Thyroid Research

REVIEW

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Subacute thyroiditis in pregnancy: a narrative review

Mahmoud Ali Kaykhaei[1,2*] and Zahra Heidari[1,2]

Abstract

Thyroid dysfunction can adversely affect pregnancy outcomes. Apart from gestational thyrotoxicosis, thyroid dysfunction during pregnancy shares similar etiologies with the non-gravid state. Graves' disease is the most common cause of spontaneous hyperthyroidism in pregnancy, followed by thyroid autonomy. Although subacute thyroiditis is a less common cause of thyrotoxicosis in pregnancy, its associated pain, systemic symptoms, and thyroid dysfunction can present diagnostic and therapeutic challenges. In its painful form, subacute thyroiditis may lead to severe disability, with systemic glucocorticoids being the best effective treatment option. When painless, the condition often comes to medical attention due to thyroid dysfunction. During the thyrotoxic phase, subacute thyroiditis should be differentiated from gestational thyrotoxicosis, Graves' disease, and thyroid autonomy. Additionally, the transient hypothyroid phase may be misdiagnosed as permanent hypothyroidism, such as in Hashimoto's thyroiditis. Once properly diagnosed, management is symptomatic and focused on correcting the predominant abnormality. In this review, we summarize the current reported cases of subacute thyroiditis in pregnancy and discuss the challenges in diagnosis and management.

Clinical trial number Not applicable.

Keywords Subacute thyroiditis, Pregnancy, Thyrotoxicosis, Hypothyroidism

Background

Pregnancy induces numerous changes in thyroid physiology. Notably, elevated levels of human chorionic gonadotropin (HCG), particularly during the first trimester, lead to significant increases in serum thyroid hormones and subsequently decreased thyroid-stimulating hormone (TSH) levels [1]. Serum TSH concentrations gradually rise during the second and third trimesters but remain significantly lower than those in nonpregnant women [2]. Additionally, pregnancy often leads to a mild increase in thyroid gland volume, which can become pronounced in iodine-deficient regions, sometimes culminating in goiter formation [3, 4]. The effects of HCG in pregnancy, referred to as gestational thyrotoxicosis, include slight thyroid enlargement, suppressed serum TSH levels, and elevated free T4 (FT4) concentrations. Importantly, gestational thyrotoxicosis must be carefully distinguished from other etiologies of thyrotoxicosis, such as Graves' disease and thyroid autonomy, due to differences in pathophysiology and management.

Subacute thyroiditis (SAT), also known as granulomatous or giant cell thyroiditis is a self-limited disorder of unknown etiology. It typically causes painful destruction of the thyroid, leading to thyrotoxicosis, followed by transient hypothyroidism, and eventually returning to euthyroidism. During the thyrotoxic phase, neck pain and systemic symptoms like fever, malaise, and myalgia can

*Correspondence:
Mahmoud Ali Kaykhaei
mazyar44@gmail.com
[1]Genetics of Non-comunicable Disease Research Center, Zahedan University of Medical Sciences, Zahedan, Iran
[2]Department of Internal Medicine, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran

be severe [5]. In some cases, pain may be minimal, necessitating differentiation of SAT from other causes of thyrotoxicosis, particularly Graves' disease [6]. Furthermore, during the hypothyroid phase, the condition should be distinguished from other causes of hypothyroidism. This is especially important if the preceding thyrotoxic phase went undiagnosed.

The incidence of SAT in the general population is primarily derived from retrospective studies, which indicate an incidence rate between 2.0 and 3.6 per 100,000 per year in different geographic areas [5, 7, 8]. However, data on the frequency of SAT during pregnancy is limited and mostly confined to a few case reports. Despite the limited data, the severity of symptoms, thyroid dysfunction that can complicate pregnancy outcomes and the need to distinguish SAT from other etiologies make it an important condition to consider during pregnancy.

Therefore, the aim of this review is to summarize the current evidence and identify potential challenges in the diagnosis and management of SAT during pregnancy.

