Autoimmune and inflammatory thyroid diseases following vaccination with SARS-CoV-2 vaccines: from etiopathogenesis to clinical management

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Abstract
Since the Covid-19 pandemic emerged in 2019, several adenoviral-vectored, mRNA-based and inactivated whole-virus vaccines have been developed. A massive vaccination campaign has been undertaken around the world, and an increasing number of SARS-CoV-2 vaccine-induced thyroid diseases have been described in the literature. Subacute thyroiditis has been reported in 52 patients, mean age 45.5 ± 1.8 years, mainly in women (n = 39). Graves’ disease is more frequent in women (n = 22) than in men (n = 10), mean age 46.2 ± 2.6 years, reported as new onset, recurrent or exacerbation of well-controlled hyperthyroidism. The mean time to symptoms onset is 9.0 ± 0.8 days in subacute thyroiditis, and 15.1 ± 2.6 days in Graves’ patients. Rare patients (n = 6) present silent or painless autoimmune thyroiditis. Thyroid function and autoimmune tests, inflammatory markers, thyroid echography with colour flow Doppler, radio-activity uptake on thyroid scan, medical treatment and follow-up are described and compared in patients with SARS-CoV-2 vaccine-induced thyroid diseases. The underlying pathogenic mechanisms of vaccine-induced thyroid diseases, molecular mimicry (various SARS-CoV-2 proteins sharing a genetic homology with a large heptapeptide human protein) or autoimmune/inflammatory syndrome induced by adjuvants (ASIA) are discussed in the context of predisposition or genetic susceptibility. The benefits of SARS-CoV-2 vaccination far outweigh the potential vaccine-induced adverse effects, but clinicians should be aware of possible autoimmune and inflammatory thyroid diseases, and can advise patients to seek medical assistance when experiencing anterior neck pain, fever or palpitations following SARS-CoV-2 vaccines. Further studies are warranted to investigate the etiopathogenesis and to clarify the factors which predispose patients to SARS-CoV-2 vaccine-induced thyroid diseases.

Keywords SARS-CoV-2 · Vaccines · Graves’ disease · Subacute thyroiditis · Autoimmune thyroiditis

Introduction
Since the emergence of the new Coronavirus (Covid-19) pandemic in December 2019, several vaccines have been approved and rapidly developed in an attempt to protect populations from Covid-19 infection. A massive vaccination campaign using several types of vaccines against SARS-CoV-2 has been undertaken around the world with benefits to morbidity and mortality, but an increasing number of autoimmune and inflammatory-related side effects are described (thrombotic thrombocytopenia, Guillain Barré syndrome, myocarditis/pericarditis, type 1 diabetes mellitus, premature ovarian failure, adrenal insufficiency). It is noteworthy that several thyroid disorders such as Graves’ disease, subacute thyroiditis and silent (painless) thyroiditis have been reported following the first or second dose of SARS-CoV-2 vaccines. Reports of such potential adverse events have been given in patients from countries in Asia, Europe, South and North America, and these are becoming more frequent in recent weeks.

Several pharmaceutical companies have developed SARS-CoV-2 vaccines:

- adenoviral-vectored vaccine (Oxford-Astra Zeneca, Johnson and Johnson Jansen),
mRNA-based vaccine (Pfizer-BioNTech, Moderna), inactivated whole-virus vaccine (Coronovac, Sinovac Life Sciences, Sinopharm BIPP2).

Adenoviral-vectored and mRNA vaccines encoding the SARS-CoV-2 spike protein antigen and inactivated whole-virus vaccine elicit antibodies and T cell response to protect against Covid-19. Most vaccines contain adjuvants which are used to increase the immunogenicity and the response to vaccination. It is suggested that in individuals who are genetically susceptible, SARS-CoV-2 vaccines can induce autoimmune and inflammatory adverse reactions by activating autoimmune cascade pathways.

Methods

The systematic review of the literature was conducted on original articles published from July 2021 to the end of January 2022, via the PubMed online databases using the following keywords: thyroid, Graves’ disease, subacute thyroiditis, chronic thyroiditis, SARS-CoV-2 and vaccines. Case reports and cases series recording data on thyroid diseases (Graves’ disease, subacute or chronic thyroiditis) in patients after SARS-CoV-2 vaccination were eligible for inclusion. Articles that were not written in English were excluded.

