Thyroid disease and pregnancy

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ABSTRACT

Several important issues must be considered when thyroid disorders occur during pregnancy. These include establishing the diagnosis (including an understanding of the effect of pregnancy and its hormonal changes on the immune system in general and the thyroid function in particular) treatment and uneventful maternal and neonatal outcome. The evaluation and treatment of women with thyroid disease during pregnancy parallels that of nonpregnant women and men, but presents unique problems. In addition some types of thyroid disorders occur only during pregnancy and the postpartum period. Pregnancy complicated by some thyroid disorders is associated with an increased rate of complications to the mother as well as to the fetus. This review will seek to discuss the diagnosis, management of different thyroid disorders during pregnancy and the postpartum period.

Keywords: Human chorionic gonadotropin, hyperthyroidism, hypothyroidism, thyroiditis, thyroxine, antithyroid drugs, thyroid nodules.

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Some recent developments and advances in the diagnosis and management of thyroid disease in pregnancy have enhanced our understanding of the interaction between maternal and fetal thyroid function including the role of the placenta. Thyroid disease is the highest occuring endocrine condition in women of childbearing age, and affects around 12 per 1000 pregnant women.[1] Pregnancy has a profound effect on the immune system in order to maintain the fetal-maternal allograft, which is not rejected despite displaying paternal histocompatability antigens. While there is no overall immunosupression during pregnancy dramatic clinical improvement usually occurs in some patients with immunological disorders. On the other hand, others may flare during pregnancy. Pregnancy manifests these effects locally, systematically, and by alteration of the function and number of the different types of lymphocytes and their cytokines production via the increased amounts of estrogen and progesterone.[2] There are some important differences in the management of thyroid disease during pregnancy.

Changes in thyroid physiology during pregnancy. Four important physiological changes occur during pregnancy, which influence thyroid activity. 1. Altered metabolism of thyroxine-binding globulin (TBG). Increased concentrations of estrogen which occur in pregnancy result in increased hepatic synthesis (2-3 folds) and greater sialylation of TBG, thus extending its half-life from 15 minutes to 3 days.[3] This results in increased total thyroid hormone levels, although the free forms remain unchanged. 2. Human chorionic gonadotrophin (hCG) Human chorionic gonadotrophin is one of the glycoprotein family of hormones that consist of 2 subunits, alpha, which is common to all hormones, and beta, which confers specificity and has great homology with thyrotropin (TSH). High levels of hCG during normal or complicated pregnancy (molar pregnancy, hyperemesis gravidarum) along with aberrant forms lead to TSH receptor stimulation. This may lead to a biochemical picture of hyperthyroidism during the first trimester. Reciprocal changes in TSH and hCG as a function of gestational age, with peak hCG and nadir TSH levels at end of first trimester were

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observed. Thyrotropin is suppressed below normal (<0.4mU/L) in 9% of normal pregnancies. First trimester free tetra-iodothyronine (T4) levels are positively correlated with hCG levels.[4] 3. Iodine deficiency. The increased renal iodine clearance due to the increase in glomerular filtration rate (GMR) during pregnancy and transplacental passage results in reduced circulating iodine, which renders the pregnant iodine deficient leading to goiter formation and fetal cretinism, particularly in endemic iodine deficient areas. The dose of thyroxine must be increased during pregnancy.[5,6] Over one 3rd of the worlds, population risk the consequences of iodine deficiency. The worst of these are on reproductive function and outcome and include more neonatal deaths, increased abortions, and defective progeny. Great progress has been made in the past decade toward the sustainable elimination of iodine deficiency, principally from the widespread introduction of iodized salt. However, availability of iodized salt does not guarantee optimal iodine nutrition, and population must be adequately monitored to protect their reproductive health.[7] Women in areas of borderline iodine sufficiency (60-l00mcg/day) have relative hypothyroxinemia, increased tri-iodothyronine (T3)/T4 ratios, and high normal TSH levels as pregnancy progresses.[8] 4. Thyroid hormones deiodination. Tri-iodothyronine has greater activity and a shorter half–life than T4, and biologically is the most important hormone, especially for intracellular functions. Three deiodinase enzymes are recognized which control the activation and inactivation of T4 and T3 in target tissues, in order to ensure adequate supply of T3 to critical areas. Deiodinase type 2 activates T4 to T3, especially intracellularly and where there is reduced availability. It is also found in the placenta. Placental type 3 deiodinase inactivates T4 to reversed tri-iodothyronine (rT3), and its concentration increases with advancing pregnancy; this accounts for the fall in circulating hormones seen later in pregnancy.

