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Thyroid Disease in Pregnancy

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1. Thyroid autoimmunity and risk of post-partum depression: a systematic review and meta-analysis of longitudinal studies

Author(s): Minaldi E.; D'Andrea S.; Castellini C.; Martorella A.; Francavilla F.; Francavilla S.; Barbonetti A.

Source: Journal of Endocrinological Investigation; Mar 2020; vol. 43 (no. 3); p. 271-277

Publication Date: Mar 2020

Publication Type(s): Review

PubMedID: 31552596

Available at Journal of endocrinological investigation - from SpringerLink - Medicine

Abstract: Purpose: The aim of this study was to systematically investigate whether, and to what extent, the detection of thyroid autoimmunity during pregnancy and in the weeks after childbirth is associated with an increased risk of developing post-partum depression (PPD), a condition associated with possible adverse outcomes for both mother and offspring. We performed a systematic review and meta-analysis of longitudinal studies, assessing the incidence of PPD in women with and without anti-thyroperoxidase antibody (TPOAb) positivity. Method(s): We searched MEDLINE, EMBASE, Web of Science, Cochrane Library, and CINAHL. Methodological quality of the studies was assessed by the Newcastle-Ottawa Scale. In the presence of even modest between-studies heterogeneity, assessed by Cochrane Q and I2 tests, risk ratios (RRs) for PPD were combined using a random effects model. Funnel plot and trim-and-fill analysis were used to assess publication bias. Result(s): Five included studies provided information on 449 women with TPOAb-positive and 2483 TPOAb-negative women. Pooled RR indicated a significantly increased risk to develop PPD in TPOAb-positive group (RR 1.49, 95% CI 1.11-2.00; P = 0.008; I2 = 47%, Pfor heterogeneity = 0.11). Consistent with a possible publication bias, the trim-and-fill test detected two putative missing studies in the funnel plot. Nevertheless, the adjustment for publication bias produced a negligible effect on the pooled estimate (adjusted RR 1.41, 95% CI 1.18-1.68, P = 0.0002). Conclusion(s): Thyroid autoimmunity during pregnancy and in the weeks after childbirth is associated with an increased risk of developing PPD. Further well-designed studies are warranted to confirm this association and elucidate underlying pathophysiological mechanisms. PROSPERO registration: CRD42019129643.

Database: EMBASE

2. Frequency and outcomes of maternal thyroid function abnormalities in early pregnancy.

Author(s): Andersen, Stine Linding

Source: Scandinavian journal of clinical and laboratory investigation; 2019; vol. 79 (no. 1-2); p. 99-107

Publication Date: 2019

Publication Type(s): Journal Article Review

PubMedID: 30616423

Abstract: Thyroid function in pregnant women is of clinical importance considering the crucial role of thyroid hormones during fetal brain development, but the current level of evidence is insufficient to recommend for or against the routine testing of thyroid function in pregnant women. As part of this debate, it is important to evaluate the frequency of undiagnosed and untreated thyroid function abnormalities in pregnant women and to address challenges related to the biochemical assessment of maternal thyroid function in early pregnancy. A hypothesis of fetal programming by maternal thyroid disease has been proposed, but more evidence in humans is needed to extend the hypothesis and to evaluate child neurodevelopmental outcomes after in utero exposure to different abnormalities in maternal thyroid function. The nationwide registers in the Nordic countries provide unique opportunities within reproductive epidemiology to study the impact of various in utero exposures, and stored blood samples from pregnant women in nationwide birth cohorts provide a valuable source for the establishment of pregnancy specific reference ranges. This review addresses the frequency and outcomes of thyroid function abnormalities in pregnant women mainly focusing on observational studies that combine data from the Danish nationwide registers and biological specimens from the Danish National Birth Cohort. Dynamic changes in the reference range of maternal TSH and free T4 during the first trimester of pregnancy are described and discussed. A high frequency of unidentified maternal thyroid function abnormalities is illustrated, and outcomes of child neurodevelopment are evaluated according to subtypes and severity of maternal thyroid dysfunction.

Database: Medline

3. Universal screening for thyroid disease during pregnancy should be performed

Author(s): Stagnaro-Green A.; Dong A.; Stephenson M.D.

Source: Best Practice and Research: Clinical Endocrinology and Metabolism; 2019

Publication Date: 2019

Publication Type(s): Review

PubMedID: 31530447

Abstract: Thyroid disease can significantly impact the pregnant woman and her child. Human and animal studies have firmly linked overt hypothyroidism and overt hyperthyroidism to miscarriage, preterm delivery and other adverse pregnancy outcomes. Overt hypothyroidism and overt hyperthyroidism affect 1% of all pregnancies. Treatment is widely available, and if detected early, results in decreased rates of adverse outcomes. Universal screening for thyroid disease in pregnancy can identify patients with thyroid disease requiring treatment, and ultimately decrease rates of complications. Universal screening is cost-effective compared to the currently accepted practice of targeted screening and may even be cost-saving in some healthcare systems. Targeted screening, which is recommended by most professional associations, fails to detect a large proportion of pregnant women with thyroid disease. In fact, an increasing number of providers are performing universal screening for thyroid disease in pregnancy, contrary to society guidelines. Limited evidence concerning the impact of untreated and treated subclinical disease and thyroid autoimmunity has distracted from the core rationale for universal screening - the beneficial impact of detecting and treating overt thyroid disease. Evidence supporting universal screening for overt disease stands independently from that of subclinical and autoimmune disease. The time to initiate universal screening is now.Copyright © 2019 Elsevier Ltd

Database: EMBASE

4. Hypothyroidism and isolated hypothyroxinemia in pregnancy, from physiology to the clinic.

Author(s): López-Muñoz, Eunice; Mateos-Sánchez, Leovigildo; Mejía-Terrazas, Gabriel Enrique; Bedwell-Cordero, Sharon Esperanza

Source: Taiwanese journal of obstetrics & gynecology; Nov 2019; vol. 58 (no. 6); p. 757-763

Publication Date: Nov 2019

Publication Type(s): Journal Article Review

PubMedID: 31759523

Abstract: Many changes occur in the physiology of the maternal thyroid gland to maintain an adequate level of thyroid hormones (THs) at each stage of gestation during normal pregnancy, however, some factors can produce low levels of these hormones, which can alter the onset and progression of pregnancy. Deficiency of THs can be moderate or severe, and classified as overt or clinical hypothyroidism, subclinical hypothyroidism, and isolated hypothyroxinemia. Overt hypothyroidism has been reported in 0.3-1.9% and subclinical hypothyroidism in approximately 1.5-5% of pregnancies. With respect to isolated hypothyroxinemia, the frequency has been reported in approximately 1.3% of pregnant women, however it can be as high as 25.4%. Worldwide, iodine deficiency is the most common cause of hypothyroidism, however, in iodine-sufficient countries like the United States, the most common cause is autoimmune thyroiditis or Hashimoto's thyroiditis. The diagnosis and timely treatment of deficiency of THs (before or during the first weeks of gestation) can significantly reduce some of the related adverse effects, such as recurrent pregnancy loss, preterm delivery, gestational hypertension, and alterations in the offspring. However, so far there is

no consensus on the reference levels of thyroid hormones during pregnancy to establish the diagnosis and there is no consensus on universal screening of women during first trimester of pregnancy to identify thyroid dysfunction, to give treatment and to reduce adverse perinatal events, so it is necessary to carry out specific studies for each population that provide information about it.

Database: Medline

5. Endocrine disorders in pregnancy

Author(s): Chong H.P.; Alazzani H.; Boelaert K.

Source: Obstetrics, Gynaecology and Reproductive Medicine; Nov 2019; vol. 29 (no. 11); p. 301-305

Publication Date: Nov 2019

Publication Type(s): Review

Abstract: Endocrine disorders in pregnancy are common. Good outcomes can be achieved with multi-disciplinary care in pregnancy. The primary objective of this review is to provide the reader with an overview of national guidelines and where applicable, recent advances with regard to care of women with endocrine disorders in pregnancy. We have outlined care for a broad range of conditions ranging from diabetes and thyroid disorders, to the rarer conditions such as phaeochromocytoma. In addition to the reading list below, we would encourage the reader to keep up to date with reports from the United Kingdom Obstetric Surveillance Service (UKOSS) which studies a range of uncommon conditions in pregnancy as well as the confidential enquiry into maternal and child death [Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK (MBRRACE-UK)]. The latter is especially useful for lessons learnt from past maternal deaths, the most common cause of which were indirect maternal deaths from pre-existing medical conditions.

Database: EMBASE

6. Thyroid hormone therapy of hypothyroidism in pregnancy.

Author(s): Shan, Zhongyan; Teng, Weiping

Source: Endocrine; Oct 2019; vol. 66 (no. 1); p. 35-42

Publication Date: Oct 2019

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article Review

PubMedID: 31617164

Available at Endocrine - from SpringerLink - Medicine

Abstract: Hypothyroidism is the most frequent pregnancy-related thyroid dysfunction, including overt and subclinical hypothyroidism. Studies show that even mild hypothyroidism may eventuate in adverse gestational outcomes and intellectual impairment of offspring. Women with overt hypothyroidism (OH) must be treated by levothyroxine (LT4) pre- and during pregnancy, however, it is controversial that when and how to initiate LT4 therapy and further optimize dosing so that pregnant women and their offspring may truly benefit. In the review we will analyze the changes in thyroid hormone requirements in pregnant women, the timing of LT4 treatment and adjustment of LT4 dose according to etiology in patients with hypothyroidism during pregnancy, and adjustment of LT4 after delivery.

