growth and prepartum maturation. *J Endocrinol.* 2014;221(3):R87-R103. doi:10.1530/joe-14-0025.
- Hillman NH, Kallapur SG, Jobe AH. Physiology of transition from intrauterine to extrauterine life. *Clin Perinatol.* 2012;39(4):769-783. doi:10.1016/j.clp.2012.09.009.
- Andersen SL, Laurberg P, Wu CS, Olsen J. Maternal thyroid dysfunction and risk of seizure in the child: a Danish nationwide cohort study. *J Pregnancy.* 2013;2013:636705. doi:10.1155/2013/636705.
- Granfors M, Åkerud H, Berglund A, Skogö J, Sundström-Poromaa I, Wikström A-K. Thyroid Testing and Management of Hypothyroidism During Pregnancy: A Population-based Study. *J Clin Endocrinol Metab.* 2013;98(7):2687-2692. doi:10.1210/jc.2013-1302.
- Nazarpour S, Ramezani Tehrani F, Simbar M, Azizi F. Pregnancy outcomes in pregnant women with hypothyroidism (A review Article). *Iranian Journal of Obstetrics, Gynecology and Infertility.* 2014;17(126):17-26. [Persian].
- Porterfield SP, Hendrich CE. The role of thyroid hormones in prenatal and neonatal neurological development--current perspectives. *Endocr Rev.* 1993;14(1):94-106. doi:10.1210/edrv-14-1-94.
- Zhang Y, Wang H, Pan X, Teng W, Shan Z. Patients with subclinical hypothyroidism before 20 weeks of pregnancy have a higher risk of miscarriage: A systematic review and meta-analysis. *PLoS One.* 2017;12(4):e0175708. doi:10.1371/journal.pone.0175708.
- Willoughby KA, McAndrews MP, Rovet JF. Effects of maternal hypothyroidism on offspring hippocampus and memory. *Thyroid.* 2014;24(3):576-584. doi:10.1089/thy.2013.0215.
- Forno E, Young OM, Kumar R, Simhan H, Celedon JC. Maternal obesity in pregnancy, gestational weight gain, and risk of childhood asthma. *Pediatrics.* 2014;134(2):e535-546. doi:10.1542/peds.2014-0439.
- Liu X, Agerbo E, Schlunssen V, Wright RJ, Li J, Munk-Olsen T. Maternal asthma severity and control during pregnancy and risk of offspring asthma. *J Allergy Clin Immunol.* 2018;141(3):886-892. e883. doi:10.1016/j.jaci.2017.05.016.
- Bobolea I, Arismendi E, Valero A, Agustí A. Early Life Origins of Asthma: A Review of Potential Effectors. *J Investig Allergol Clin Immunol.* 2019;29(3):168-179. doi:10.18176/jiaci.0361.
- den Dekker HT, Jaddoe VVW, Reiss IK, de Jongste JC, Duijts L. Fetal and Infant Growth Patterns and Risk of Lower Lung Function and Asthma. The Generation R Study. *Am J Respir Crit Care Med.* 2018;197(2):183-192. doi:10.1164/rccm.201703-0631OC.
- Liu H, Shan Z, Li C, et al. Maternal subclinical hypothyroidism, thyroid autoimmunity, and the risk of miscarriage: a prospective cohort study. *Thyroid.* 2014;24(11):1642-1649. doi:10.1089/thy.2014.0029.
- Shrestha A, Chawla C. Abnormal thyroid function and recurrent pregnancy loss. *Nepal Journal of Obstetrics and Gynaecology.* 2014;17(1):29-32. doi:10.3126/njog.v9i1.11184.