Influence of thyroid autoantibodies on fertility. Anti-thyroid antibodies (ATA) present during pregnancy may be a marker for increased miscarriage as shown by 2 large studies of 730 pregnant women,[9] and 487 infertile patients who became pregnant following assisted reproductive techniques.[10] It has been found that there is a significantly higher incidence of ATA (36%) in recurrent aborters compared to controls (9%).[11] In contrast to this data Epslin et al[12] concluded that women with a history of recurrent pregnancy loss do not have an increased incidence of ATA although an association was found between the presence of autoantibodies before pregnancy and miscarriage in women without a history of habitual abortion.[13] However it appears that thyroid antibodies may be a marker for autoimmune mediated recurrent spontaneous abortion in some patients although the mechanism is unknown.

Maternal hypothyroxinemia/hypothyroidsm. I broad screening program, it has been found that measuring TSH at the time of AFP measurement, 2.5% have TSH>6.0 and 0.4% (1 in 250) have TSH>l0.[14]

Several studies examining hypothyroid women who had less than optimal prenatal care (first prenatal visit near midgestation, T4 therapy not begun until midgestation, or inadequate T4 replacement) have shown increased incidence of preeclampsia/ gestational hypertension, abruption, anemia, and postpartum hemorrhage, and babies were small for gestational age.[15] Therefore, with adequate thyroxine treatment, these complications are minimized. The importance of T4 for postnatal neural development is evident from experience with children with congenital hypothyroidism. If T4 therapy is begun within the first month of life, development is normal. Maternal thyroid hormone crosses the placenta as shown by the presence of T4 and T3 in the neural tissue of the first trimester abortuses (prior to fetal thyroid functioning). In addition, Vulsma et al[16] measured neonatal T4 levels in infants with total organification defects, demonstrating this was from a maternal source.

Iodine deficiency is a model to observe the extreme effects of thyroid hormone deficiency in utero on neural development. It impairs the capacity of both maternal and fetal thyroids to supply adequate hormone amounts. Timing of therapy is critical and gives insights into effects on brain development. Studies from Papua New Guinea and China have shown that iodine therapy pre-conception or in early gestation protect the fetal brain from effects of iodine deficiency, but iodine is not effective if given in the 3rd trimester for the first time. Therefore, iodine and by extension thyroid hormone are important for neural development in the first trimester, prior to functioning of fetal thyroid. The clinical importance of maternal T4 on somatic growth during gestation is provided by a recent case report of a mother who had a thyroidectomy for Graves' disease at age 11 and was taking 0.2mg/day L-T4 prior to conception (TSH <0.O5mU/L, free T4 2.1 ng/dL).[17] At the first pre-natal visit at 29 weeks, TSH 72.4mU/L, free T4 0.6 ng/dl. L-T4 dosage incrementally increased to 0.25mg and 0.3mg per day, with normalization of the serum by 32 weeks gestation. Neonatal thyroid function was normal. However, by ultrasound there was marked delay in fetal growth (biparietal diameter, cranial circumference, humerus and femur length), with normalization of extremity but not head measurements by 39 weeks. The clinical importance of maternal T4 on cognitive development during gestation was first evaluated by Man who reports low intelligence quotient (IQ) score in progeny of

Table 1 - Maternal hypothyroidism during pregnancy and child development.[18]