Database: Medline

7. Levothyroxine treatment and pregnancy outcomes in women with subclinical hypothyroidism: a systematic review and meta-analysis.

Author(s): Nazarpour, Sima; Ramezani Tehrani, Fahimeh; Amiri, Mina; Bidhendi Yarandi, Razieh; Azizi, Fereidoun

Source: Archives of gynecology and obstetrics; Oct 2019; vol. 300 (no. 4); p. 805-819

Publication Date: Oct 2019

Publication Type(s): Journal Article Review

PubMedID: 31399840

Abstract:PURPOSETo evaluate the benefits of LT4 treatment on pregnancy outcomes in SCH women.STUDY DESIGNPubMed [including Medline], Web of Science, Wiley, Google Scholar, Science direct and Scopus were searched for identifying and retrieving all English articles published up to May 2018 on the effects of levothyroxine treatment on pregnancy outcomes in pregnant women with SCH compared to untreated or healthy controls. In this systematic review and meta-analysis, both fixed and random effect models were applied to estimate the pooled effect size. Heterogeneity and publication bias were evaluated using the I-squared (I2) and Begg's statistics, respectively. We also explored heterogeneity sources using meta-regression models and sensitivity analysis.RESULTSData of 13 cohort studies and randomized controlled trials with a total of 11,503 participants were analyzed. This meta-analysis showed that pregnant women with SCH treated with levothyroxine had lower chances of pregnancy loss (OR 0.78, 95% CI 0.66-0.94; I2 = 0%) and higher chances for live birth rates (OR 2.72, 95% CI 1.44-5.11; I2 = 25%) than the placebo group. Compared to euthyroid women, SCH patients treated with levothyroxine had higher odds ratio for preterm labor (OR 1.82, 95% CI 1.14-2.91; I2 = 0%).CONCLUSIONSResults of this study showed that the effects of treatment with levothyroxine in SCH pregnant women are not the same for all pregnancy outcomes. Levothyroxine treatment in these patients can reduce pregnancy loss. Considering the limited number of studies available, further studies are warranted to document more precise data on other consequences.

Database: Medline

8. Graves' hyperthyroidism in pregnancy

Author(s): Nguyen C.T.; Mestman J.H.

Source: Current Opinion in Endocrinology, Diabetes and Obesity; Oct 2019; vol. 26 (no. 5); p. 232-240

Publication Date: Oct 2019

Publication Type(s): Review

PubMedID: 31389810

Available at Current opinion in endocrinology, diabetes, and obesity - from Ovid (LWW Total Access Collection 2019 - with Neurology)

Abstract: Purpose of reviewGraves' hyperthyroidism is associated with significant obstetric, maternal, fetal, and neonatal complications. Early diagnosis and an understanding of the management of Graves' hyperthyroidism in pregnancy can help to prevent these complications. Antithyroid drugs (ATD) should be avoided in early pregnancy, given their association with congenital malformations.Recent findingsTSH-receptor antibodies (TRAb) are integral in the management of Graves' hyperthyroidism in pregnancy and in the preconception period. TRAb are indicative of the current activity of Graves' hyperthyroidism and the likelihood of relapse. Furthermore, TRAb predicts the risk of fetal and neonatal hyperthyroidism.The incidence of congenital malformations is roughly the same for propylthiouracil (PTU) and methimazole (MMZ). Exposure to both ATDs in early pregnancy has been associated with increased incidence of congenital malformations compared with exposure to either ATD alone.SummaryThe goal of the physician is maintaining euthyroidism throughout pregnancy and delivery of a healthy, euthyroid baby. An understanding of the natural progression of Graves' hyperthyroidism in pregnancy and the proper utilization of TRAb enables the physician to minimize the risks associated with Graves' hyperthyroidism and side effects of ATDs unique to pregnancy. The physician should prioritize preconception counseling in women with Graves' hyperthyroidism in order to avoid hyperthyroidism and having to use ATDs in pregnancy.

Database: EMBASE

9. Subclinical hypothyroidism in pregnancy

Author(s): Toloza F.J.K.; Abedzadeh-Anaraki S.; Maraka S.

Source: Current Opinion in Endocrinology, Diabetes and Obesity; Oct 2019; vol. 26 (no. 5); p. 225-231

Publication Date: Oct 2019

Publication Type(s): Review

PubMedID: 31356254

Available at Current opinion in endocrinology, diabetes, and obesity - from Ovid (LWW Total Access Collection 2019 - with Neurology)

Abstract: Purpose of reviewSubclinical hypothyroidism (SCH) is a common diagnosis among women of reproductive age. The importance of sufficient maternal thyroid supply during pregnancy is well known. Nevertheless, the effects of SCH during pregnancy and the efficacy of its treatment on maternofetal outcomes are not well established. This review discusses the recent evidence on SCH in pregnancy and how this evidence is reflected in current clinical care.Recent findingsRecent observational studies have found a positive association between SCH during pregnancy and adverse maternal, neonatal and offspring outcomes, mainly in thyroid peroxidase autoantibody positive women. Although interventional studies have shown a benefit of levothyroxine (LT4) treatment on selected pregnancy outcomes, there was no effect on offspring neurodevelopment.SummaryCurrent evidence strengthens the association between SCH with both maternofetal and offspring adverse outcomes. An earlier and more individualized diagnostic assessment taking into consideration predictors of thyroid dysfunction and major risk factors for complications could result in better management of SCH during pregnancy. The effectiveness of LT4 on improving maternofetal and long-term offspring outcomes is still not fully elucidated.

Database: EMBASE

10. Hyperthyroidism and Pregnancy.

Author(s): Kobaly, Kristen; Mandel, Susan J

Source: Endocrinology and metabolism clinics of North America; Sep 2019; vol. 48 (no. 3); p. 533-545

Publication Date: Sep 2019

Publication Type(s): Journal Article Review

PubMedID: 31345521

Abstract: Clinical hyperthyroidism affects 0.1% to 0.4% of pregnancies. Gestational thyrotoxicosis is due to homology of the structure of TSH and HCG, which weakly stimulates the TSH receptor. Graves' disease (GD) most commonly causes clinically significant hyperthyroidism. Given concerns for teratogenicity from antithyroid drugs, these may be discontinued in low-risk GD patients. High-risk patients are treated with propylthiouracil in the first trimester then may transition to methimazole. Surgery is reserved for special circumstances; radioactive iodine is contraindicated. In late pregnancy, GD may remit; postpartum relapse is common. Measurement of serum thyrotropin receptor antibodies identifies pregnancies at-risk for fetal and neonatal hyperthyroidism.

Database: Medline

11. Hypothyroidism in Pregnancy.

Author(s): Taylor, Peter N; Lazarus, John H

Source: Endocrinology and metabolism clinics of North America; Sep 2019; vol. 48 (no. 3); p. 547-556

Publication Date: Sep 2019

Publication Type(s): Journal Article Review

PubMedID: 31345522

Abstract: Thyroid hormone is essential for pregnancy and ensuring fetal development. Pregnancy also places substantial demands on the thyroid axis. Overt hypothyroidism is associated with substantial adverse obstetric and offspring outcomes and requires treatment. Borderline thyroid dysfunction is common in women and associated with adverse obstetric and offspring outcomes, although benefits of screening for and treating borderline thyroid function are unclear. Many women are established on thyroid hormone replacement before pregnancy and doses need increasing during pregnancy. Care is taken to prevent overreplacement. Universal thyroid screening in pregnancy is being undertaken in several countries, although it remains a matter of debate.

Database: Medline

12. Association of Thyroid Function Test Abnormalities and Thyroid Autoimmunity with Preterm Birth: A Systematic Review and Meta-analysis

Author(s): Korevaar T.I.M.; Derakhshan A.; Meima M.; Chaker L.; Peeters R.P.; Taylor P.N.; Chen L.; Lu X.; Bliddal S.; Feldt-Rasmussen U.; Carty D.M.; Delles C.; Meems M.; Pop V.J.M.; Vaidya B.; Shields B.; Ghafoor F.; Popova P.V.; Grineva E.N.; Tkachuck A.S.; Mosso L.; Oken E.; Suvanto E.; Hisada A.; Yoshinaga J.; Brown S.J.; Bassols J.; Walsh J.P.; Auvinen J.; Bramer W.M.; Lopez-Bermejo A.; Dayan C.; Boucai L.; Vafeiadi M.; Vrijkotte T.G.; Guxens M.; Sunyer J.; Riano I.; Murcia M.; Chatzi L.; Jimenez-Zabala A.; Mukhtar S.; Nelson S.M.; Alexander E.K.; Mannisto T.; Pearce E.N.; Steegers E.A.P.