For each included article we recorded reference data (authors, journal, year of publication), and for each patient we collected demographic data (sex, age), previous history of autoimmune or thyroid disease, type of administered vaccines (mRNA vaccine, inactivated virus or vector vaccine), timing of thyroid disease onset following vaccination, signs and symptoms at presentation, laboratory tests (TSH, freeT4, anti-TPO, anti-Tg, anti-TSH receptor antibodies, C-reactive protein, erythrocyte sedimentation rate) and other diagnostic exams (ultrasonography with colour flow doppler, thyroid scintigraphy), specific medical therapies and clinical or hormonal follow-up.

Patients with SARS-CoV-2 vaccine-induced thyroid diseases

Subacute thyroiditis

Subacute thyroiditis usually occurs following viral upper respiratory tract infection, and several patients have been described as presenting with this following Covid-19 infection. This self-limited inflammatory and benign thyroid disease usually follows a triphasic pattern: an initial thyrotoxic phase is characterised by severe pain, swelling and a tender thyroid gland with follicular destruction and release of preformed thyroid hormones responsible for thyrotoxicosis, with signs of systemic inflammation and high inflammatory markers. Then granulomatous thyroid tissue can be associated with transient hypothyroidism, and followed by spontaneous resolution with a recovery phase.

The first cases of subacute thyroiditis associated with SARS-CoV-2 vaccines were described by Iremli et al. [1] in 3 female patients, and cases or case series continued to be reported, with there being 52 patients at the time of writing this manuscript (Table 1) [1–23]. The median age of the patients is 45.5 ± 1.8 years, ranging from 26 to 75, and subacute thyroiditis is more prevalent in women (n = 39, 75%) than in men (n = 13, 25%). Seventeen percent of patients have a personal history of thyroid disease (nodular thyroid disease n = 5, subacute thyroiditis n = 2, Hashimoto thyroiditis n = 1). Patients develop subacute thyroiditis after receiving mRNA (60%), inactivated whole-virus (25%) and adenoviral-vectored (13.5%) vaccines, either after the first (62%) or the second (38%) dose. The mean time from vaccination to symptom onset is 9.0 ± 0.8 days, with a range of 1–21. The most frequent symptom is neck pain (97%) followed by signs of thyrotoxicosis (palpitations 71%, weight loss 29%, night sweats 12.5%, tremor 12.5%) and signs of systemic inflammation (fever 54%, fatigue 34.5%, headaches 11.5%, myalgia 7%). Thyrotoxicosis is confirmed by increased thyroid hormones (free T4 = 30.0 ± 2.8 pmol/L, free T3 = 34.3 ± 10.8 pmol/L) with decreased TSH (0.29 ± 0.10 mU/L) concentrations. In all patients except one (concurrent subacute thyroiditis and Graves’ disease) anti TSH-receptor antibodies are negative, and TPO-antibodies are present in only 4 (9.5%) patients. Erythrocyte sedimentation rate (53 ± 3 mm/hour) and C-reactive protein (87 ± 14 mg/L) are significantly increased (p < 0.02) compared to SARS-CoV-2 vaccine-induced Graves’ disease. Ultrasound sonography with colour flow Doppler, in the majority of patients reveals normal or increased heterogeneous thyroid gland with hypoechoic areas and decreased blood flow, and decreased uptake on thyroid scan. Finally, at the inflammatory phase of the subacute thyroiditis, post-surgical pathology (destroyed follicles, presence of macrophages and inflammatory cells) [6] or cytology (mononuclear lymphocytes infiltrate, presence of macrophages and multinucleated giant cells) examen after fine needle aspiration [14, 17, 20, 21] are compatible with a diagnosis of subacute thyroiditis.