IQ Score	Children of Untreated Hypothyroid Women (N=48)	Control Children (N=124)
Mean IQ score	100	107
IQ score < 85	19%	5%
N - number, IQ - intelligence quotient		

inadequately treated hypothyroid women. A recent study by Haddow and colleagues systematically[18] retrospectively identified 62 women who had been hypothyroid at 17 weeks gestation (mean TSH 13.2, range 5-100 mU/L). All infants had normal thyroid function at birth. Neuropsychological testing (15 tests relating to intelligence, attention, language, reading ability, school attainments, and visual-motor performance) of their children was performed at ages 7 years - 9 years and compared to control children, matched for sex and age, as well as maternal age, education, and occupation. Overall the average full-scale IQ score was 4 points lower in children born to hypothyroid mothers as compared with controls (103 versus 107, p=0.06). However, it was 7 points lower in children born to the mothers with untreated gestational hypothyroidism (presumably undiagnosed) as compared to controls (100 versus. 107), while the IQ of those progeny born to treated hypothyroid women, albeit not fully treated, was normal. Children of untreated hypothyroid women also had lower scores for language development, school performance, and motor performance. Autoimmune thyroid disease was the cause as antithyroid antibodies were present in 77% of these women retrospectively and in 58% of the undiagnosed hypothyroid women, permanent hypothyroidism was eventually diagnosed one to 10 years after delivery (median 5 years).

Therapy for maternal hypothyroidism during pregnancy. Certainly women should be counseled on the importance of optimal iodine intake, by giving them an iodine-containing prenatal vitamin. Identifying women at risk of autoimmune thyroid disease, based on the presence of goiter or a personal family history of thyroid disease or other autoimmune diseases, and carefully monitoring women on thyroid hormone to guarantee normal TSH level throughout pregnancy are also extremely important.[19] Several studies have now confirmed that thyroxine requirements of hypothyroid women increase during pregnancy (mean increase 45%).[5,6] There are several reasons for the increased dose requirement, which may vary in importance depending upon time of gestation. These include: 1. estrogen-induced increased TBG concentration; 2. altered volume of distribution (both hepatic and fetal-placental unit); 3. Increased placental T4 degradation and transport. The magnitude of this increased requirement may in part depend upon the etiology of the hypothyroidism. In women with a previous history of radioiodine ablation for hyperthyroidism, the mean dose increase was 46% (1.75 to 2.25mcg/kg), whereas in those with Hashimoto's, the mean dose increase was 26% (1.7 to 1.9mcg/kg). Increase occurs as early as 5 weeks gestation and persists throughout pregnancy. It is important to remember that 25% of those with initial normal serum TSH levels in the first trimester and 37% of those with initial normal serum TSH concentrations in the 2nd trimester will later require dosage increases.[6] Women with subclinical hypothyroidism who are taking less than replacement dosages of levothyroxine may not require a dosage increase during gestation as the residual thyroid gland is able to increase synthesis of thyroid hormone. These women may be at increased risk for postpartum thyroiditis. Recommendation is to check TSH as soon as pregnancy test is positive and then every 8 weeks during gestation, unless a dose adjustment is needed, in which case the TSH should be rechecked sooner. The goal is to maintain normal TSH level. Dosage may be reduced to the pre-pregnancy amount immediately after delivery, and the serum TSH should be rechecked at the 6 week postpartum visit. Because of iron's potential interference with thyroxine absorption, women should separate ingestion of prenatal vitamins and thyroid hormone by at least 6 hours.

Maternal hyperthyroidism. The most common cause of hyperthyroidism is Graves, disease (85-90%), which affects one in 1500-2000 pregnancies. However, other etiologies are accounted (namely nodular goiters/toxic nodules, thyroiditis, hydatidiform mole, gestational hCG-associated thyrotoxicosis and hyperemesis gravidarum). A spectrum of hCG-induced hyperthyroidism occurs during pregnancy and this entity has recently been referred to as "gestational thyrotoxicosis".[20,21] It is postulated that hCG activates the TSH receptor by a spillover mechanism due to the molecular similarity between these 2 glycoproteins. Findings range from an isolated subnormal serum TSH concentration (up to 18% of pregnancies) to elevations of free thyroid hormone levels in the clinical setting of hyperemesis gravidarum. In women without symptoms of thyrotoxicosis, the serum TSH level may be subnormal but detectable in approximately 9% and undetectable (<0.05 mU/L) in an additional 9%. Systematic screening of 1900 consecutive pregnant women at their initial antenatal visit demonstrated low serum TSH and elevated free T4 levels in 2.4%, half of whom had weight loss, lack of weight gain, or unexplained tachycardia.[20] In all these women, normalization of the free T4 paralleled the decrease