Source: JAMA - Journal of the American Medical Association; Aug 2019; vol. 322 (no. 7); p. 632-641

Publication Date: Aug 2019

Publication Type(s): Review

PubMedID: 31429897

Abstract: Importance: Maternal hypothyroidism and hyperthyroidism are risk factors for preterm birth. Milder thyroid function test abnormalities and thyroid autoimmunity are more prevalent, but it remains controversial if these are associated with preterm birth. Objective(s): To study if maternal thyroid function test abnormalities and thyroid autoimmunity are risk factors for preterm birth. Data Sources and Study Selection: Studies were identified through a search of the Ovid MEDLINE, EMBASE, Web of Science, the Cochrane Central Register of Controlled Trials, and Google Scholar databases from inception to March 18, 2018, and by publishing open invitations in relevant journals. Data sets from published and unpublished prospective cohort studies with data on thyroid function tests (thyrotropin [often referred to as thyroid-stimulating hormone or TSH] and free thyroxine [FT4] concentrations) or thyroid peroxidase (TPO) antibody measurements and gestational age at birth were screened for eligibility by 2 independent reviewers. Studies in which participants received treatment based on abnormal thyroid function tests were excluded. Data Extraction and Synthesis: The primary authors provided individual participant data that were analyzed using mixed-effects models. Main Outcomes and Measures: The primary outcome was preterm birth (<37 weeks'

gestational age). Result(s): From 2526 published reports, 35 cohorts were invited to participate. After the addition of 5 unpublished data sets, a total of 19 cohorts were included. The study population included 47045 pregnant women (mean age, 29 years; median gestational age at blood sampling, 12.9 weeks), of whom 1234 (3.1%) had subclinical hypothyroidism (increased thyrotropin concentration with normal FT4 concentration), 904 (2.2%) had isolated hypothyroxinemia (decreased FT4 concentration with normal thyrotropin concentration), and 3043 (7.5%) were TPO antibody positive; 2357 (5.0%) had a preterm birth. The risk of preterm birth was higher for women with subclinical hypothyroidism than euthyroid women (6.1% vs 5.0%, respectively; absolute risk difference, 1.4% [95% CI, 0%-3.2%]; odds ratio [OR], 1.29 [95% CI, 1.01-1.64]). Among women with isolated hypothyroxinemia, the risk of preterm birth was 7.1% vs 5.0% in euthyroid women (absolute risk difference, 2.3% [95% CI, 0.6%-4.5%]; OR, 1.46 [95% CI, 1.12-1.90]). In continuous analyses, each 1-SD higher maternal thyrotropin concentration was associated with a higher risk of preterm birth (absolute risk difference, 0.2% [95% CI, 0%-0.4%] per 1 SD; OR, 1.04 [95% CI, 1.00-1.09] per 1 SD). Thyroid peroxidase antibody-positive women had a higher risk of preterm birth vs TPO antibody-negative women (6.6% vs 4.9%, respectively; absolute risk difference, 1.6% [95% CI, 0.7%-2.8%]; OR, 1.33 [95% CI, 1.15-1.56]). Conclusions and Relevance: Among pregnant women without overt thyroid disease, subclinical hypothyroidism, isolated hypothyroxinemia, and TPO antibody positivity were significantly associated with higher risk of preterm birth. These results provide insights toward optimizing clinical decision-making strategies that should consider the potential harms and benefits of screening programs and levothyroxine treatment during pregnancy.

Database: EMBASE

13. Thyroxine replacement for subfertile women with euthyroid autoimmune thyroid disease or subclinical hypothyroidism.

Author(s): Akhtar, M Ahsan; Agrawal, Rina; Brown, Julie; Sajjad, Yasmin; Craciunas, Laurentiu

Source: The Cochrane database of systematic reviews; Jun 2019; vol. 6 ; p. CD011009

Publication Date: Jun 2019

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article Systematic Review

PubMedID: 31236916

Available at The Cochrane database of systematic reviews - from Cochrane Collaboration (Wiley)

Abstract:BACKGROUNDThyroid disease is the second most common endocrine disorder affecting women of reproductive age. Subclinical hypothyroidism is diagnosed by an elevated thyroid-stimulating hormone concentration with a normal concentration of free thyroxine hormone. Autoimmune thyroid disease (ATD) is diagnosed by the presence of thyroid autoantibodies, regardless of thyroid hormone levels. Thyroxine may be a useful treatment for subfertile women with these two specific types of thyroid disease for improving pregnancy outcomes during assisted reproduction.OBJECTIVESTo evaluate the efficacy and harms of levothyroxine replacement in subfertile women with subclinical hypothyroidism or with normal thyroid function and thyroid autoimmunity (euthyroid autoimmune thyroid disease, or euthyroid ATD) undergoing assisted reproduction.SEARCH METHODSWe searched the Cochrane Gynaecology and Fertility (CGF) Group specialised register, CENTRAL, MEDLINE, Embase, PsycINFO, CINAHL and two trials registers together with reference checking and contact with study authors and experts in the field to identify studies. We searched for all published and unpublished randomised controlled trials (RCTs) comparing thyroxine with no treatment or placebo, without language restrictions, from inception to 8 April 2019, and in consultation with the Cochrane CGF Information Specialist.SELECTION CRITERIAWe included women undergoing assisted reproduction treatment, meaning both in vitro fertilisation and intracytoplasmic sperm injection, with a history of subfertility and with subclinical hypothyroidism or

with euthyroid ATD. We excluded women with a previously known clinical hypothyroidism or already taking thyroxine or tri-iodothyronine. RCTs compared thyroxine (levothyroxine) with either placebo or no treatment.DATA COLLECTION AND ANALYSISWe used standard methodological procedures expected by Cochrane. Our primary review outcomes were live birth and adverse events of thyroxine; our secondary outcomes were clinical pregnancy, multiple pregnancy and miscarriage.MAIN RESULTSThe review included four studies with 820 women. The included studies were of overall low risk of bias. Using GRADE methodology, we assessed the quality of evidence for the primary outcomes of this review to be very low- to low-quality evidence. Evidence was downgraded for imprecision as it was based on single, small trials with wide confidence intervals (CI). We were able to include data from three of the four included studies.In one study of women with both subclinical hypothyroidism and positive or negative anti-TPO antibodies (autoimmune disease), the evidence suggested that thyroxine replacement may have improved live birth rate (RR 2.13, 95% CI 1.07 to 4.21; 1 RCT, n = 64; low-quality evidence) and it may have led to similar miscarriage rates (RR 0.11, 95% CI 0.01 to 1.98; 1 RCT, n = 64; low-quality evidence). The evidence suggested that women with both subclinical hypothyroidism and positive or negative anti-TPO antibodies would have a 25% chance of a live birth with placebo or no treatment, and that the chance of a live birth in these women using thyroxine would be between 27% and 100%.In women with normal thyroid function and thyroid autoimmunity (euthyroid ATD), treatment with thyroxine replacement compared with placebo or no treatment may have led to similar live birth rates (risk ratio (RR) 1.04, 95% CI 0.83 to 1.29; 2 RCTs, number of participants (n) = 686; I2 = 46%; low-quality evidence) and miscarriage rates (RR 0.83, 95% CI 0.47 to 1.46, 2 RCTs, n = 686, I2 = 0%; low-quality evidence). The evidence suggested that women with normal thyroid function and thyroid autoimmunity would have a 31% chance of a live birth with placebo or no treatment, and that the chance of a live birth in these women using thyroxine would be between 26% and 40%.Adverse events were rarely reported. One RCT reported 0/32 in the thyroxine replacement group and 1/32 preterm births in the control group in women diagnosed with subclinical hypothyroidism and positive or negative anti-TPO antibodies. One RCT reported 21/300 preterm births in the thyroxine replacement group and 19/300 preterm births in the control group in women diagnosed with positive anti-TPO antibodies. None of the RCTs reported on other maternal pregnancy complications, foetal complications or adverse effects of thyroxine.AUTHORS' CONCLUSIONSWe could draw no clear conclusions in this systematic review due to the very low to low quality of the evidence reported.

Database: Medline

14. Hyperthyroidism in the pregnant woman: Maternal and fetal aspects.

Author(s): Moleti, Mariacarla; Di Mauro, Maria; Sturniolo, Giacomo; Russo, Marco; Vermiglio, Francesco

Source: Journal of clinical & translational endocrinology; Jun 2019; vol. 16 ; p. 100190

Publication Date: Jun 2019

Publication Type(s): Journal Article Review

PubMedID: 31049292

Available at Journal of clinical & translational endocrinology - from Unpaywall

Abstract: Hyperthyroidism during pregnancy is uncommon. Nonetheless, prompt identification and adequate management of hyperthyroidism in a pregnant woman is essential, because uncontrolled thyrotoxicosis significantly increases the risk of maternal and fetal complications. Also, fetal prognosis may be affected by the transplacental passage of maternal thyroid stimulating antibodies or thyrostatic agents, both of which may disrupt fetal thyroid function. Birth defects have been reported in association with the use of antithyroid drugs during early pregnancy. Although rarely, offspring of mothers with Graves' disease may develop fetal/neonatal hyperthyroidism, the management of which requires a close collaboration between endocrinologists, obstetricians, and neonatologists. Because of the above considerations, the management of pregnant and lactating women with hyperthyroidism requires special care, bearing in mind that both maternal thyroid excess per se and related treatments may adversely affect the newborn's health. In this review we discuss the diagnosis and management of hyperthyroidism in pregnancy, along with the impact of thyrotoxicosis and medications on fetal outcome.