Methods

A comprehensive literature search was independently performed by two authors across PubMed, ISI Web of Science, and Scopus databases, encompassing all available studies published through November 23, 2024. The inclusion criteria required studies to document at least one case of subacute thyroiditis occurring during pregnancy.

The search strategy incorporated the following keywords: [(Thyroiditis) OR (Thyroiditides)] AND [(Subacute) OR (Subacute Painful) OR (Granulomatous) OR (Giant Cell) OR (De Quervain)] AND [(Pregnancy) OR (Gestation)], with the search restricted to English-language publications. From an initial pool of 248 studies, 229 were excluded based on title screening, 13 were identified as duplicates, and one was excluded following a relevance assessment. Consequently, five articles describing six cases of subacute thyroiditis during pregnancy were selected.

An additional two cases were identified through cross-referencing citations within these articles. Due to the limited number of reported cases, conducting a systematic review was deemed impractical [9, 10]. Instead, we conducted a comprehensive narrative analysis of all eight cases to synthesize the available data.

Case review and summary

The first documented cases of subacute thyroiditis in pregnancy were reported by Hirawa et al. in 2006, involving two patients who presented with neck pain during pregnancy [11]. Since then, six additional cases have been reported from various regions worldwide [12–17]. The clinical and laboratory characteristics of these patients are summarized in Table 1.

In brief, all reported cases occurred during the first half of pregnancy, with a median gestational age of 6 weeks. All patients experienced varying degrees of neck pain and tenderness.

Elevated inflammatory markers, including erythrocyte sedimentation rate (ESR) and/or C - reactive protein (CRP), were observed in all cases. Thyroid ultrasound consistently revealed hypo-echogenicity and/or hypovascularity. Five of the cases exhibited the classic triphasic pattern of thyrotoxicosis, hypothyroidism, and eventual return to euthyroidism.

Management strategies varied significantly, ranging from conservative approaches with no treatment to more aggressive interventions involving glucocorticoids and thyroid hormone replacement therapy.

Notably, apart from a single case of pregnancy termination at 11 weeks of gestation, no severe complications were reported for either the mothers or their fetuses. The patient in this case experienced severe hyperemesis gravidarum accompanied by neck pain and odynophagia, which initially responded to oral prednisolone. However, due to poor adherence to the prescribed treatment, the patient developed intractable nausea, vomiting, and progressive weight loss. Consequently, she elected to terminate the pregnancy and was subsequently lost to follow-up, leaving the post-pregnancy course unknown [13]. Additionally, one case of SAT during pregnancy resulted in the development of permanent hypothyroidism [17].

Epidemiology

Subacute thyroiditis (SAT) predominantly affects middle-aged individuals, with a marked preference for females [18]. Although the exact cause of SAT remains unclear, viral infections are significantly associated with its onset [19, 20], with additional contributions from genetic predisposition and autoimmune mechanisms [21–23].

Incidence rates range from 2.4 per 100,000 per year in Denmark to 4.9 per 100,000 in the United States [5, 7]. Some studies have also noted an increased incidence of SAT during the COVID-19 pandemic, though results are inconsistent [24–26]. Additionally, SAT has been reported rarely following COVID-19 vaccination [27]. Based on these figures, SAT is estimated to affect approximately 5 to 20 pregnancies per one million; however, cases in pregnancy are rarely documented.

Several factors may contribute to this discrepancy. First, mildly symptomatic cases of SAT may be misdiagnosed as gestational thyrotoxicosis, with some progressing to hypothyroidism undiagnosed as SAT. Second, SAT primarily affects women in their fifth and sixth decades, whereas pregnancy typically occurs in younger