in hCG. It has been observed that hyperemesis gravidarum, defined as severe nausea and vomiting in pregnancy resulting in weight loss and fluid and electrolyte disturbances, has been associated with abnormal thyroid function tests. Suppressed serum TSH levels may occur in 60% of these patients, with elevated free T4 levels in almost 50%.[22] Serum hCG concentrations correlate positively with the free T4 levels and inversely with TSH determinations. The magnitude of the deviation from normal values increases with the severity of nausea and vomiting. The vomiting may be related to the elevated hCG-mediated estradiol production since estradiol levels are higher in hyperemesis subjects than controls, rather than to the thyroid stimulation itself.[22] In addition, a recent case report further supports the concept of hCG-induced thyrotoxicosis. A woman and her mother with recurrent gestational thyrotoxicosis were found to have a missense mutation in the extracellular domain of their TSH receptor that caused a 2-3 fold increase in activation (cAMP generation) when exposed to hCG compared to wild type receptor.[23] Gestational thyrotoxicosis is transient and usually resolves within 10 weeks of the diagnosis.[21] Clinically, this disorder differs from Graves' disease in several ways: 1. Nonautoimmune origin, with negative antithyroid and anti-TSH receptor antibodies; 2. Absence of goiter; 3. Resolution in almost all patients after 20 weeks gestation.[21] Hyperthyroid symptoms such as weight loss, or lack of normal pregnancy weight increase and tachycardia are present in 50% of women with gestational thyrotoxicosis.[20] However, ophthalmopathy, which is autoimmune in origin, is not seen with this disorder. Treatment with antithyroid drugs is controversial, but is generally not recommended. Patients with hyperemesis who remain symptomatic after 20 weeks gestation with elevated thyroid hormone concentrations and suppressed TSH levels may be considered for antithyroid drug therapy. More than likely, such patients probably have mild Graves' Disease.

Diagnosis. Diagnosis can be difficult as pregnancy is a hyperadrenergic state. Free and total T4 and T3 levels are above the normal range for pregnancy, T3U is useful, as it is not as reduced as expected given increase in TBG. Suppressed serum TSH (<0.4mU/L) can occur in up to 9% of normal pregnancies with 14% having increased free T4.[24]

Clinical course. Graves' disease may present for the first time in the first trimester, or if a patient has pre-existing Graves' disease, it may be exacerbated at this time. Similar to other autoimmune disorders, Graves' disease usually improves and may remit in the 3rd trimester, which is a time of immune tolerance. During the postpartum period of immunologic rebound, Graves' disease may also occur for the first time.

Risks to mother. If uncontrolled hyperthyroidism, maternal risks include preterm labor and congestive heart failure.[25]

Risks to fetus. Uncontrolled maternal hyperthyroidism: The incidences of small for gestational age births, stillbirths, and possibly congenital malformations (for first trimester untreated hyperthyroidism) are increased.[25]

Antithyroid drug therapy (ATD) therapy for maternal hyperthyroidism has implications for the fetus due to transplacental passage and subsequent inhibition of fetal thyroid function. In most reference literature, transplacental passage of propylthiouracil (PTU) is reported as lower than that of methimazole. However, the sole quoted supporting study investigated only 6 patients without thyroid problems who were undergoing abortion at end of the first trimester. Just prior to the procedure, 4 received a single injection of 35S-PTU and 2 received 35S-methimazole. The fetal serum PTU concentration was < one 3rd of maternal concentration, but for methimazole, the fetal concentration was over 80% The conclusion was that the placenta was 3 times more permeable to methimazole than PTU.[26] Nine years later, Cooper et al[27] measured maternal and cord serum PTU concentrations at term in hyperthyroid women who had received chronic PTU throughout pregnancy and found that cord serum PTU was higher than maternal in all 6 cases. Serum maternal PTU levels correlated with cord serum free T4.