Database: Medline

15. Maternal and Fetal Thyroid Physiology

Author(s): Sterrett M.

Source: Clinical Obstetrics and Gynecology; Jun 2019; vol. 62 (no. 2); p. 302-307

Publication Date: Jun 2019

Publication Type(s): Review

PubMedID: 31026229

Available at Clinical obstetrics and gynecology - from Ovid (LWW Total Access Collection 2019 - with Neurology)

Abstract: This study was a brief review of maternal and fetal thyroid function and pathology during pregnancy.

Database: EMBASE

16. 2017 ATA guidelines on the management of thyroid dysfunctions in pregnancy: what do OB/GYNs need to know?

Author(s): Rotondi M.; Capelli V.; Chiovato L.; Nappi R.E.

Source: Gynecological Endocrinology; Apr 2019; vol. 35 (no. 4); p. 276-279

Publication Date: Apr 2019

Publication Type(s): Review

PubMedID: 30721102

Abstract: In the past two decades, the issue of thyroid dysfunctions during pregnancy and the postpartum period received increasing attention by both endocrinologists and obstetrics/gynecologists (OB/GYNs), the latter often became the first to diagnose an impaired thyroid function in pregnant women. In this setting, a series of different clinical guidelines have been published and reviewed, the latest ones being represented by the 2017 ATA guidelines, which extensively address a wide variety of topics, including iodine supplementation, thyroid autoimmunity, hyper- and hypo-thyroidism, thyroid nodules and cancer, post-partum management, as well as the need for pre-conception screening. Aim of this editorial is to offer a practical guidance to the OB/GYN reader by focusing upon evidence-based changes introduced by the latest guidelines, with particular regard to: (a) prescribing further endocrine testing before referral; (b) providing evidence-based answers to some of the frequently asked questions.Copyright © 2019, © 2019 Informa UK Limited, trading as Taylor & Francis Group.

Database: EMBASE

17. Endocrine causes of recurrent pregnancy loss

Author(s): Amrane S.; McConnell R.

Source: Seminars in Perinatology; Mar 2019; vol. 43 (no. 2); p. 80-83

Publication Date: Mar 2019

Publication Type(s): Review

PubMedID: 30665726

Abstract: Objective: To review the available data on endocrine disorders and recurrent pregnancy loss. Finding(s): Our group found that most endocrine disorders do not seem to be correlated with a diagnosis of recurrent pregnancy loss (RPL). The exception to this is testing for thyroid stimulating hormone and thyroid antibodies, which is recommended due to a strong correlation with recurrent pregnancy loss and positive anti-thyroid peroxidase antibodies. Conclusion(s): The available literature supports testing thyroid function and antibodies in women with RPL. Testing for other endocrine disorders is only warranted if otherwise clinically indicated, independent from a history of recurrent pregnancy loss.Copyright © 2018

Database: EMBASE

18. Meta-analysis of the association between maternal subclinical hypothyroidism and gestational diabetes mellitus

Author(s): Jia M.; Lin B.; Shi Y.; Zhang Q.; Lin Y.; Zhang Y.; Wu Y.; Wang S.

Source: International Journal of Gynecology and Obstetrics; Mar 2019; vol. 144 (no. 3); p. 239-247

Publication Date: Mar 2019

Publication Type(s): Review

PubMedID: 30578669

Available at International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics - from Wiley Online Library

Abstract: Background: Subclinical hypothyroidism (SCH) and gestational diabetes mellitus (GDM) are common endocrine disorders that occur during pregnancy. Objective(s): To determine whether the risk of GDM differs between pregnant women with normal thyroid function and those with SCH. Search strategy: MEDLINE, EMBASE, the Cochrane Library, and Web of Science were searched for studies published in English from inception to March 1, 2017, using combinations of the search terms "thyroid dysfunction", "thyroid diseases", "subclinical hypothyroidism", "hypothyroxinemia", "thyrotropin", "gestational diabetes", "hyperglycemia in pregnancy", and "adverse pregnancy outcomes". Selection Criteria: We selected cohort studies that included pregnant women with SCH; in which the outcome of interest was, or included, the incidence of GDM; and that had data available for both the SCH and GDM groups. Studies were excluded if assisted reproductive technologies were used to achieve pregnancy; reviews, abstracts, and case reports were also excluded. Data Collection and Analysis: Eleven studies were included in the analysis. Summary odds ratios (ORs) for the risk of GDM were calculated. Main Result(s): SCH with positive antithyroid autoantibodies markedly increased GDM risk (OR 3.22, 95% confidence interval 1.72-6.03, I2=55%). Conclusion(s): SCH with positive antithyroid autoantibodies in pregnancy is associated with an increased risk of GDM.

Database: EMBASE

19. Management for women with subclinical hypothyroidism in pregnancy.

Author(s): Wiles, Kate

Source: Drug and therapeutics bulletin; Feb 2019; vol. 57 (no. 2); p. 22-26

Publication Date: Feb 2019

Publication Type(s): Journal Article Review

PubMedID: 30709859

Available at Drug and therapeutics bulletin - from BMJ Journals

Available at Drug and therapeutics bulletin - from ProQuest (Health Research Premium) - NHS Version

Database: Medline

20. Differences in Diagnostic Criteria Mask the True Prevalence of Thyroid Disease in Pregnancy: A Systematic Review and Meta-Analysis.

Author(s): Dong, Allan Chen; Stagnaro-Green, Alex

Source: Thyroid : official journal of the American Thyroid Association; Feb 2019; vol. 29 (no. 2); p. 278-289

Publication Date: Feb 2019

Publication Type(s): Meta-analysis Journal Article Systematic Review

PubMedID: 30444186

Abstract:BACKGROUNDThe reported prevalence of thyroid disease in pregnancy varies widely through the published literature. These discrepancies are due to differences in criteria for euthyroidism, nationality, iodine status, and gestational age at screening. As a result, currently, an accepted rate of prevalence does not exist for the various thyroid diseases in pregnancy. Understanding the true prevalence rates of these disorders has important implications for clinical management and the ongoing discussion regarding universal screening. The aims of this study were to assess (i) the true prevalence of thyroid disorders in pregnancy and (ii) the impact of diagnostic methodology on these rates.METHODSA systematic review was conducted of the existing literature, including the Pubmed database and references from relevant review articles. Sixty-three studies reporting prevalence of overt hypothyroidism, subclinical hypothyroidism, isolated hypothyroxinemia, subclinical hyperthyroidism, and overt hyperthyroidism in pregnant women were included. Studies were further classified by thyrotropin (TSH) cutoff for diagnosis in hypothyroid disease and timing of screening for hyperthyroid disease. Meta-analysis yielded pooled prevalence rates, with subgroup analyses for TSH cutoff and timing of screening. Analysis of studies using the 97.5th percentile TSH cutoff was assessed to yield the most accurate prevalence rates for hypothyroidism.RESULTSPooled prevalence rates for hypothyroidism calculated from studies using the 97.5th percentile as an upper limit for TSH were 0.50% for overt hypothyroidism, 3.47% for subclinical hypothyroidism, and 2.05% for isolated hypothyroxinemia. Pooled prevalence rates in the first and second trimesters for hyperthyroidism were 0.91% and 0.65%, respectively, for overt hyperthyroidism and 2.18% and 0.98%, respectively, for subclinical hyperthyroidism.CONCLUSIONPopulation-based, trimester-specific TSH cutoffs for diagnosis of hypothyroid disease in pregnancy result in more accurate diagnosis and better estimates for prevalence of disease. Prevalence of hyperthyroidism in pregnancy varies depending on timing of screening. The prevalence rates reported in this study represent the best estimate to date of the true rates of thyroid disease in pregnancy.

Database: Medline

21. Thyroid function and thyroid disorders during pregnancy: a review and care pathway.

Author(s): Delitala, Alessandro P; Capobianco, Giampiero; Cherchi, Pier Luigi; Dessole, Salvatore; Delitala, Giuseppe

Source: Archives of gynecology and obstetrics; Feb 2019; vol. 299 (no. 2); p. 327-338

Publication Date: Feb 2019

Publication Type(s): Journal Article Review

PubMedID: 30569344

Available at Archives of gynecology and obstetrics - from SpringerLink - Medicine

Abstract:PURPOSETo review the literature on thyroid function and thyroid disorders during pregnancy.METHODSA detailed literature research on MEDLINE, Cochrane library, EMBASE, NLH, ClinicalTrials.gov, and Google Scholar databases was done up to January 2018 with restriction to English language about articles regarding thyroid diseases and pregnancy.RESULTSThyroid hormone deficiencies are known to be detrimental for the development of the fetus. In particular, the function of the central nervous system might be impaired, causing low intelligence quotient, and mental retardation. Overt and subclinical dysfunctions of the thyroid disease should be treated appropriately in pregnancy, aiming to maintain euthyroidism. Thyroxine (T4) replacement therapy should reduce thyrotropin (TSH) concentration to the recently suggested fixed upper limits of 2.5 mU/l (first and second trimester) and 3.0 mU/l (third trimester). Overt hyperthyroidism during pregnancy is relatively uncommon but needs prompt treatment due to the increased risk of preterm delivery, congenital malformations, and fetal death. The use of antithyroid drug (methimazole, propylthiouracil, carbimazole) is the first choice for treating overt hyperthyroidism, although they are not free of side effects. Subclinical hyperthyroidism tends to be asymptomatic and no pharmacological treatment is usually needed. Gestational transient hyperthyroidism is a self-limited non-autoimmune form of hyperthyroidism with negative antibody against TSH receptors, that is related to hCG-induced thyroid hormone secretion. The vast majority of these patients does not require antithyroid therapy, although administration of low doses of β-blocker may by useful in very symptomatic patients.CONCLUSIONSNormal maternal thyroid function is essential in pregnancy to avoid adverse maternal and fetal outcomes.