SARS-CoV-2 vaccine-induced subacute thyroiditis appears to follow a clinical course and responds to conventional treatment in an identical way to classic subacute thyroiditis. Patients with palpitations or tachycardia are given beta-adrenergic blockers (31%). During the inflammatory phase, patients were initially given non-steroidal anti-inflammatory drugs (52%) and/or oral glucocorticoids (48%), which were considered when the patient presented.
| No | Author (Ref) | Gender | Age | Type of vaccine | Dose | Time (days) | Neck pain | TSH | FT4 | ESR | CRP | Thyroid ultrasound, Colour flow Doppler | Thyroid scintigraphy | Treatment | Follow-up |
|----|--------------|--------|-----|-----------------|------|-------------|-----------|-----|-----|-----|-----|---------------------------------------|-----------------|-----------|-----------|
| 1  | Iremli [1]   | F      | 35  | Inactivated virus | 2nd  | 4           | Y         | 0.47| 14.1| 53  | 100.5 | Bilateral focal hypoechoic area, decreased blood flow | ND               | Methylprednisolone, propanolol | Disappeared within 1 day, recovery 4 weeks |
| 2  | Iremli [1]   | F      | 34  | Inactivated virus | 1st  | 4           | Y         | 0.01| 5.2 | 19  | 6    | Bilateral focal hypoechoic area, decreased blood flow | ND               | Methylprednisolone, propanolol | Myalgia, neck pain during tapering methylprednisolone, recovery 10 weeks |
| 3  | Iremli [1]   | F      | 37  | Inactivated virus | 2nd  | 7           | Y         | 0.9 | 13.85| 25  | 2.4  | Bilateral focal hypoechoic area, decreased blood flow | ND               | Rarely paracetamol | No treatment, recovery 8 weeks |
| 4  | Oyibo [2]    | F      | 55  | Adenovirus vectored | 1st  | 21          | Y         | 0.09| 25.2| 51  | 87   | Enlarged, heterogenous thyroid gland | ND               | Propanolol, ibuprofen, paracetamol | Hypothyroidism at 6 weeks treated by LT4, recovery 12 weeks |
| 5  | Franquemont [3] | F      | 42  | mRNA | 1st  | 5           | Y         | <0.01| 58.95| 62  | NA   | Bilateral focal hypoechoic area, decreased blood flow | ND               | Rarely paracetamol | No treatment, recovery 12 weeks |
| 6  | Schimmel [4] | F      | 57  | mRNA | 2nd  | 1           | Y         | 0.008| 24.7 | NA  | NA   | Increased size, hypoechoic area | ND               | Ibuprofen, propanolol, prednisone | Hypothyroidism at 1 month, levothyroxine treatment |
| 7  | Saygili [5]  | F      | 38  | Inactivated virus | 2nd  | 14          | Y         | 0.008| 59.8| 78  | 87.6 | Increased size, hypoechoic area | ND               | Increased size, hypoechoic area | Normal thyroid function at 1 month |
| 8  | Sigstad [6]  | F      | 30  | mRNA | 1st  | 6           | Normal    | 13  | NA  | NA  | NA   | Thyroiditis, hypoechoic nodule | Minimal isotope uptake | NSAID | Resolution symptoms in 6 weeks, euthyroid 8 weeks |