Antithyroid drugs affect the fetal thyroid in 2 ways: 1. Changes in fetal thyroid function; 2. Fetal goiter.

Changes in thyroid function. Infants born to hyperthyroid mothers treated with minimal doses of PTU at term (100-200mg/day) still have increased TSH levels (40-60mU/L) on days 1-3 after birth, which normalize by 7 days of life.[28] Three studies of over 287 pregnancies have reported that neonatal thyroid dysfunction is related to PTU/methimazole dose at term. Momotani et al correlated maternal and cord free T4 (FT4) levels. All babies born to mothers who had increased FT4 at delivery had fetal FT4 levels in the normal range and of those born to mothers with FT4 in the upper 3rd of normal range, 90% had normal FT4. Over 50% of babies born to mothers with normal FT4 had either a low FT4 or an elevated TSH.[29]

Goiter (not associated with neonatal hyperthyroidism). Goiter may cause a danger of airway obstruction in the neonate and usually resolves in the first 2 weeks of life. The transplacental transport of PTU/methimazole impairs fetal thyroid hormone production and the deficient concentration of circulating thyroid hormones leads to increase in pituitary TSH secretion, stimulating thyroid growth. Goiter occurred more commonly in

the past with iodide therapy, with an incidence as high as 25% in women receiving iodide and PTU. With ATD alone, the incidence is much lower. The dose-relationship less clear as goiter has occurred when mothers have received as little as 100mg PTU or 5mg methimazole. Pre-natal detection is by ultrasound in the 3rd trimester. Treatment with intra-amniotic thyroxine injections (250 mcg at 35, 36, 37 weeks) after confirmation of fetal hypothyroxinemia with percutaneous umbilical blood sampling leads to decreased goiter size by almost 50% at 38 weeks, but simultaneously the maternal ATD dose was also lowered. The goiter decreased by almost 50% at 38 weeks, but simultaneously the maternal ATD dose was also lowered.[30] Therefore, it is difficult to distinguish the relative importance of each factor on the resolution of the fetal goiter. Another recent case report demonstrated that cessation of maternal ATD therapy alone resulted in decrease in the fetal goiter documented ultrasonographically.[31] In cases of fetal goiter where hypothyroidism is suspected due to transplacental ATD, it may be prudent to discontinue or substantially decrease maternal ATD, and follow the goiter with sequential ultrasounds. If reduction in size does not occur within 2-3 weeks, periumbilical blood sampling should be performed to determine fetal thyroid function. If still low, intra-amniotic levothyroxine therapy should be given.

Congenital malformations. Antithyroid drug therapy and incidence of congenital malformations have been discussed in the literature. Untreated maternal hyperthyroidism is associated with a risk of congenital malformations and there does not appear to be an increased risk in general with ATD therapy. However aplasia cutis has been associated with methimazole therapy. Although the incidence of reported aplasia cutis cases in babies born to women taking methimazole is not higher than would be expected from the sporadic incidence rate, there are no reported cases of aplasia cutis in infants born to mothers treated with PTU.[32]

Fetal/neonatal graves' disease. This is reported to complicate 1% of all pregnancies in women with either active Graves' disease or those who have previously undergone radioiodine ablation. The mechanism is the transplacental transfer of maternal thyroid stimulating antibodies at the end of the 2nd or the early 3rd trimester. In utero, there may be increased fetal activity, fetal tachycardia>160/min, intrauterine growth retardation (IUGR), or goiter. Diagnosis is best made with ultrasound to detect persistent fetal tachycardia and goiter if present. Commercial assays for thyroid stimulating immunoglobulins (TSI) may not be as helpful as levels of TSH receptor binding inhibitory immunoglobulins (TBII). Treatment is difficult, but may involve maternal PTU administration, even if the mother is euthyroid (T4 may have to be given simultaneously), with close monitoring of the fetal heart rate, fetal thyroid, and growth. After birth, the hyperthyroidism usually persists for the duration of maternal antibodies (3 months) and requires ATD therapy.