Table 1 Data summary of reported cases of subacute thyroiditis in pregnancy

Year Reported	Age (Years)	Gestational age (Weeks)	Clinical findings	Laboratory findings	Ultrasound Findings	Treatment	Thyroid Function Phases	Maternal outcomes	Fetal outcomes
Case 1 2006 [11]	35	11	Neck pain, Enlarged and tender thyroid	ESR ↑, TSH ↓, FT4 ↑, FT3 ↑	Low echogenicity, Goiter	Prednisolone, Liothyronine, Levothyroxine	Thyrotoxicosis, Hypothyroidism	No complications	No complications
Case 2 2006 [11]	31	6	Neck pain, Enlarged right lobe and tenderness	ESR ↑, TSH ↓, FT4 Nl, FT3 Nl	Low echogenicity	No treatment	Euthyroidism	No complications	No complications
Case 3 2011 [12]	30	6	Neck pain, Enlarged and tender thyroid	ESR ↑, TSH ↓, FT4 ↑, FT3 ↑	Low echogenicity, Goiter	Levothyroxine	Thyrotoxicosis, Hypothyroidism, Euthyroidism	No complications	No complications
Case 4 2012 [16]	29	5	Neck pain, Enlarged and tender thyroid	ESR ↑, TSH ↓, FTI4 ↑, T3 Nl	Decreased vascularity and blood flow	Prednisolone, Levothyroxine	Thyrotoxicosis, Hypothyroidism, Euthyroidism	No complications	No complications
Case 5 2015 [13]	29	7	Neck pain, Enlarged and tender thyroid	CRP ↑, TSH ↓, FT4 ↑, T3 Nl	Heterogeneous echogenicity, Not increased vascularity	Prednisolone	Thyrotoxicosis	No follow up	Terminated at 11th weeks
Case 6 2017 [15]	33	13	Neck pain, Enlarged and tender thyroid	ESR, TSH ↓, FT4 ↑, FT3 ↑	Not increased vascularity, Goiter	Acetaminophen, Levothyroxine	Thyrotoxicosis, Hypothyroidism, Euthyroidism	No complications	No complications
Case 7 2022 [14]	27	17	Neck pain, Enlarged and tender thyroid	ESR ↑, TSH ↓, FT4 Nl, FT3 Nl	Low echogenicity of left lobe	Prednisolone, Levothyroxine	Thyrotoxicosis, Hypothyroidism, Euthyroidism	No complications	No complications
Case 8 2024 [17]	35	12	Neck pain, Enlarged and tender thyroid	ESR ↑, TSH ↓, FT4 ↑, FT3 ↑	Heterogeneous echogenicity, Decreased blood flow	Ibuprofen, Levothyroxine	Thyrotoxicosis, Hypothyroidism	No complications	No complications

Abbreviations: ESR: Erythrocyte sedimentation rate; TSH: Thyroid stimulating hormone; FT4: Free thyroxine; FT3: Free triiodothyronine; FTI4: Free thyroxine index; ↑: High; ↓: Low; Nl: Normal

populations [5, 7]. Third, pregnancy's immune modulation may reduce inflammatory responses, especially in the second and third trimesters [28, 29]. Fourth, it is possible that some patients with SAT present to specialties other than endocrinology, such as general practitioners, leading to underdiagnosis or misdiagnosis. Lastly, the lower likelihood of publishing SAT cases in pregnancy, when similar cases have already been reported, introduces reporting bias, further contributing to the underrepresentation of SAT in pregnancy in the literature.

Diagnosis of subacute thyroiditis in pregnancy

Diagnosing subacute thyroiditis in pregnancy is generally straightforward when classical symptoms manifest, such as thyroid discomfort, tenderness, elevated inflammatory markers, and thyrotoxicosis, alongside typical ultrasound features. However, in cases without overt symptoms, particularly in painless form, the diagnosis may require further investigation, including fine-needle aspiration (FNA) of the thyroid [12].

The painful thyroid in pregnancy

The primary causes of neck pain, with or without goiter, during pregnancy are similar to those observed in non-pregnant women (Table 2). However, the relatively younger age of pregnant women makes certain diagnoses, such as thyroid lymphoma, less likely. In this context, subacute thyroiditis (SAT) and hemorrhage into a thyroid cyst or nodule are considered the most common causes of neck pain in pregnancy, which can be readily distinguished through thyroid ultrasound [30, 31].