| 9  | Jeeyavudeen [7] | F      | NA  | mRNA | 2nd  | 14          | Y         | <0.01| 27   | NA  | 23   | Heterogeneity, decreased vascularity | Moderate to severely decreased uptake | Predictive index, propanolol | Euthyroid state at 7 weeks |
| 10 | Soltanpoor [8] | F      | 34  | Inactivated virus | 1st  | 5           | Y         | 0.05| 60  | 9.8  | ND   | Heterogeneity, decreased vascularity | Marked reduction of uptake | Ibuprofen | Normal thyroid function at 1 month |
| 11 | Ratnayake [9] | M      | 75  | Adenovirus vectored | 1st  | 14          | Y         | 0.01| 28.2| NA  | NA   | Heterogeneity, hypoechoic nodule | Marked reduction of uptake | Ibuprofen | Normal thyroid function at 1 month |
| 12 | Sozen [10]   | M      | 41  | mRNA | 2nd  | 3           | Y         | 0.01| 40.9| 32  | 124  | Heterogeneity, hypoechoic nodule, decreased blood flow | Acetylsalicylic acid, propanolol | Control at 1 month, euthyroid | Transient hypothyroidism, complete remission, euthyroid |
| 13 | Sozen [10]   | F      | 40  | mRNA | 2nd  | 6           | Y         | 0.18| 20.34| 80  | 34   | Heterogeneity, hypoechoic nodule, decreased blood flow | Acetylsalicylic acid, propanolol | Control at 1 month, euthyroid | Control at 1 month, euthyroid |
| 14 | Sozen [10]   | M      | 40  | mRNA | 1st  | 4           | Y         | 1.1 | 19.95| 28  | 15   | Heterogeneous, hypoechoic nodule | Acetylsalicylic acid, propanolol | Control at 2 weeks, euthyroid | Control at 2 weeks, euthyroid |
| 15 | Sozen [10]   | F      | 26  | mRNA | 1st  | 20          | Y         | 0.01| 26   | 34  | 27   | Heterogeneity, hypoechoic nodule, decreased blood flow | Acetylsalicylic acid, propanolol | Control at 1 month, euthyroid | Control at 1 month, euthyroid |
| 16 | Sozen [10]   | F      | 44  | mRNA | 2nd  | 9           | Y         | 0.24| 20.33| 44  | 18   | Heterogeneity, hypoechoic nodule, decreased blood flow | Acetylsalicylic acid, propanolol | Control at 1 month, euthyroid | Control at 1 month, euthyroid |
| 17 | Kyriacou [11] | F      | 40  | mRNA | 2nd  | 1           | Y         | 0.11| 33.74| 67  | 174.3| Heterogeneity, hypoechoic nodule, decreased blood flow | Predictive index, propanolol | Resolution symptoms in 2 days, euthyroid TSH 2.74, 1 month |
| 18 | Patel [12]   | M      | 48  | 2nd  | 7           | Y         | 0.01| 46.34| Increased | Increased | Heterogeneity, hypoechoic nodule, decreased blood flow | NSAID, prednisone | Resolution symptoms in 1 day, euthyroid |
| 19 | Sahin tekin [13] | M      | 67  | Inactivated virus | 2nd  | 17          | Y         | 0.005| 36.9| 67  | 5.9  | Hypothyroidism, goiter | NSAID, prednisone | Ibuprofen | Relief of symptoms in few days |
| 20 | Bornemann [14] | F      | 26  | Adenovirus vectored | 1st  | 16          | Y         | 1.75| 11.97 | NA  | 29.4 | Heterogeneity, hypoechoic nodule, decreased blood flow | Ibuprofen, prednisone | Resolution symptoms in 1 day, euthyroid TSH 2.74, 1 month | Resolution symptoms in 1 day, euthyroid |