Therapy for maternal hyperthyroidism. There is a good case for preconception clinic for patients with Grave's disease who wish to become pregnant. Firstly, education regarding the effects of the disease on maternal health and fetal well being can be given to allay fears, which are commonly present in these women. As a first choice, PTU is recommended, as no cases of aplasia cutis have been reported with its use. However, if a patient has difficulty swallowing many pills, or a problem with taste, methimazole (MMI) or carbimazole (CM) will be the 2nd choice.[33] The following guidelines, preferably should be followed: 1. Use the lowest ATD dosage to maintain maternal thyroid hormone levels in the high normal to slightly elevated range for pregnancy (free T4 2.0-2.5ng/dl, total T4 of l2-l4mcg/dl, total T3 in mid to high 200's ng/dl). However, thyroid hormone levels must be interpreted in the context of clinical progression of the pregnancy! In the 3rd trimester, if permitted by thyroid function tests (TFT's), make every effort to titrate dosage down and discontinue prior to delivery. 2. B-blockers can be used in small doses for a short period of time, in order to control the hyperadrenergic symptoms, as it is not harmful to the fetus in small doses. High doses for longer periods may lead to intrauterine growth retardation (IUGR), fetal bradycardia, and hypoglycemia. 3. Follow thyroid function tests monthly (TSH may not be helpful initially as it is suppressed). 4. Consider fetal ultrasound at 28-30 weeks to evaluate for (a) fetal goiter (hypothyroidism), especially if dosage requirements have been high, and (b) fetal tachycardia (hyperthyroidism). Also measure maternal TBII to evaluate risk of fetal thyrotoxicosis. 5. Subtotal thyroidectomy is usually only considered during pregnancy as therapy for maternal Graves' disease if consistently high levels of ATD (PTU >600mg/day, MMI >40mg/day) are required to control maternal hyperthyroidism, if a patient is nonadherent or allergic to ATD therapy, or if compressive symptoms exist due to goiter size. If a woman has experienced severe ATD-related side effects such as agranulocytosis, she should receive transient therapy with supersaturated potassium iodide solution (50-100mg per day) for 10-14 days prior to surgery. Thyroidectomy is usually performed in the 2nd trimester. 6. Iodine may be used safely for short periods of time and may be especially helpful pre-op, but TFT's must be monitored and maintained as above. 7. Radioactive iodine treatment is contraindicated during pregnancy.

Lactation. Over the last 2 decades, several such studies have been published, which include almost 200 infants of thyrotoxic lactating mothers taking PTU, MMI, or CM. The methodologies of these

reports vary, with some having a rigorous schedule of thyroid function testing of the infant and others, a more variable surveillance. However, in summary, maternal ATD use during lactation appears to be safe, whether it is continued after gestation or initiated in the postpartum period. For MMI, doses of up to 20mg daily have been documented not to affect infants' thyroid function.[34,35] For PTU, the number of reported infants is smaller and thyroid function was followed in only 3 infants whose mothers were taking high doses (750mg daily one woman and 600 mg daily 2 women).[36] Therefore, to be prudent, PTU doses used during lactation should be 450mg or less. A mother should take her ATD dose just after breast-feeding, which should provide a 3-4 hour interval before she lactates again. Although maternal thyroid hormone levels must be monitored with appropriate ATD adjustment, it appears that the child's thyroid function does not need to be checked regularly as long as somatic and mental development are progressing normally.[37]

