

# Thyroid Cancer and Pregnancy

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**Published Date:** November 15, 2016

## ABSTRACT

Thyroid cancer is the second most common cancer diagnosed during pregnancy and with an incidence of 14 per 100,000 live births. History and physical examination, ultrasound and thyroid function tests are the optimal diagnostic strategies for thyroid nodules detected during pregnancy. Thyroid ultrasound is the most accurate tool for detecting thyroid nodules, determining their features, monitoring their growth, and evaluating cervical lymph nodes.

There is a perioperative risks to mother and fetus of surgery for thyroid cancer during pregnancy. Therefore surgery for thyroid carcinoma during the second trimester of pregnancy has not been demonstrated to be associated with increased maternal or fetal risk. Up to this time all patients should be monitored until the 24th week by ultrasound. However, if it remains stable by midgestation or if it is diagnosed in the second half of pregnancy, surgery may be performed after delivery.

Surgery during pregnancy is indicated for patients with larger (tumor  $\geq 4$  cm), more aggressive (anaplastic cancer) or rapidly growing cancers, in the presence of extensive nodal or distant metastasis, any tumor size and history of childhood head and neck radiation and the presence of the airway pressure. The safest time for any type of surgery during pregnancy is the second trimester. Type of thyroid cancer discovered during pregnancy may have impact on prognosis. In the majority of studies reported tumor recurrence or death, of women diagnosed during pregnancy/postpartum for well differentiated types of thyroid cancer did not differ from controls.

Radioactive iodine (RAI) ablative therapy and levothyroxine (**LT4**) therapy are the other treatment options. Exposure to radioactive iodine during pregnancy is contraindicated, and the hazards of this exposure include fetal hypothyroidism and cognitive disorders and mental retardation. LT4 treatment is indicated, if cytopathology confirmed the diagnosis with differentiated thyroid cancer and the surgery was decided to be post-partum, it is advisable to start treatment with LT4. Suppressive treatment with LT4 aims to keep TSH level below 0.1–1 mU/l, with monthly monitoring of TSH and T4 level. If surgery was done during pregnancy, LT4 therapy should be started immediately after surgery.

The management of thyroid cancer during pregnancy is not a difficult clinical problem if managed through a multidisciplinary team using guidelines adopted by American Thyroid Association (**ATA**) and The Endocrine Society (**ENDO**).

## INTRODUCTION

Thyroid cancer is the second most common cancer type seen after the breast cancer at/during pregnancy and its incidence is 14 in every 100,000 live births [1]. 3,3/100,000 of the patients before the delivery, 0,3/100,000 during the delivery and 10,8/100,000 in a year after delivery are diagnosed. The incidence increases with the age. The risk is greater at the ages over 45. Papillary thyroid cancer is the most frequent diagnosed pathologic type [1].

Ionized radiation history, iodine deficiency and the presence of genetic family history (especially MEN2) are the most important risk factors for thyroid cancer. In addition to these, estrogen hormone use, late menarche, long menstrual period, the parity over 3 are reported in the studies to have increased the risk [2].

The physiology of thyroid gland changes/transforms with pregnancy. An increase in Bhcg in the circulation and estrogen levels are two most important causes. TSH and Bhcg are two glycoproteins that have similar structures. TSH receptors are activated through an increased Bhcg binding, which results in an increase in the size of thyroid gland. When Bhcg level is decreased, TSH levels return to normal in the following weeks [3]. As for increased estrogen levels, they cause physiological changes on the gland, affecting thyroid gland in the receptor level [4].

## DIAGNOSIS

Firstly, the detailed histories of the patients who were detected to have thyroid nodules should be taken. Radiation history of head and neck in childhood, the period the nodule developed in, the presence of thyroid disease in the family, family medullary thyroid cancer, multiple endocrine neoplasia type 2 (MEN-2), and the presence of family papillary thyroid cancer are all important. Head and neck should be palpated during the physical examination and cervical nodules should be inspected. If the nodule has grown progressively, then fine-needle aspiration biopsy should be administered. And in the presence of persistent cough and dysphonia, malign lesion is supposed to be taken into consideration [5].