Database: Medline

22. Maternal Thyroid Function During Pregnancy or Neonatal Thyroid Function and Attention Deficit Hyperactivity Disorder: A Systematic Review.

Author(s): Drover, Samantha S M; Villanger, Gro D; Aase, Heidi; Skogheim, Thea S; Longnecker, Matthew P; Zoeller, R Thomas; Reichborn-Kjennerud, Ted; Knudsen, Gun P; Zeiner, Pål; Engel, Stephanie M

Source: Epidemiology (Cambridge, Mass.); Jan 2019; vol. 30 (no. 1); p. 130-144

Publication Date: Jan 2019

Publication Type(s): Research Support, N.i.h., Extramural Research Support, N.i.h., Intramural Journal Article Systematic Review

PubMedID: 30299402

Available at Epidemiology (Cambridge, Mass.) - from Ovid (LWW Total Access Collection 2019 - with Neurology)

Available at Epidemiology (Cambridge, Mass.) - from Unpaywall

Abstract:BACKGROUNDAttention deficit hyperactivity disorder (ADHD) is the most common neurobehavioral disorder in children, yet its etiology is poorly understood. Early thyroid hormone disruption may contribute to the development of ADHD. Disrupted maternal thyroid hormone

function has been associated with adverse neurodevelopmental outcomes in children. Among newborns, early-treated congenital hypothyroidism has been consistently associated with later cognitive deficits.METHODSWe systematically reviewed literature on the association between maternal or neonatal thyroid hormones and ADHD diagnosis or symptoms. We searched Embase, Pubmed, Cinahl, PsycInfo, ERIC, Medline, Scopus, and Web of Science for articles published or available ahead of print as of April 2018.RESULTSWe identified 28 eligible articles: 16 studies of maternal thyroid hormones, seven studies of early-treated congenital hypothyroidism, and five studies of neonatal thyroid hormones. The studies provide moderate evidence for an association between maternal thyroid hormone levels and offspring ADHD, some evidence for an association between early-treated congenital hypothyroidism and ADHD, and little evidence for an association between neonatal thyroid hormone levels and later ADHD.CONCLUSIONSThe reviewed articles suggest an association between maternal thyroid function and ADHD, and possibly between early-treated congenital hypothyroidism and ADHD. Study limitations, however, weaken the conclusions in our systematic review, underlining the need for more research. Importantly, there was much variation in the measurement of thyroid hormone function and of ADHD symptoms. Recommendations for future research include using population-based designs, attending to measurement issues for thyroid hormones and ADHD, considering biologically relevant covariates (e.g., iodine intake), and assessing nonlinear dose-responses.

Database: Medline

23. Effect of Thyroid Hormones on Neurons and Neurodevelopment.

Author(s): Prezioso, Giovanni; Giannini, Cosimo; Chiarelli, Francesco

Source: Hormone research in paediatrics; 2018; vol. 90 (no. 2); p. 73-81

Publication Date: 2018

Publication Type(s): Journal Article Review

PubMedID: 30157487

Abstract: This review focuses on the current knowledge of the effects of thyroid hormones on central nervous system differentiation and development in animals and the human fetal brain. The outcomes of children with congenital hypothyroidism and of newborns with hypothyroid pregnant mothers are emphasized, focusing on how therapies could affect and especially improve the outcomes.

Database: Medline

24. Graves' disease and pregnancy.

Author(s): Illouz, Frédéric; Luton, Dominique; Polak, Michel; Besançon, Alix; Bournaud, Claire

Source: Annales d'endocrinologie; Dec 2018; vol. 79 (no. 6); p. 636-646

Publication Date: Dec 2018

Publication Type(s): Practice Guideline Journal Article Review

PubMedID: 30224035

Abstract: This section deals with the specificities of managing Graves' disease during pregnancy. Graves' disease incurs risks of fetal, neonatal and maternal complications that are rare but may be severe: fetal hyper- or hypothyroidism, usually first showing as fetal goiter, neonatal dysthyroidism, premature birth and pre-eclampsia. Treatment during pregnancy is based on antithyroid drugs alone, without association to levothyroxine. An history of Graves' disease, whether treated radically or not, with persistent maternal anti-TSH-receptor antibodies must be well identified. Fetal monitoring should be initiated in a multidisciplinary framework that should be continued throughout pregnancy. Neonatal monitoring is also crucial if the mother still shows anti-TSH-receptor antibodies at end of pregnancy or underwent antithyroid treatment. The risk of recurrence of hyperthyroidism in the weeks following delivery requires maternal monitoring. The long-term neuropsychological progression of children of mothers with Graves' disease is poorly known.

Database: Medline

25. Thyroid screening in early pregnancy: Pros and cons

Author(s): Lazarus J.H.; Okosieme O.; Zouras S.; Min T.; Nagarahaj K.; Taylor P.N.

Source: Frontiers in Endocrinology; Oct 2018; vol. 9

Publication Date: Oct 2018

Publication Type(s): Review

Available at Frontiers in endocrinology - from Europe PubMed Central - Open Access

Available at Frontiers in endocrinology - from Free Medical Journals . com

Available at Frontiers in endocrinology - from Unpaywall

Abstract: Universal thyroid screening in pregnancy is a key debate in thyroidology and obstetrics. It is well-established that thyroid hormones are essential for maintaining pregnancy and optimal fetal development. Thyroid dysfunction is common in women of childbearing age and also results in substantial adverse obstetric and child neurodevelopmental outcomes. Furthermore, thyroid dysfunction is readily diagnosed with reliable blood tests and easily corrected with inexpensive and available treatments. Screening only high-risk patients appears to miss the majority of cases and economic models show that compared to high-risk screening, universal screening is cost effective even if only overt hypothyroidism was assumed to have adverse obstetric effects. As a result, several countries now implement universal screening. Opponents of universal thyroid screening argue that asymptomatic borderline thyroid abnormalities such as subclinical hypothyroidism and isolated hypothyroxinemia form the bulk of cases of thyroid dysfunction seen in pregnancy and that there is a lack of high quality evidence to support their screening and correction. This review critically appraises the literature, examines the pros and cons of universal thyroid screening using criteria laid down by Wilson and Jungner. It also highlights the growing evidence for universal thyroid screening and indicates the key challenges and practicalities of implementation.

Database: EMBASE

26. Impact of levothyroxine therapy on obstetric, neonatal and childhood outcomes in women with subclinical hypothyroidism diagnosed in pregnancy: a systematic review and meta-analysis of randomised controlled trials.

Author(s): Yamamoto, Jennifer M; Benham, Jamie L; Nerenberg, Kara A; Donovan, Lois E

Source: BMJ open; Sep 2018; vol. 8 (no. 9); p. e022837

Publication Date: Sep 2018

Publication Type(s): Meta-analysis Journal Article Systematic Review

PubMedID: 30196268

Abstract:OBJECTIVETo determine in women with subclinical hypothyroidism diagnosed in pregnancy whether levothyroxine treatment compared with control, impacts important obstetrical or childhood outcomes (specifically IQ) in randomised controlled trials.DESIGNSystematic review and meta-analysis.STUDY ELIGIBILITY CRITERIARandomised trials which met all the following were included: (1) reported original data of women with subclinical hypothyroidism diagnosed in pregnancy (by any prespecified study definition); (2) randomised to either levothyroxine or control (placebo or no treatment); (3) reported obstetrical outcomes and/or childhood neurodevelopmental outcomes and (4) published from 1980 to January 2018 in either English or French language.DATA SOURCESMedline, EMBASE, CINAHL, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials and ClinicalTrials.gov.OUTCOME MEASURESObstetrical, neonatal and childhood outcomes including: miscarriage, gestational hypertension, pre-eclampsia, preterm delivery, mode of delivery, neonatal intensive care unit admission, birth weight, gestational age at delivery, childhood IQ and neurodevelopmental scores. Risk of bias assessment Cochrane Risk of Bias Tool (Modified) for Quality Assessment of Randomised Controlled Trials RESULTS: Three trials of low to unclear risk of bias with 1837 participants were included. Two studies were meta-analysed for maternal and neonatal outcomes and two studies for childhood IQ. No statistically significant differences were found for any clinical outcomes with levothyroxine therapy compared with control.LIMITATIONSOnly three trials were identified for inclusion.CONCLUSIONSThis review, based on three randomised trials in women with subclinical hypothyroidism diagnosed in pregnancy, found no evidence of benefit of levothyroxine therapy on obstetrical, neonatal, childhood IQ or neurodevelopmental outcomes. Current trial evidence does not support the treatment of subclinical hypothyroidism diagnosed in pregnancy.PROSPERO REGISTRATION NUMBERCRD4201707980.