Postpartum thyroiditis. Etiology. Postpartum thyroiditis (PPT) is an autoimmune disorder with the occurrence of hyper- or hypothyroidism, or both during the postpartum period in women who were euthyroid during and prior to pregnancy. In the United States of America, overall PPT occurs after 8%-10% of all pregnancies. Pregnancy is time of immunosuppression followed by a postpartum rebound of immunologic activity. Postpartum thyroiditis is associated with thyroid autoantibodies and with T-cell phenotypic changes. Between 75%-100% of women who develop PPT are positive for thyroid autoantibodies directed against thyroid peroxidase (anti-microsomal) or thyroglobulin. Antithyroid antibody titers decline beginning in the first trimester, nadir in the 3rd trimester, and surge postpartum. There is a positive correlation between antibody titer and disease, and women with the highest titers develop PPT. In addition, there is a decline in the helper CD4+/suppresser CD8+ T- cell ratio. In women who develop PPT, this ratio is less suppressed at all stages of pregnancy and postpartum.[38] Recently, it has been reported the occurrence of autoimmune thyroiditis after miscarriage. This can occur after a pregnancy lasting only 6-8 weeks. Likewise, it appears to occur more frequently in antibody positive women.[38] The clinician should be alert to this possibility.

Clinical course. Typically, the hyperthyroid phase occurs from 1-6 months postpartum, and lasts for 1-2 months. This may be followed by the hypothyroid phase at 4 months to one year postpartum, which lasts 4-6 months. The majority of women are euthyroid by one year. There is a 20% rate of recurrence with subsequent pregnancies and the risk of longterm hypothyroidism is 20%. Patients may not always be diagnosed with both hyper- and hypothyroid phases. Postpartum depression occurs with increased frequency among women with the hypothyroid phase of PPT.

Treatment. The hyperthyroid phase is transient and painless. Beta-blockers may be given for cardiac symptomatolgy. If the hyperthyroid phase persists beyond 2 months, then this may represent Graves' disease, which may also first present in the postpartum period and accounts for 10% of postpartum thyrotoxicosis. Thyroxine therapy should be given during the hypothyroid phase and should empirically be continued for 6-8 months, at which point it can be stopped and the TSH rechecked at 3-4 weeks to ensure return of normal thyroid function.

Nodular thyroid disease. Ten percent of pregnant women are claimed to develop thyroid nodules. The investigation of choice during pregnancy, in addition to other tests such as thyroid function test, is fine needle aspiration biopsy (FNABx) and in one report[39] yielded a malignancy/ suspicious result in 35%. Thyroid malignancy is usually of the differentiated type that might be surgically resected in the 2nd trimester. In some cases it can be delayed safely to the postpartum period. It has been found that there is no difference in terms of outcome (recurrences and metastases) between those who were treated during the 2nd trimester and those who were treated postpartum.[40] The impact of pregnancy on thyroid cancer seems to be minimal in that there is no difference in rates of metastases or recurrence compared to nonpregnant women with the same disease.[41,42] Current evidence suggests that differentiated thyroid cancer should not inhibit an intended pregnancy.[42] Previous radioactive iodine therapy does not result in demonstrable adverse events in subsequent pregnancy.[43]

Summary. Reviewing the above mentioned manuscript and the accompanied references indicates that much work has occurred in the area of thyroid disease and pregnancy. The physiological changes of thyroid function as well as the importance of adequate iodine supply and the effects of iodine inadequacy on the fetus and maternal health during pregnancy have been discussed. The role of hCG in mediating hyperthyroidism, diagnosis and management has been discussed. The role of thyroid antibodies as a cause of miscarriage and infertility needs to be clarified further. The management of hyperthyroidism has been discussed extensively taking into consideration the best regimen of ATD and the proper follow up of the pregnant woman and her fetus. The importance of intensifying treatment of maternal hypothyroidism during pregnancy has been discussed, as well as its adequacy to avoid any psychological and somatic consequences to their neonates. Significant advances in understanding the pathogenesis and management of PPT have been discussed extensively. The issue of the proper management of nodular thyroid disease has been reviewed emphasizing the role of fine needle aspiration biopsy (FNABx) in aiding the diagnosis.

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