Table 1: Clinical characteristics, laboratory results and imaging findings of patients with SARS-CoV-2 vaccine-induced subacute thyroiditis.
| No  | Author (Ref) | Gender | Age  | Type of vaccine | Dose | Time (days) | Neck pain | TSH   | FT4   | ESR  | CRP   | Thyroid ultrasound, Colour flow Doppler | Thyroid scintigraphy | Treatment                                      | Follow-up                                      |
|-----|--------------|--------|------|-----------------|------|-------------|-----------|-------|-------|------|-------|----------------------------------------|---------------------|-----------------------------------------------|-----------------------------------------------|
| 21  | Bornemann [14] | F      | 49   | mRNA            | 1st  | 14          | Y         | 0.01  | 12.1  | NA   | 219  | Normal size, hypoechoic areas, decreased vascularity | Ibufrofen, prednisolone | Resolution symptoms 2 weeks, euthyroid 6 weeks | TSH 0.83 Symptoms improved in 2 weeks |
| 22  | Lee [15]     | F      | 39   | Adenovirus vectored | 2nd  | 4           | Y         | 0.113 | 31.4  | 63   | 28.6 | Ill defined, hypoechoic lesion            | Decreased uptake    | Symptoms improved in 2 weeks                  |                                 |
| 23  | Lee [15]     | F      | 73   | Adenovirus vectored | 1st  | 11          | Y         | 0.012 | 94.7  | 85   | 34.6 | Ill defined, hypoechoic lesion            |                     |                                 |                                 |
| 24  | Lee [15]     | M      | 39   | Adenovirus vectored | 1st  | 14          | Y         | 0.012 | 39.9  | 74   | 36.5 | Ill defined, hypoechoic lesion            |                     |                                 |                                 |
| 25  | Siosos [16]  | F      | 51   | mRNA            | 1st  | 4           | Y         | 0.08  | 24.8  | 103  | 135  | Markedly decreased thyroid uptake         |Prednisolone              | Resolution fever and neck pain in 2 days |                                 |
| 26  | Pujol [17]   | F      | 38   | mRNA            | 1st  | 8           | Y         | <0.008| 23.94 | NA   | NA   | Enlarged right lobe, diffuse hypoechochogenicity | Ibufrofen, propanolol, prednisone | Improvement of symptoms in 1 week |                                 |
| 27  | Pandya [18]  | M      | 37   | mRNA            | 1st  | 15          | Y         | <0.01 | 89.58 | 51   | NA   | Enlarged and heterogenous thyroid gland  | Ibufrofen, propanolol, prednisone |                                 |                                 |
| 28  | Pandya [18]  | M      | 35   | mRNA            | 1st  | 10          | Y         | 0.07  | 39.13 | NA   | NA   | Enlarged and heterogenous thyroid gland  | Ibufrofen, propanolol |                                 |                                 |
| 29  | Pandya [18]  | F      | 41   | mRNA            | 2nd  | 20          | Y         | 0.019 | 32.43 | NA   | NA   | Enlarged and heterogenous thyroid gland  |                     |                                 |                                 |
| 30  | Pla Pleris [19] | M     | 57   | mRNA            | 1st  | <14         | No        | <0.005| 64.36 | 30   | 88   | Heterogeneous echogenicity, diffuse hypoechochogenic area, decreased vascularity | NA                    | NSAID                           | Improvement in 2 weeks, subclinical hypothyroidism |
| 31  | Pla Pleris [19] | M     | 67   | mRNA            | 1st  | <14         | Y         | <0.005| 45.05 | 60   | 120  | Unstructured thyroid, diffuse hypoechochogenic area, decreased vascularity | Decreased uptake NSAID | Improvement in 2 weeks, subclinical hypothyroidism at 4 weeks |                                 |
| 32  | Pla Pleris [19] | M     | 47   | mRNA            | 1st  | <14         | Y         | 0.005 | 33.46 | 70   | 92   | Unstructured thyroid, diffuse hypoechochogenic area, decreased vascularity | Decreased uptake NSAID | Improvement of symptoms in 2 weeks, normal thyroid function at 5 weeks |                                 |
| 33  | Pla Pleris [19] | F     | 69   | mRNA            | 1st  | <14         | Y         | <0.005| 23.17 | 75   | 120  | Enlarged thyroid gland, heterogenous echogenicity, diffuse hypoechochogenic pattern | Methylprednisolone, NSAID | NSAID                           |                                 |
| 34  | Das [20]     | F      | 47   | Adenovirus vectored | 1st  | 14          | Y         | 0.06  | NA   | NA   | NA   | Bulky thyroid with bilateral hypoechochogenic nodules | No tracer uptake Propanolol | Improvement and complete resolution and normal TSH at 8 weeks |                                 |