Database: Medline

27. Effect of levothyroxine supplementation on pregnancy outcomes in women with subclinical hypothyroidism and thyroid autoimmuneity undergoing in vitro fertilization/intracytoplasmic sperm injection: an updated meta-analysis of randomized controlled trials.

Author(s): Rao, Meng; Zeng, Zhengyan; Zhao, Shuhua; Tang, Li

Source: Reproductive biology and endocrinology : RB&E; Sep 2018; vol. 16 (no. 1); p. 92

Publication Date: Sep 2018

Publication Type(s): Meta-analysis Journal Article Review Systematic Review

PubMedID: 30249251

Abstract:BACKGROUNDEvidence suggests that subclinical hypothyroidism (SCH) and thyroid autoimmunity (TAI) are associated with adverse pregnancy outcomes. This systematic review and meta-analysis was conducted to determine whether levothyroxine (LT4) supplementation would improve pregnancy outcomes among infertile women with SCH and/or TAI who underwent in vitro fertilization (IVF) or intracytoplastic sperm injection (ICSI).METHODSWe searched databases of PubMed, EMBASE, Web of Science, Cochrane Controlled Trials Register databases, and Clinicaltrials.gov up to April 2018 to identify eligible studies. Studies that focused on the treatment effect of LT4 on pregnancy outcomes of women with SCH and/or TAI who underwent IVF/ICSI were included in the data synthesis. We only included randomized controlled trials (RCTs). Relative risks (RR) and 95% confidence intervals (CI) were calculated using a random-effects model to assess the results of pregnancy outcomes, including clinical pregnancy rate, miscarriage rate, live birth rate and preterm birth rate.RESULTSFour published RCTs including 787 infertile couples undergoing IVF/ICSI were included in this meta-analysis. Notably, the study observed no significant associations of LT4 treatment with the clinical pregnancy rate (RR = 1.46, 95% CI: 0.86-2.48), live birth rate (RR = 2.05, 95% CI: 0.96-4.36), or preterm birth rate (RR = 1.13, 95% CI: 0.65-1.96). However, patients receiving LT4 supplementation had a significantly decreased miscarriage rate relative to those receiving a placebo or no treatment (RR = 0.51, 95% CI: 0.32-0.82). A further sub-group analysis showed that LT4 supplementation did not improve the miscarriage rates among patients with SCH (RR = 0.67, 95% CI: 0.39-1.15) or TAI (RR = 0.28, 95% CI: 0.07-1.06).CONCLUSIONSGiven its potential to reduce the miscarriage rate, LT4 supplementation is recommended for infertile women with SCH and/or TAI who are undergoing IVF/ICSI. However, additional population-based RCTs are needed to confirm this recommendation.

Database: Medline

28. Thyroid and pregnancy

Author(s): Belmahi N.; El Ouahabi H.; Boujraf S.

Source: Reproductive and Developmental Medicine; Sep 2018; vol. 2 (no. 3); p. 162-170

Publication Date: Sep 2018

Publication Type(s): Review

Available at Reproductive and Developmental Medicine - from Unpaywall

Abstract: Thyroid diseases are common in women of childbearing age. Different factors of maternal thyroid function occur during pregnancy; therefore, guidelines recommend trimester-specific pregnancy reference range for thyroid-stimulating hormone. Manifestly, thyroid dysfunctions have deleterious obstetrical and neonatal outcomes. Therefore, an adequate treatment is important to prevent adverse pregnancy complications. Furthermore, iodine deficiency during pregnancy could originate maternal and fetal problems. Consequently, scientific organizations recommend prenatal iodine supplementation for all pregnant women. However, treatment of thyroid autoimmunity is intriguing, but adequately powered randomized controlled trials are needed. The aim of this article was to summarize the reported results of the literature related to the management of thyroid disease during pregnancy in order to help endocrinologists in decision-making processes.Copyright © 2018 Reproductve and Developmental Medicine Published by Wolters Kluwer - Medknow.

Database: EMBASE

29. Autoimmune thyroid disease during pregnancy

Author(s): De Leo S.; Pearce E.N.

Source: The Lancet Diabetes and Endocrinology; Jul 2018; vol. 6 (no. 7); p. 575-586

Publication Date: Jul 2018

Publication Type(s): Review

PubMedID: 29246752

Abstract: Understanding of changes in thyroid function and the consequences of thyroid disease during pregnancy has rapidly grown in the past two decades, and revised American Thyroid Association guidelines on this topic were published in 2017. This Review explores the association between thyroid autoimmunity and complications during and after pregnancy. Thyroid autoimmunity refers to the presence of antibodies to thyroperoxidase or thyroglobulin, or thyroid-stimulating hormone receptor antibodies (TRAbs), or a combination of these, and is present in up to 18% of pregnant women. Thyroid antibodies in pregnant women with normal functioning thyroids (ie, euthyroid) have been associated with several complications, including miscarriage and premature delivery. Treatments to improve pregnancy outcomes are being studied. Whether thyroid antibodies are associated with infertility and assisted reproductive technology outcomes is unclear; although, treatment with low doses of levothyroxine, which is usually used to treat hypothyroidism, can be considered in such situations. Additionally, thyroid antibodies have been associated with other neonatal and maternal complications. All these associations require confirmation in larger prospective studies, and their pathogenic mechanisms need to be better understood. Post-partum thyroiditis is substantially more frequent in women who have thyroid antibodies during pregnancy than in those who do not have thyroid antibodies; however, whether treatment can prevent post-partum thyroiditis in women who are or have been antibody positive is unknown. Finally, TRAbs cross the placenta from the mother to the fetus and can cause fetal or neonatal hyperthyroidism. Therefore, women who are positive for TRAbs during pregnancy should be monitored.Copyright © 2018 Elsevier Ltd

Database: EMBASE

30. Maternal autoimmune disorders and fetal defects

Author(s): Panaitescu A.M.; Nicolaides K.

Source: Journal of Maternal-Fetal and Neonatal Medicine; Jul 2018; vol. 31 (no. 13); p. 1798-1806

Publication Date: Jul 2018

Publication Type(s): Review

PubMedID: 28627279

Abstract: Maternal autoantibodies can cross the placenta and cause fetal damage. This article summarizes the development and management of fetal thyroid goiter in response to maternal Graves' disease and/or its treatment with antithyroid medication, fetal heart block due to maternal anti-Ro and anti-La antibodies, fetal athrogryposis multiplex congenita in association with maternal myasthenia gravis and fetal brain hemorrhage due to maternal autoimmune thrombocytopenia.

Database: EMBASE

31. Subclinical Hypothyroidism in Women Planning Conception and During Pregnancy: Who Should Be Treated and How?

Author(s): Maraka, Spyridoula; Singh Ospina, Naykky M; Mastorakos, George; O'Keeffe, Derek T

Source: Journal of the Endocrine Society; Jun 2018; vol. 2 (no. 6); p. 533-546

Publication Date: Jun 2018

Publication Type(s): Journal Article Review

PubMedID: 29850652

Abstract: Subclinical hypothyroidism (SCH), a mild form of hypothyroidism defined as elevated TSH with normal free thyroxine levels, is a common diagnosis among women of reproductive age. In some, but not all, studies, it has been associated with infertility, an increased risk of adverse pregnancy and neonatal outcomes, and possibly with an increased risk of neurocognitive deficits in offspring. Despite well-established recommendations on treatment of overt hypothyroid pregnant women, a consensus has not yet been reached on whether to treat women with SCH. This review focuses on examining the evidence informing the clinical strategy for using levothyroxine (LT4) in women with SCH during pregnancy and those who are planning conception. A crucial first step is to accurately diagnose SCH using the appropriate population-based reference range. For pregnant women, if this is unavailable, the recommended TSH upper normal limit cutoff is 4.0 mIU/L. There is evidence supporting a decreased risk for pregnancy loss and preterm delivery for pregnant women with TSH > 4.0 mIU/L receiving LT4 therapy. LT4 treatment has been associated with better reproductive outcomes in women with SCH undergoing artificial reproductive techniques, but not in those who are attempting natural conception. Thyroid function tests need to be repeated throughout pregnancy to monitor LT4 therapy. In addition to potential harms, LT4 contributes to treatment burden. During a consultation, clinicians and patients should engage in a careful consideration of the current evidence in the context of the patients' values and preferences to determine whether LT4 therapy initiation is the best next step.