Ultrasonography that can be administered easily is non-invasive and the most suitable method for the diagnosis. The detection of the nodule, the follow up of the growth of the nodule and the screening of cervical lymph nodules may be able to be administered. Biopsy is not recommended if the nodule is smaller than 10 mm. If the nodule longer than the width of the nodule's length and the presence of microcalcification are findings which make us think of malignity [6].

In all the patients with thyroid nodule, TSH and free T4 values are to be examined/checked. It should always be kept in mind that in patients with thyroid cancer, the thyroid function tests are usually normal. As for serum calcitonin levels, they are not recommended in routine measurement; however, they are recommended to patients with family medullar thyroid cancer or MEN2 history.

Fine-needle aspiration biopsy, which is a reliable diagnostic procedure in pregnancy, can be administered in any trimester [7,8]. Neither thyroid gland nor lymph node leads to any risk in fine-needle aspiration biopsy.

Radionucleotide scanning is contraindicated in/during the pregnancy and is not recommended [9].

## MANAGEMENT AND TREATMENT

Thyroid nodules are likely to be able to show progression during the pregnancy. Even if any benign nodule has been detected during the fine-needle aspiration biopsy, biopsy is to be repeated when growing is fast and a malign change is detected ultrasonographically. If there is no change in appearance or growth, any new invasive procedure for nodules detected to be benign is not recommended during the pregnancy [10]. In the presence of any nodule which is large, grows extremely fast and puts on pressure on trachea and esophagus, urgent surgery is necessary in whatever period the pregnancy is.

Primary and standard cure of thyroid cancer is surgery. A total or near-total thyroidectomy is preferred. When thyroid cancer is diagnosed, the most important point of the management is to determine the time for the surgery. As far as ATA guidelines are concerned, it has been declared that the follow-up of the patient with a well-differentiated thyroid cancer who was diagnosed in

the early gestational week is likely to be able to be done ultrasonographically [10]. Ultrasonography is to be repeated in every trimester. If a 50 % increase in the volume of nodule and a 20% increase in the diameter are detected in/during the follow-up, then in the 24th week of the pregnancy the surgery is to be carried out. In addition to this, in the follow-up period, if the patient undergoes lymph-node metastasis, then urgent surgery is to be performed in the second trimester. In the presence of pressure of anaplastic histologic type, trachea and esophagus, urgent surgery is a necessity. Except for the available conditions, the delay of the surgery until after the delivery is a suitable approach in the presence of a well-differentiated thyroid cancer[11].Thyroid hormone suppression treatment are to be scheduled in the patients who are differentiated-thyroid cancer and whose surgery is delayed until postpartum period. The aim of LT4 (levotiroksin) suppression treatment is to help to keep the TSH levels between 0,1 and 1,5mU/L.

Delaying the surgery after the delivery will be the safest choice in the patients with the third-trimester diagnosis because in these patients there is a risk possibility which is likely to develop during surgery [11].

There are patients with thyroid nodule whose fine-needle aspirations are reported to have potential cancer risk. Even though there are prospective studies evaluating the current situation, in 30 % of these nodules good-differentiated thyroid cancer develops. In spite of the fact that a great majority of the patients are considered to have benign thyroid nodule(s), if not urgent, delaying the surgery until postpartum is considered to be much better. For these patients, LT4treatment during the pregnancy is recommended.

The surgery performed in the second-trimester is safe from the point of fatal and maternal views and there is no major morbidity. Prolonged hospital stay and cost increase may be mentioned among the drawbacks of the surgery performed in the second-trimester [12-15].