| 35  | Raven [21]   | F      | 35   | mRNA            | 1st  | 4           | Y         | 2.03  | 11.4  | NA   | NA   | 11 mm right thyroid nodule                | No treatment                  | Resolution of pain in 2 weeks             |                                 |
| 36  | Chatzi [22]  | F      | 35   | mRNA            | 1st  | 12          | Y         | 75    | 498   |      |      | Increased gland, heterogeneous appearance, hypoechochogenic regions | Low uptake Prednisolone |                                 |                                 |
| 37  | Chatzi [22]  | F      | 32   | mRNA            | 2nd  | 4           | Y         | 40    | 10    |      |      | Increased gland, heterogeneous appearance, hypoechochogenic regions | Low uptake Prednisolone |                                 |                                 |
| 38  | Oguz [23]    | F      | 42   | mRNA            | 1st  | 4           | <0.015   | 51.4  | 74   | 44.4 | Patchy heterogenous hypoechochogenic areas in right lobe | Partially suppressed thyroid uptake NSAID | Remission 14 weeks |                                 |
| 39  | Oguz [23]    | F      | 48   | Inactivated virus | 2nd  | 1           | Y         | 0.051 | 48    | 58   | Patchy heterogenous, hypoechochogenic areas | NA Prednisolone | Remission 5 weeks |                                 |
| N° | Author (Ref) | Gender | Age | Type of vaccine | Dose | Time (days) | Neck pain | TSH  | FT4  | ESR | CRP | Thyroid ultrasound, Colour flow Doppler | Thyroid scintigraphy | Treatment | Follow-up            |
|----|--------------|--------|-----|----------------|------|-------------|-----------|------|------|-----|-----|--------------------------------------|----------------------|-----------|----------------------|
| 40 | Oguz [23]    | F      | 47  | mRNA           | 1st  | 10          | 0.54      | 13.42| 55   |     | 48.5| Patchy heterogenous, hypoechoic areas | NA                   | Paracetamol | Remission 13 weeks |
| 41 | Oguz [23]    | F      | 72  | mRNA           | 2nd  | 15          | 11.81     | 10   | 7.7  |     | 10.2| Patchy heterogenous, hypoechoic areas in the right lobe | NA                   | No treatment | Remission 5 weeks |
| 42 | Oguz [23]    | M      | 50  | Inactivated virus | 1st  | 1           | 0.127     | 11.4 | 41   |     | 10.2| Ill-edged heterogenous hypoechoic area in right lobe | NA                   | NSAID     | Remission 6 weeks |
| 43 | Oguz [23]    | F      | 61  | Inactivated virus | 2nd  | 15          | 4.44      | 10.99| 34   |     | 11.6| Patchy heterogenous, hypoechoic areas | NA                   | Methylprednisolone | Remission 20 weeks |
| 44 | Oguz [23]    | F      | 36  | Inactivated virus | 2nd  | 4           | 0.47      | 19.11| 53   |     | 105 | Patchy heterogenous, hypoechoic areas, decreased vascularisation | NA                   | Methylprednisolone | No remission |
| 45 | Oguz [23]    | F      | 38  | Inactivated virus | 2nd  | 7           | 0.018     | 26.1 | 44   |     | 3   | Patchy heterogenous, hypoechoic areas, decreased vascularisation | NA                   | No treatment | Remission 11 weeks |
| 46 | Oguz [23]    | F      | 38  | mRNA           | 1st  | 10          | <0.01     | 51.48| 55   |     | 136.3| Patchy heterogenous, hypoechoic areas | NA                   | NSAID     | Remission 4 weeks |
| 47 | Oguz [23]    | F      | 38  | Inactivated virus | 1st  | 13          | 0.032     | 12.23| 42   |     | 19  | Patchy heterogenous, hypoechoic areas | NA                   | Paracetamol, NSAID | Remission 12 weeks |
| 48 | Oguz [23]    | F      | 36  | mRNA           | 2nd  | 7           | 0.01      | 37.7 | 429  |     | 429 | Patchy heterogenous, hypoechoic areas, decreased vascularisation | Low thyroid uptake (24 h RAIU 1%) | Methylprednisolone, NSAID | Remission 11 weeks |
| 49 | Oguz [23]    | F      | 60  | mRNA           | 1st  | 3           | 0.6       | 14   | 33   |     | 52  | Patchy heterogenous, hypoechoic areas | NA                   | No treatment | Not in remission |
| 50 | Oguz [23]    | F      | 46  | mRNA           | 1st  | 1           | 0.43      | 14.08| 60   |     | 17  | Patchy heterogenous, hypoechoic areas | NA                   | NSAID, methylprednisolone | Remission 18 weeks |
| 51 | Oguz [23]    | F      | 34  | Inactivated virus | 1st  | 4           | 0.03      | 31.65| 18   |     | 6   | Patchy heterogenous, hypoechoic areas, decreased vascularisation | NA                   | Methylprednisolone and then methimazole after GD diagnosis | Not in remission |
| 52 | Oguz [23]    | M      | 71  | mRNA           | 1st  | 10          | 0.038     | 17.27| 67   |     | 36.5| Patchy heterogenous, hypoechoic areas, decreased vascularisation | NA                   | Prednisolone | Not in remission |