When diffuse neck pain is the main presenting symptom, SAT is the most likely diagnosis. However, the presence of unilateral thyroid involvement does not exclude SAT, as "creeping" thyroiditis is a recognized variant [5, 32]. Conversely, while the absence of pain reduces the

Table 2 Causes of painful thyroid and some discriminating features

Category	Cause	Characteristic Features
Common	Subacute thyroiditis	Diffuse pain (may be localized), increased inflammatory markers
	Hemorrhage into a thyroid cyst or nodule	Localized pain, detectable nodule/cyst on physical examination or ultrasound
Less common	Acute infectious (suppurative) thyroiditis	Localized pain, history of immunosuppression or congenital anomaly (e.g., piriform sinus fistula), abscess formation
	Thyroid trauma	Diffuse or localized pain, history of trauma
	Radiation-induced thyroiditis	Diffuse pain, history of radiation exposure (contraindicated in pregnancy)
	Rapid enlargement of thyroid carcinoma	Localized pain, detectable tumor often with extrathyroidal extension
Rare	Autoimmune thyroiditis	Diffuse pain, positive immune markers (thyroid peroxidase and thyroglobulin antibodies)
	Drug-induced thyroiditis (e.g., amiodarone)	Diffuse pain, positive drug history
	Thyroid lymphoma	Localized pain, very firm and enlarged thyroid, extrathyroid involvement common

likelihood of SAT, it does not rule it out entirely [6, 33]. Indeed, diagnosing SAT in pregnancy can be particularly challenging when pain or tenderness is absent, as its constitutional symptoms and thyrotoxicosis can easily be attributed to physiological changes of pregnancy, such as gestational thyrotoxicosis.

Another important, though less common, cause of painful and often unilateral thyroid enlargement is acute infectious (suppurative) thyroiditis. This condition typically occurs in individuals with underlying pathology, such as immunosuppression or a piriform sinus fistula [34, 35]. Notably, the only case of acute infectious thyroiditis reported during pregnancy occurred following a cesarean section wound infection [36].

Differential diagnosis of thyrotoxicosis in pregnancy

While all etiologies of hyperthyroidism may theoretically complicate pregnancy, most are rare. Gestational thyrotoxicosis is the most common cause of thyrotoxicosis during pregnancy, with a prevalence ranging from 2 to 11% [37–39]. Graves' disease is the second most frequent cause, although it occurs at a much lower rate (0–0.05%) in pregnancy [40, 41]. Thyroid autonomy, due to one or more hyperfunctioning thyroid nodules, is another rare cause of hyperthyroidism in pregnancy [41, 42]. Since an autonomous nodule typically needs to be at least 2.5–3.0 cm in diameter to produce hyperthyroidism, these nodules are usually detectable through thyroid examination or ultrasound [43].

Silent thyroiditis is recognized as a common cause of transient thyrotoxicosis, particularly in the postpartum period [44]. However, it is rare during pregnancy, with only one reported case [45].

Similarly, SAT is uncommon in pregnancy, yet its transient thyrotoxic phase, followed by subsequent hypothyroidism, requires differentiation from more common causes of hyperthyroidism.

Given these various etiologies, SAT must be distinguished primarily from gestational thyrotoxicosis and Graves' disease (Table 3). However, differentiation based solely on thyroid function tests can be challenging, as TSH levels may be suppressed in all three conditions, and free T4 (FT4) levels may remain within trimester-specific reference ranges in cases of Graves' disease and SAT, representing subclinical hyperthyroidism [46, 47]. Nonetheless, in cases where TSH is low, a markedly elevated FT4 or total T4 beyond trimester-specific ranges reduces the likelihood of gestational thyrotoxicosis as a diagnosis [46, 48].

As part of evaluation, it is essential to thoroughly review the patient's medication history. Certain drugs can affect thyroid function tests, leading to diagnostic confusion. For example, heparins can cause falsely elevated FT4 levels [49].