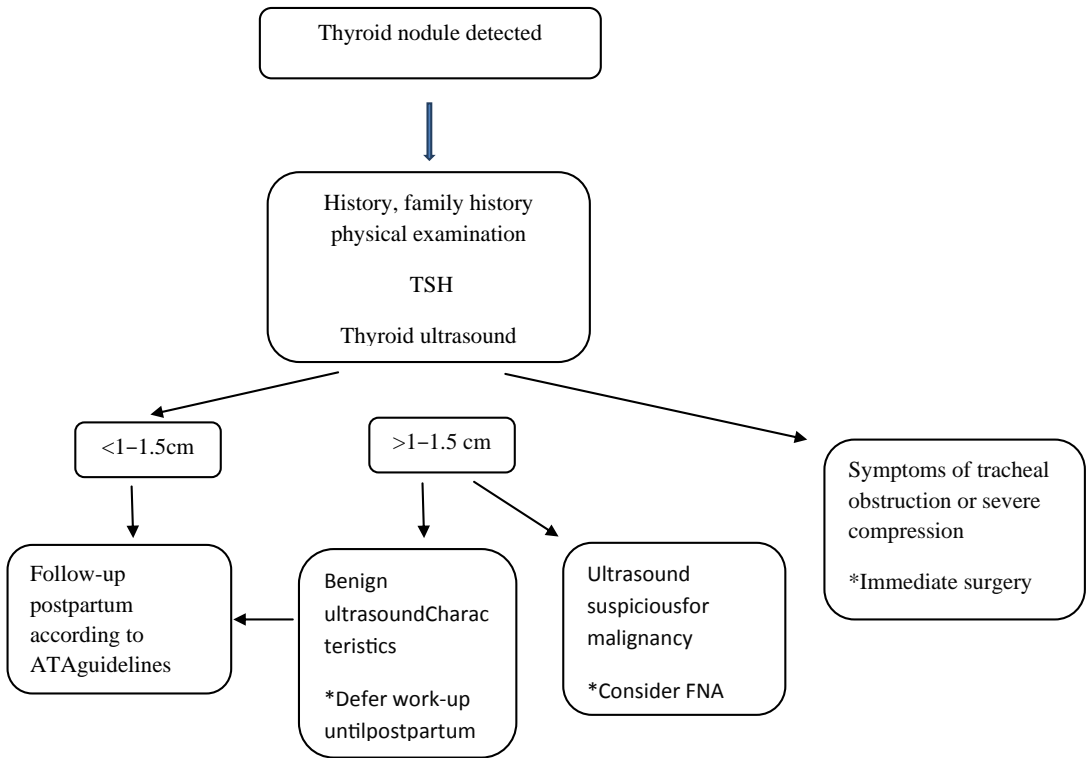
In the follow-up of the patients who underwent thyroid cancer and LT4 treatment, the measurement of TSH is of considerable importance. LT4 treatment of pregnant in whom surgery is delayed until the second-trimester or postpartum can be administered with different indications like suppression treatment [16].

In the cases with persistent diseases, the serum TSH level is to be kept under 0,1mU/L. In the cases that were treated due to high risk tumor but no biochemical disease was diagnosed, the TSH serum level is to be kept between 0,1mU/L-0,5mU/L. In low risk cases with no diseases, keeping the TSH level between 0,3mU/L-1,5mU/L is suggested.