Database: Medline

32. The Association Between Maternal Subclinical Hypothyroidism and Growth, Development, and Childhood Intelligence: A Meta-analysis

Author(s): Liu, Yahong; Chen, Hui; Jing, Chen; Li, FuPin

Source: Journal of clinical research in pediatric endocrinology; Jun 2018; vol. 10 (no. 2); p. 153-161

Publication Date: Jun 2018

Publication Type(s): Meta-analysis Journal Article

PubMedID: 28958983

Abstract:OBJECTIVETo explore the association between maternal subclinical hypothyroidism (SCH) in pregnancy and the somatic and intellectual development of their offspring.METHODSUsing RevMan 5.3 software, a meta-analysis of cohort studies published from inception to May 2017, focusing on the association between maternal SCH in pregnancy and childhood growth, development and intelligence, was performed. Sources included the Cochrane Library, Pub-Med, Web of Science, China National Knowledge Infrastructure and Wan Fang Data.RESULTSAnalysis of a total of 15 cohort studies involving 1.896 pregnant women with SCH revealed that SCH in pregnancy was significantly associated with the intelligence (p=0.0007) and motor development (p<0.00001) of the offspring. SCH was also significantly associated with the child's weight in four studies involving 222 women (p=0.02). Maternal SCH in pregnancy was identified as a risk factor for fetal growth restriction with a combined relative risk (RR) value of 2.4 [95% confidence interval (CI): 1.56, 3.7]. Meta-analysis of 10 studies that provided numbers of preterm infants revealed a significant association between maternal SCH in pregnancy and premature delivery, with a combined RR of 1.96 (95% CI: 1.34, 2.88). There was a significant effect of maternal SCH in pregnancy on fetal distress in utero (p=0.003).CONCLUSIONMaternal SCH in pregnancy is associated with increased risk of adverse neonatal outcomes, including delayed intellectual and motor development, low birth weight, premature delivery, fetal distress and fetal growth restriction.

Database: Medline

33. Management of Subclinical Hypothyroidism in Pregnancy: A Comment from the Italian Society of Endocrinology and the Italian Thyroid Association to the 2017 American Thyroid Association Guidelines-"The Italian Way"

Author(s): Rotondi M.; Chiovato L.; Pacini F.; Bartalena L.; Vitti P.

Source: Thyroid; May 2018; vol. 28 (no. 5); p. 551-555

Publication Date: May 2018

Publication Type(s): Review

PubMedID: 29644934

Abstract: The 2017 American Thyroid Association guidelines for the diagnosis and management of thyroid disease during pregnancy and the postpartum were published six years after the previous ones. They provide comprehensive clinical recommendations for the whole spectrum of thyroid diseases, as well as for optimal iodine intake during pregnancy, postpartum, and lactation. The present position statement mainly regards the recommended flow chart for therapeutic decision making in pregnant women being diagnosed with subclinical hypothyroidism. Here, we comment on the major biochemical and clinical situations and the corresponding therapeutic recommendations. In particular, we welcome the critical revision of the thyrotropin (TSH) reference range in pregnancy, and we agree that there is no need to treat thyroid peroxidase antibody-negative women with a serum TSH ranging from 2.5 muIU/mL to the upper limit of the reference range. This recommendation will hopefully reduce the huge proportion of healthy pregnant women in whom, according to the previous guidelines, levothyroxine therapy had to be initiated. On the other hand, we are concerned with the recommendation to only "consider treatment" in thyroid peroxidase antibody-negative pregnant women with a serum TSH ranging from the upper limit of the reference range to 10.0 muIU/mL. This is because thyroid antibodies may be falsely negative during gestation, and serum negative chronic autoimmune thyroiditis is a well-known clinical entity even outside pregnancy. Based on these and other arguments, we recommend treatment with levothyroxine in pregnant women with TSH levels ranging between the upper limit of the reference range and 10.0 muIU/mL independently from their thyroid antibody status.

Database: EMBASE

34. Pregnancy Complications Associated With Maternal Hypothyroidism: A Systematic Review.

Author(s): Shinohara, Danielle Rosani; Santos, Thais da Silva; de Carvalho, Hayalla Corrêa; Lopes, Laíza Cristina Bahls; Günther, Luciene Setsuko Akimoto; Aristides, Sandra Mara Alessi; Teixeira, Jorge Juarez Vieira; Demarchi, Izabel Galhardo

Source: Obstetrical & gynecological survey; Apr 2018; vol. 73 (no. 4); p. 219-230

Publication Date: Apr 2018

Publication Type(s): Journal Article Review Systematic Review

PubMedID: 29701867

Abstract: ImportanceHypothyroidism is one of the most prevalent diseases in pregnancy, but there is no consensus about its management in pregnant women.ObjectiveIn this systematic review, we evaluated the association between pregnancy complications and treated or untreated maternal hypothyroidism.Evidence AcquisitionPubMed and reference lists were searched for the Medical Subject Headings terms "pregnancy complications" and "hypothyroidism." The eligibility criteria for inclusion in the study were an original study published between 2002 and 2013. Six reviewers independently selected the studies, and 3 extracted the data. Two reviewers assessed the risk of bias and quality of the studies.ResultsEighteen studies were included in the systematic review. The most prevalent complications associated with maternal hypothyroidism were abortion, intrauterine fetal death, preterm delivery, and preeclampsia. The pregnancy outcome depended on the treatment that was received by the patient.ConclusionsStrong evidence indicates that maternal hypothyroidism is associated with maternal-fetal complications, but no consensus was found among the studies reviewed herein. The dose of levothyroxine that is required to maintain euthyroidism is still questioned, but studies have suggested that levothyroxine should be adjusted according to the gestational period and laboratory profile.

Database: Medline

35. Appraisal of clinical practice guidelines on the management of hypothyroidism in pregnancy using the Appraisal of Guidelines for Research and Evaluation II instrument.

Author(s): Fang, Yuan; Yao, Liang; Sun, Jing; Zhang, Jian; Li, Yanxia; Yang, Ruifei; Yang, Kehu; Tian, Limin

Source: Endocrine; Apr 2018; vol. 60 (no. 1); p. 4-14

Publication Date: Apr 2018

Publication Type(s): Journal Article Review

PubMedID: 29445919

Available at Endocrine - from SpringerLink - Medicine

Abstract:PURPOSEThis study aimed to systematically evaluate the quality of guidelines for the management of hypothyroidism in pregnancy.METHODSystematic searches were conducted to identify hypothyroidism in pregnancy guidelines published in electronic databases and developers' websites. Four reviewers independently evaluated eligible guidelines using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument. Agreement among reviewers was measured using the intraclass correlation coefficient (ICC). The number of recommendations, strength of recommendations, and levels of evidence were determined. The software used for analysis was SPSS version 12.0.RESULTSNine guidelines met the inclusion criteria and were appraised. The scope and purpose (65%) and clarity of presentation (70%) domains achieved relatively high scores, whereas the stakeholder involvement (41%), rigor of development (33%), applicability (36%), and editorial independence (31%) domains yielded low scores. The American Thyroid Association (ATA) guideline ranked the highest, whereas the 2012 Chinese Society of Endocrinology (CSE) guideline ranked the lowest among all the guidelines. The British Thyroid Association (BTA) and ATA guidelines were strongly recommended as dependable and helpful references to aid clinical decisions for medical providers, whereas the CSE guideline was not recommended. Most recommendations of the guidelines were relatively consistent. However, the nine guidelines varied with respect to their recommendations on thyroid scanning, dose of levothyroxine (L-T4) treatment, and target thyroid-stimulating hormone(TSH) level of L-T4 therapy.CONCLUSIONSThe quality of the guidelines on the management of hypothyroidism in pregnancy is highly variable. Additionally, these guidelines need significant improvement, especially in the rigor of development and applicability domains. Some improvements should be made to promote the development and implementation of guidelines, for example, conducting a comprehensive search strategy to include more potential evidence and establishing a standard grading system to evaluate the quality of evidence.

Database: Medline

36. Maternal thyroid hormone insufficiency during pregnancy and risk of neurodevelopmental disorders in offspring: A systematic review and meta-analysis.

Author(s): Thompson, William; Russell, Ginny; Baragwanath, Genevieve; Matthews, Justin; Vaidya, Bijay; Thompson-Coon, Jo

Source: Clinical endocrinology; Apr 2018; vol. 88 (no. 4); p. 575-584

Publication Date: Apr 2018

Publication Type(s): Research Support, Non-u.s. Gov't Meta-analysis Journal Article Systematic Review

PubMedID: 29325223

Abstract:BACKGROUNDIn the last 2 decades, several studies have examined the association between maternal thyroid hormone insufficiency during pregnancy and neurodevelopmental disorders in children and shown conflicting results.AIMThis systematic review aimed to assess the evidence for an association between maternal thyroid hormone insufficiency during pregnancy and neurodevelopmental disorders in children. We also sought to assess whether levothyroxine treatment for maternal thyroid hormone insufficiency improves child neurodevelopment outcomes.METHODSWe performed systematic literature searches in MEDLINE, EMBASE, PSYCinfo, CINAHL, AMED, BNI, Cochrane, Scopus, Web of Science, GreyLit, Grey Source and Open Grey (latest search: March 2017). We also conducted targeted web searching and performed forwards and backwards citation chasing. Meta-analyses of eligible studies were carried out using the random-effects model.RESULTSWe identified 39 eligible articles (37 observational studies and 2 randomized controlled trials [RCT]). Meta-analysis showed that maternal subclinical hypothyroidism and hypothyroxinaemia are associated with indicators of intellectual disability in offspring (odds ratio [OR] 2.14, 95% confidence interval [CI] 1.20 to 3.83, P = .01, and OR 1.63, 95% CI 1.03 to 2.56, P = .04, respectively). Maternal subclinical hypothyroidism and hypothyroxinaemia were not associated with attention deficit hyperactivity disorder, and their effect on the risk of autism in offspring was unclear. Meta-analysis of RCTs showed no evidence that levothyroxine treatment for maternal hypothyroxinaemia or subclinical hypothyroidism reduces the incidence of low intelligence quotient in offspring.LIMITATIONSAlthough studies were generally of good quality, there was evidence of heterogeneity between the included observational studies (I2 72%-79%).CONCLUSIONMaternal hypothyroxinaemia and subclinical hypothyroidism may be associated with intellectual disability in offspring. Currently, there is no evidence that levothyroxine treatment, when initiated 8- to 20-week gestation (mostly between 12 and 17 weeks), for mild maternal thyroid hormone insufficiency during pregnancy reduces intellectual disability in offspring.