In summary, in cases where neck pain accompanies thyrotoxicosis during pregnancy, the diagnosis is most likely subacute thyroiditis (SAT). Confirmation can be achieved by measuring inflammatory markers, such as erythrocyte sedimentation rate (ESR), and performing a thyroid ultrasound. When neck pain is absent or minimal—though no cases have been reported during pregnancy to date—elevated inflammatory markers, decreased vascularity on thyroid ultrasound and negative TSH receptor antibodies (TSHR-Abs) suggest SAT. Conversely, increased vascularity, the presence of goiter, and positive TSHR-Abs indicate Graves' disease. Additionally, the presence of positive TSHR-Abs effectively rules out gestational thyrotoxicosis and SAT while confirming Graves' hyperthyroidism.

The main diagnostic challenge lies in differentiating painless SAT from gestational thyrotoxicosis. This distinction can be made through the assessment of inflammatory markers and specific thyroid ultrasound features (see Table 3). When Graves' disease is not a consideration in the differential diagnosis and symptoms of thyrotoxicosis are mild, close monitoring for the development of neck pain or progression to hypothyroidism may be sufficient.

Hypothyroidism in pregnancy: diagnostic challenges

Primary hypothyroidism accounts for approximately 99% of all hypothyroidism cases and may be either permanent

Table 3 Features useful in differentiating subacute thyroiditis, gestational thyrotoxicosis and Graves' disease

Characteristic	Subacute Thyroiditis	Gestational Thyrotoxicosis	Graves' Disease
Clinical			
Onset	Sudden	Rapid	Gradual
Timing (trimester)	Any [a]	First	First [b]
Personal or family history of autoimmune thyroiditis	No	No	May present
Neck pain/tenderness	Yes	No	No
Thyroid enlargement	Mild	Mild	Moderate to severe
Severity of hyperthyroidism	Mild to moderate	Mild to moderate	Mild to severe
Infiltrative orbitopathy	No	No	Can occur
Infiltrative dermopathy	No	No	Rare
Associated conditions	Systemic symptoms, "Creeping" thyroiditis	Hyperemesis gravidarum	Unusual
Spontaneous recovery	Yes	Yes	No
Response to glucocorticoids	Rapid, Complete	No	Delayed, Partial
Hypothyroidism phase	Common	No	No
Laboratory findings			
Inflammatory markers (ESR/CRP)	Elevated	Normal	Normal
T4/T3 Ratio	T4 > T3	T4 > T3	T3 > T4
TSH Receptor Antibodies	Negative	Negative	Positive
Ultrasound Features	Low echogenicity, Decreased vascularity and blood flow	Normal echogenicity, Increased vascularity	Low echogenicity, Goiter, Increased vascularity and blood flow

a. Almost all reported cases occurred in the first half of pregnancy

b. Rarely may emerge in other trimesters

or transient [50–52]. Aside from iodine deficiency, autoimmune thyroiditis is the most common cause of primary hypothyroidism [52], a pattern that holds true during pregnancy as well [53, 54]. High titers of antibodies against thyroid peroxidase (TPO) and/or thyroglobulin (Tg) help distinguish autoimmune thyroiditis from other, less common causes of hypothyroidism in pregnancy [55]. However, differentiating between permanent and transient hypothyroidism during pregnancy is challenging, as it is typically infeasible to observe a hypothyroid pregnant patient without treatment.

Research indicates that transient hypothyroidism can occur in association with or independently of a preceding thyrotoxic phase in cases of SAT [5, 7, 56]. Fortunately, the hypothyroid phase of SAT is generally not associated with high titers of thyroid autoantibodies and rarely results in permanent hypothyroidism. Thus, spontaneous, antibody-negative hypothyroidism following a thyrotoxic episode strongly suggests a diagnosis of SAT. This also applies to isolated hypothyroidism with negative antibodies and the absence of ultrasound features typical of autoimmune thyroiditis, such as diffuse hypoechogenicity, micro/pseudonodules, and heterogeneous parenchyma [57, 58].