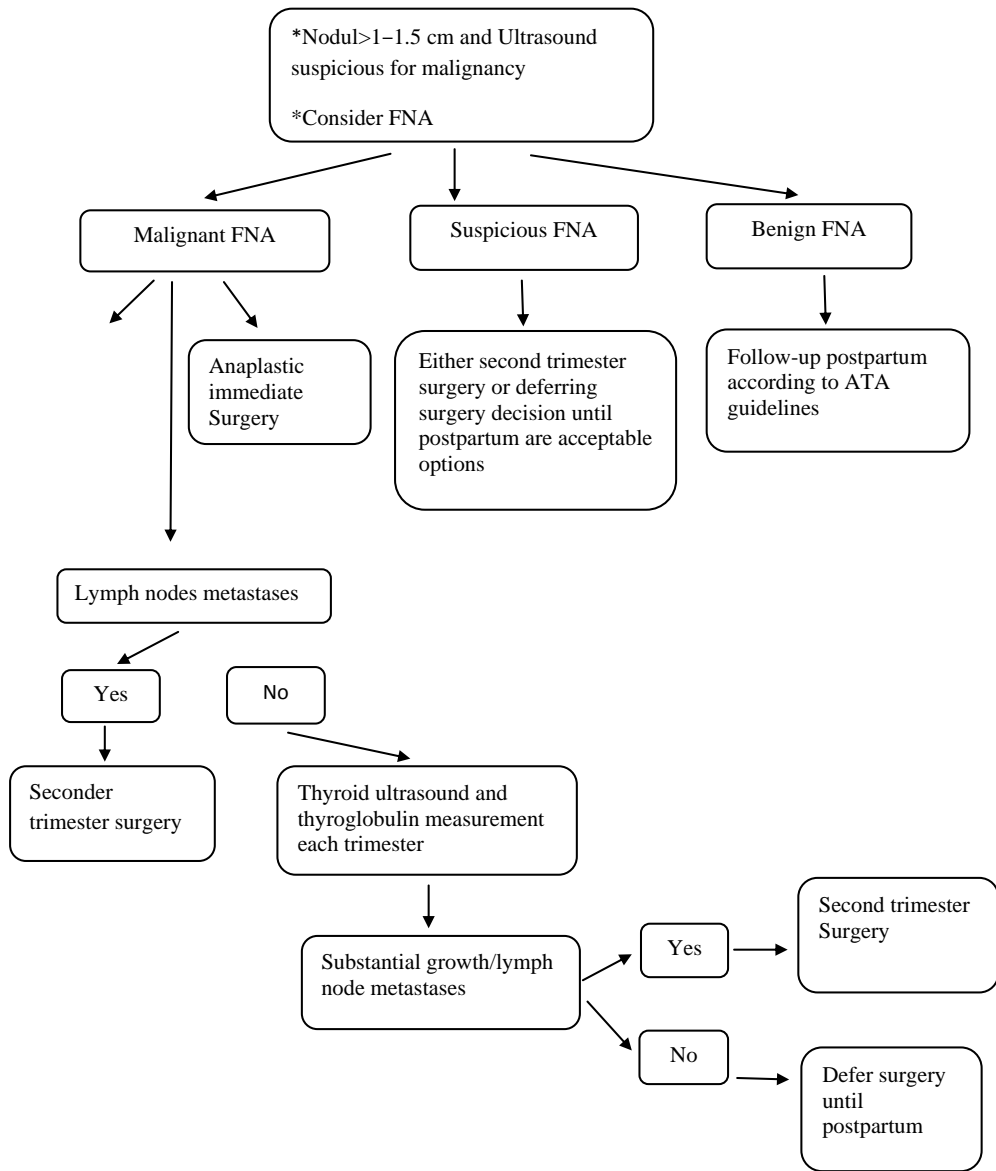
The TSH levels in patients who had a differentiated thyroid cancer treatment should be kept in preconceptional range. During the follow-up period, when the pregnancy is determined, the follow-up of thyroid function tests is necessary. The need for thyroxine hormone in pregnancy increases 20-30 %, so LT4 doses are also to be increased. Thyroid function tests should be controlled once every four weeks until the 16th to 20th weeks, and in the later periods only once

between the 26th and 30th week. Functional tests should be repeated 4 weeks after every LT4 dosage.

Because the ablation treatment with radioactive iodine is contraindicated in the pregnancy, it must be confirmed that there is no pregnancy before the treatment. The relations of the treatment with fatal hypothyroidism, cognitive disorders and mental retardations have been declared [17]. In patients who require post partum RAI treatment, breast feeding is to be stopped at least 6 weeks before the treatment, and the patient should be informed about this situation. No negative effect of RAI ablation treatment on fertility or later pregnancy has been mentioned [18]. Following the RAI ablation treatment, the delay of pregnancy is of vital importance in order to supply both remission and sufficient hormone replacement treatment.



**Figure 1:** An algorithm for the work-up and treatment of a thyroid nodule detected during pregnancy.



**Figure 2:** An algorithm for the work-up and treatment of a thyroid nodule detected during pregnancy.

## PROGNOSIS

There are some studies evaluating how the pregnancy affects a well-differentiated thyroid cancer prognosis. Most of these studies have shown that there is no difference in such prognostic findings as tumor recurrence or death among the patients who had a diagnosis both/either

during pregnancy and/or in one year after post partum compared to the control groups. In one of the studies, in the presence of well-differentiated thyroid cancer during the pregnancy and post partum, the persistence and recurrence of tumor was evaluated and its relation with bad-prognosis was determined [19-25].

Most of the studies have shown that pregnancy has not affected differentiated thyroid cancer prognosis negatively; however, all the studies are retrospective and some of them seem to have limited patient number. The evaluation of different prime routes is another limitation.

## CONCLUSION

Pregnancy has not affected differentiated thyroid cancer prognosis negatively. The management of thyroid cancer during pregnancy is not a difficult clinical problem if managed through a multidisciplinary team using guidelines adopted by American Thyroid Association (ATA) and The Endocrine Society (ENDO).

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