Database: Medline

37. Graves' hyperthyroidism in pregnancy: A clinical review

Author(s): Nguyen C.T.; Sasso E.B.; Barton L.; Mestman J.H.

Source: Clinical Diabetes and Endocrinology; Mar 2018; vol. 4 (no. 1)

Publication Date: Mar 2018

Publication Type(s): Review

Available at Clinical diabetes and endocrinology - from BioMed Central

Available at Clinical diabetes and endocrinology - from SpringerLink - Medicine

Available at Clinical diabetes and endocrinology - from ProQuest (Health Research Premium) - NHS Version

Available at Clinical diabetes and endocrinology - from Unpaywall

Abstract: Background: Graves' hyperthyroidism affects 0.2% of pregnant women. Establishing the correct diagnosis and effectively managing Graves' hyperthyroidism in pregnancy remains a challenge for physicians. Main: The goal of this paper is to review the diagnosis and management of Graves' hyperthyroidism in pregnancy. The paper will discuss preconception counseling, etiologies of hyperthyroidism, thyroid function testing, pregnancy-related complications, maternal management, including thyroid storm, anti-thyroid drugs and the complications for mother and fetus, fetal and neonatal thyroid function, neonatal management, and maternal post-partum management. Conclusion(s): Establishing the diagnosis of Graves' hyperthyroidism early, maintaining euthyroidism, and achieving a serum total T4 in the upper limit of normal throughout pregnancy is key to reducing the risk of maternal, fetal, and newborn complications. The key to a successful pregnancy begins with preconception counseling.

Database: EMBASE

38. Hypothyroidism during pregnancy and its association to perinatal and obstetric morbidity: a review.

Author(s): Martínez, María; Soldevila, Berta; Lucas, Anna; Velasco, Inés; Vila, Lluis; Puig-Domingo, Manel

Source: Endocrinologia, diabetes y nutricion; Feb 2018; vol. 65 (no. 2); p. 107-113

Publication Date: Feb 2018

Publication Type(s): Journal Article Review

PubMedID: 29396214

Abstract: There is currently no consensus among the different scientific societies on screening for thyroid dysfunction in the first trimester of pregnancy. Indeed, diagnosis and treatment of subclinical hypothyroidism during pregnancy are controversial, as no cut-off value for thyrotropin (TSH) is universally accepted. TSH measurement may be influenced by different factors throughout pregnancy, but especially during the first trimester. The association between overt hypothyroidism during pregnancy and obstetric and perinatal complications is well established. It is also accepted that thyroid hormones are important for neurodevelopment of the offspring. However, there is no scientific evidence available about the impact of subclinical hypothyroidism and its treatment during the first trimester of pregnancy on children's neurodevelopment. In recent years, studies conducted in the offspring of mothers with subclinical hypothyroidism have reported new biochemical parameters which may eventually serve as biomarkers of offspring neurodevelopment and which are more reproducible and are measured at an earlier time than the conventional clinical tests.

Database: Medline

39. Maternal Thyrotropin Receptor Antibody Concentration and the Risk of Fetal and Neonatal Thyrotoxicosis: A Systematic Review.

Author(s): van Dijk, Myrthe M; Smits, Iris H; Fliers, Eric; Bisschop, Peter H

Source: Thyroid : official journal of the American Thyroid Association; Feb 2018; vol. 28 (no. 2); p. 257-264

Publication Date: Feb 2018

Publication Type(s): Journal Article Systematic Review

PubMedID: 29325496

Abstract:BACKGROUNDIn pregnant women with Graves' disease, maternal thyrotropin receptor antibodies (TRAb) can cross the placenta and induce fetal or neonatal thyrotoxicosis. Symptoms of fetal thyrotoxicosis are tachycardia, intrauterine growth restriction, and intra-uterine death. Recommendations on an upper limit of TRAb concentrations below which intensive fetal monitoring can be safely omitted vary between different guidelines. The objective of this study was to define an evidence-based cutoff level for maternal TRAb necessitating additional fetal monitoring during pregnancy.METHODSA literature search was performed to identify studies on pregnant women with Graves' disease and fetal and/or neonatal thyrotoxicosis. Only studies that reported TRAb were included.RESULTSFrom a total of 229 identified titles, 20 articles could be included in the analysis. A total of 53 cases of fetal and/or neonatal thyrotoxicosis were described. The lowest level of maternal TRAb leading to neonatal thyrotoxicosis was 4.4 U/L, which corresponds to 3.7 times the upper limit of normal. The level of evidence for this threshold is moderate to low.CONCLUSIONIn women with Graves' disease, intensive fetal monitoring is recommended when maternal TRAb concentrations are >3.7 times the upper limit of normal. This cutoff level should be interpreted with caution, since evidence is limited.

Database: Medline

40. The role of levothyroxine in obstetric practice.

Author(s): Velasco, Inés; Taylor, Peter

Source: Annals of medicine; Feb 2018; vol. 50 (no. 1); p. 57-67

Publication Date: Feb 2018

Publication Type(s): Comparative Study Journal Article Review

PubMedID: 28972798

Abstract: Thyroid hormones play a pivotal role in somatic growth, metabolic regulation and neurodevelopment. There is growing evidence regarding adverse obstetric and perinatal consequences of maternal thyroid hypofunction during early stages of pregnancy. These include: early pregnancy loss, preterm delivery and lower intelligence quotient (IQ) in children. Different clinical guidelines have been published by scientific societies for the management of thyroid diseases during pregnancy and levothyroxine (LT4) has become a therapeutic agent increasingly prescribed by obstetricians. The aim of this work was to search for both similarities and controversial clinical aspects from the currently available literature. Guidelines published from 2011 onwards have been analysed and compared, in order to clarify the evidence about the involvement of thyroid dysfunction in pregnancy complications and the impact of LT4 use in their prevention and/or treatment. This review summarizes the most updated knowledge about the effectiveness of LT4 for pregnancy complications, the current recommendations and its application into clinical practice. KEY MESSAGES The use of levothyroxine in obstetric practices requires a correct diagnosis and to consider the specific recommendations for each thyroid dysfunction entity. The effectiveness and safety of levothyroxine treatment in preventing adverse perinatal events in pregnant women with clinical hypothyroidism is supported by all the current guidelines. Levothyroxine therapy is strongly recommended in all cases of overt hypothyroidism and in cases of subclinical hypothyroidism associated to positive thyroid autoimmunity.

Database: Medline

Strategy 818447

#	Database	Search term	Results
1	Medline	exp HYPERTHYROIDISM/ OR exp HYPOTHYROIDISM/	67544
2	Medline	(hyperthyroidism OR hypothyroidism).ti	22048
3	Medline	(1 OR 2)	69523
4	Medline	(pregnan* OR maternal).ti	290406
6	Medline	exp PREGNANCY/ OR exp "PREGNANCY COMPLICATIONS"/	911345
7	Medline	(4 OR 6)	960690
8	Medline	(3 AND 7)	5153
9	Medline	8 [DT FROM 2018] [Document type Review] [Languages English]	33
10	Medline	8 [DT FROM 2018] [Document type Guideline] [Languages English]	2
11	EMBASE	exp HYPERTHYROIDISM/	57812
12	EMBASE	exp HYPOTHYROIDISM/	65191
13	EMBASE	(hyperthyroidism OR hypothyroidism).ti	23223
14	EMBASE	(11 OR 12 OR 13)	109147
15	EMBASE	(pregnan* OR maternal).ti	322586
16	EMBASE	exp PREGNANCY/	652009
17	EMBASE	exp "PREGNANCY COMPLICATION"/	119879

18	EMBASE	(15 OR 16 OR 17)	782356
19	EMBASE	(14 AND 18)	7077
20	EMBASE	19 [DT FROM 2018] [Publication types Review] [Languages English]	92
21	EMBASE	*"PRACTICE GUIDELINE"/	71228
22	EMBASE	(19 AND 21)	65
24	Medline	8 [DT FROM 2018] [Document type Meta-analysis]	8