One of the most complex scenarios is the immediate post-thyrotoxic hypothyroid phase, where low free T4 (FT4) may be accompanied by persistently low thyroid-stimulating hormone (TSH) levels [15, 16]. This phenomenon, which is well recognized after radioiodine therapy for hyperthyroidism [59], can also occur following other causes of thyrotoxicosis, such as SAT and silent thyroiditis [60]. When hypothyroidism is preceded by a recognized thyrotoxic phase, diagnosis based on low FT4 is straightforward. However, if the prior thyrotoxicosis was undiagnosed, this condition must be differentiated from central hypothyroidism, severe non-thyroidal illness, and drug effects. Although central hypothyroidism is extremely rare during pregnancy, a single case was reported in a patient with Graves' disease [61]. Differentiating these conditions is critical, as their diagnostic and therapeutic approaches vary significantly. In challenging cases, additional evaluation of other hypothalamic-pituitary axes, such as the hypothalamic-pituitary-adrenal axis, may be necessary.

Non-thyroidal illness (NTI) syndrome is a spectrum of disorders resulting from systemic illnesses that impact thyroid function tests proportionally to illness severity [62]. In severe NTI, both TSH and FT4 levels may be low, mimicking central hypothyroidism. Similarly, the post-thyrotoxic hypothyroid phase of SAT can present with low TSH and FT4 levels, requiring differentiation from NTI. However, in NTI, low TSH typically occurs in critically ill patients and is associated with low free T3 (FT3), facilitating differentiation [62].

Finally, certain drugs, such as high-dose aspirin, carbamazepine and phenytoin, can reduce total T4 (TT4)

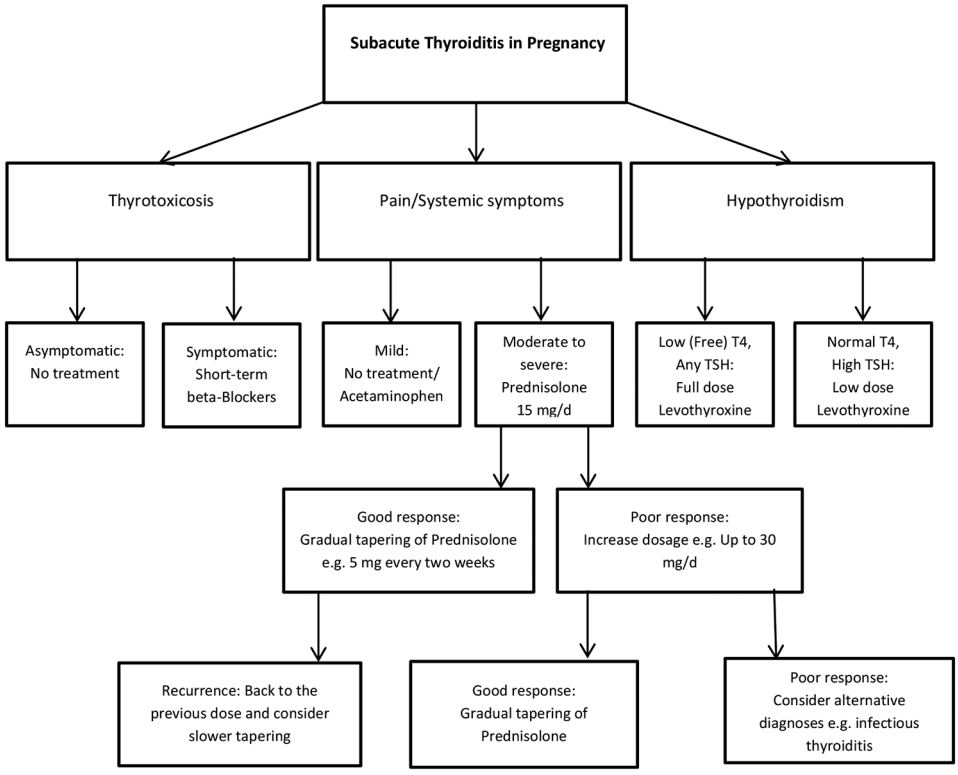

Fig. 1 Proposed therapeutic approach for managing subacute thyroiditis during pregnancy

levels while maintaining inappropriately normal TSH levels [63]. This possibility should be considered in the differential diagnosis of post-thyrotoxic hypothyroidism [64–66].

Management and treatment strategies

Since there are no specific treatment options for SAT, management during pregnancy is primarily conservative, focusing on symptom relief until spontaneous recovery occurs. Supportive care serves as the cornerstone of management, as SAT often resolves without the need for targeted therapeutic interventions (Fig. 1).

Pain control

Nonsteroidal anti-inflammatory drugs (NSAIDs) have traditionally been the primary pharmacologic intervention for pain relief in subacute thyroiditis (SAT), a practice that remains prevalent. However, due to the gastrointestinal side effects associated with older NSAIDs, such as aspirin, selective cyclooxygenase-2 (COX-2) inhibitors are often preferred for managing SAT-related pain [67]. During pregnancy, the use of NSAIDs is associated with potential risks, particularly in later trimesters such as increased risk of premature closure of the fetal ductus arteriosus [68, 69]. Current guidelines generally advise against NSAID use during pregnancy; however, short-term use before the 20th week is considered relatively safe in select cases [70]. Notably, one reported case of SAT involved a pregnant patient in the 12th week of gestation who received ibuprofen for five weeks without any complications [17].

For mild to moderate pain and systemic symptoms in SAT, acetaminophen—a widely used analgesic without anti-inflammatory properties—is often regarded as a safer alternative during pregnancy [71]. In a case study by Yildiz et al., acetaminophen was successfully used to manage SAT-related pain without adverse effects on pregnancy outcomes [15].

Glucocorticoids remain the most effective agents for managing both pain and systemic symptoms in SAT. However, the use of glucocorticoids may carry potential risks for both mother and fetus. For instance, maternal corticosteroid use has been weakly associated with orofacial clefts in the fetus, highlighting the need for further research to confirm and better understand this association [72]. Prednisolone, which minimally crosses the placenta, is typically preferred for treating SAT in pregnant patients [73]. To minimize potential side effects, it is advisable to prescribe the lowest effective dose. Research indicates that a daily dose of 15 mg of prednisolone can be as effective as 30 mg in terms of pain relief, recurrence prevention, and reducing the prevalence of hypothyroidism [67, 74].

A recent comparative review showed that 42.9% of pregnant patients and 79.3% of non-pregnant patients received prednisolone as part of their SAT management. For pregnant patients, the initial dose was consistently set at 15 mg, while in non-pregnant patients, the initial doses varied between 5 and 30 mg [75]. In contrast, a 2012 case report by Kaykhaei et al. described an initial prednisolone dose of 1 mg/kg body weight in a pregnant SAT patient [16].

One recommended approach to glucocorticoid therapy in SAT during pregnancy mirrors treatment in non-pregnant patients: an initial dose of 15 mg/day of prednisolone, followed by a taper of 5 mg every two weeks, with regular evaluation of symptoms to guide further adjustments [76]. In cases of unsatisfactory symptom relief, gradual increases in the prednisolone dosage may be considered (Fig. 1).

Recently, intrathyroidal steroid injections have demonstrated potential in providing more rapid symptom relief with fewer side effects compared to oral prednisolone in non-pregnant patients. However, this approach has been evaluated in a single-center study with a limited sample size, necessitating further research to confirm its efficacy and safety [77]. Consequently, its applicability during pregnancy remains unknown, and it is not currently recommended.

Notably, while there are no documented cases directly linking subacute thyroiditis (SAT) in pregnancy to adverse outcomes, untreated pain, severe systemic symptoms, and inflammation—consistent with other inflammatory conditions—may adversely impact pregnancy outcomes, such as the neurocognitive development of offspring [78–80]. Singh et al. reported a case of SAT in early pregnancy where the patient did not adhere to treatment, experiencing intractable nausea, vomiting, significant weight loss, and ultimately opting for therapeutic abortion [13]. These observations highlight the necessity of proactive management of severe symptoms in SAT during pregnancy to alleviate maternal anxiety, potentially contributing to improved pregnancy outcomes.

Considering that all therapeutic options for managing pain during pregnancy may affect mother and fetus, efforts must be made to minimize drug exposure while ensuring maternal and fetal well-being.

Thyrotoxicosis

In cases of SAT, thyrotoxicosis is typically mild and transient, and many patients—apart from experiencing neck pain—remain asymptomatic [5, 7]. For those with pronounced thyrotoxic symptoms, short-term treatment with beta-blockers may be considered [76]. However, the generally young age of pregnant patients, combined with the naturally hypermetabolic state of pregnancy, reduces the need for beta-blockers in most cases. Notably, none of the reported cases in the literature have required beta-blocker therapy. Although low doses and short-term beta-blocker use in pregnancy have been shown to be safe [81], their use remains uncommon in this context.

Cholestyramine, a bile acid sequestrant, can interrupt the enterohepatic circulation of thyroid hormones and has demonstrated efficacy in treating hyperthyroidism [82, 83]. Since cholestyramine is not absorbed from the gastrointestinal tract, it may be an option in severe, symptomatic cases of SAT. However, it is associated with gastrointestinal side effects such as constipation and can interfere with the absorption of fat-soluble vitamins. Additionally, it reduces cholesterol levels, which are essential for fetal development [84]. In this regard, low doses of cholestyramine may mitigate these adverse effects while still effectively lowering thyroid hormone levels [82].

Hypothyroidism

Subacute thyroiditis (SAT) typically progresses through three distinct phases: an initial thyrotoxic phase characterized by follicular destruction and the subsequent release of thyroid hormones, a hypothyroid phase marked by decreased hormone synthesis, and, finally, a return to euthyroidism as follicular regeneration occurs. Due to this sequence, the hypothyroid phase in SAT is generally transient, with most cases eventually returning to euthyroidism. However, up to 15% of patients may develop permanent hypothyroidism, while approximately 34% experience transient hypothyroidism [5]. Despite this usual course, it remains unclear whether transient hypothyroidism leaves any lasting adverse effects. Importantly, SAT-induced transient hypothyroidism can persist for several months [5]. Until there is conclusive evidence that transient hypothyroidism during pregnancy is not linked to adverse outcomes, treatment with levothyroxine (LT4) is recommended to mitigate potential risks. Pregnant patients receiving LT4 therapy should be closely monitored to maintain TSH levels within the lower half of the trimester-specific reference range [46, 85, 86]. If trimester-specific reference ranges are unavailable, it is recommended to aim for TSH levels below 2.5 mIU/L [46] (Fig. 1).

Notably, hypothyroidism that follows the resolution of thyrotoxicosis may present uniquely, with low FT4 levels despite a low or normal TSH concentration [87]. This phenomenon has also been observed during the progression of SAT in pregnancy [12, 15, 16]. In such cases, initiating LT4 replacement therapy can be beneficial. The primary objective of treatment should be to maintain TT4 or FT4 levels within the upper normal reference range for pregnancy until TSH levels recover from suppression (Fig. 1).

Conclusions

Subacute thyroiditis (SAT) during pregnancy is a rarely reported condition, with neck pain and tenderness as prominent clinical features. To manage pain, acetaminophen is recommended for mild discomfort, while prednisolone may be necessary in more severe cases. The hypothyroid phase should be managed with levothyroxine therapy to support optimal maternal and fetal outcomes. Clinicians should remain vigilant for atypical presentations of SAT that may arise during pregnancy.

Abbreviations

HCG	Human chorionic gonadotropin
TSH	Thyroid-stimulating hormone
SAT	Subacute thyroiditis
FT4	Free T4
ESR	Erythrocyte sedimentation rate
CRP	C - reactive protein
TPO	Thyroid peroxidase
Tg	Thyroglobulin
NTI	Non-thyroidal illness
FT3	Free T3
TT4	Total T4
NSAIDs	Nonsteroidal anti-inflammatory drugs

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Author contributions
Both authors contributed equally to the conception and design of the study. M.K. and Z.H. conducted the literature search and data extraction. M.K. drafted the initial manuscript, which was reviewed and approved by Z.H. All authors have read and approved the final version of the manuscript.

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