Age in years, Time in days, TSH in mU/L, and FT4 in pmol/l
Gender F female, M male, Y yes, N not present, ESR Erythrocyte sedimentation rate (mm/h), CRP C-reactive protein (mg/l), NSAID non-steroidal anti-inflammatory drug, NA Not available
Graves’ disease

Graves’ disease is a Th1-mediated immune disease caused by the stimulation of the follicular thyroid cells by anti-TSH receptor antibodies. Graves’ disease is the most common cause of hyperthyroidism in young adults, mainly in women. After SARS-CoV-2 vaccination, the mean age of Graves’ disease patients is 46.2 ± 2.6 years, ranging from 28 to 73 (Table 2) [15, 17, 19, 21, 23–35]. Graves’ hyperthyroidism is more frequent in women (n = 22) than in men (n = 10). Seven patients have a personal history of thyroid disease, autoimmune hypothyroidism (n = 3) or past history of Graves’ disease (n = 3). Graves’ hyperthyroidism following SARS-CoV-2 vaccination is reported as:

- new onset or newly diagnosed Graves’ disease with no previous history of thyroid disease [24, 35], after recovering from a mildly symptomatic Covid-19 infection [28], or in a patient associated with the conversion of pre-existing type 2 diabetes mellitus into type 1 immune diabetes [30],

- exacerbation of well-controlled hyperthyroidism on low-dose thioamide treatment [31],

- recurrent hyperthyroidism following a long-period of remission after medical treatment [25],

- after long standing stable hypothyroidism on thyroxine replacement [29],

- following an episode of subacute thyroiditis [15, 19, 23], a thyroid storm [35].

Newly diagnosed or recurrent Graves’ hyperthyroidism is reported following adenoviral-vectorised (28%) and mRNA (72%) SARS-CoV-2 vaccines following the first dose (62%), the second dose (34%) or a booster dose (3%) of Covid-19 vaccines. No patient received an inactivated whole-virus vaccine. The mean time from vaccination to thyrotoxicosis onset is 15.1 ± 2.6 days, with a range of 1 to 60 days. Patients present palpitations (53%), weight loss (34%), tremor (22%), sweating (12.5%), and heat intolerance (3%).

After SARS-CoV-2 vaccination, thyrotoxicosis is confirmed by increased free thyroid hormones concentrations (free T4 = 43.3 ± 4.0 pmol/L, free T3 = 39.0 ± 20.1 pmol/L) and low TSH (0.002 ± 0.0008 mU/L) concentrations. All patients with Graves’ hyperthyroidism except two have positive anti-TSH-receptor antibodies or thyroid stimulating immunoglobulins, and anti-TPO antibodies are positive in 73% of patients. Most patients have an increased vascularity of normal sized or enlarged thyroid gland during thyroid ultrasound with Colour flow Doppler, with a diffuse and markedly increased uptake of the radiotracer activity during thyroid scintigraphy.

In classic Graves’ disease, treatment should control the thyrotoxic symptoms and decrease the thyroid hormone synthesis either with thioamides, radiiodine ablation or surgical thyroideectomy. After SARS-CoV-2 vaccination, 32% patients have symptomatic treatment with beta-adrenergic blockers and 89% require antithyroid drugs, while 11% patients receive no treatment. Rapid improvement of signs and symptoms of thyrotoxicosis is observed in most patients, response to standard or low-dose medical treatment is good with rapid restoring of normal thyroid hormone concentrations in under 8 weeks, and a decrease or normalisation of anti-TSH receptor antibodies in 2 or 3 months. A rare recurrence of hyperthyroidism is observed in patients with Graves’ disease following Covid-19 vaccination [23, 32].

Silent autoimmune thyroiditis

Autoimmune thyroiditis (Hashimoto’s thyroiditis, lymphocytic thyroiditis) is the most common form of thyroiditis with lymphocytic infiltration of the thyroid gland, and is characterised by the presence of high serum thyroid antibodies (anti-thyroperoxidase, anti-thyroglobulin) concentrations and heterogeneous goiter, while TSH concentration is variable and in most patients within the normal range. Silent or painless thyroiditis, a variant form of autoimmune thyroiditis, can be exhibited through thyrotoxicosis, often followed by a transient hypothyroidism and then a full recovery to normal thyroid function.

Few patients (3 women, 3 men) with variable forms of autoimmune thyroiditis are reported after SARS-CoV-2 vaccines (Table 3) [15–17, 36, 37]. Patients have a personal (type 1 diabetes mellitus) or family history (Hashimoto’s thyroiditis) of autoimmune diseases. The mean age is 33 ± 1 year, and the time from vaccination to onset of symptoms ranges from 1 to 21 days. Silent autoimmune thyroiditis following mRNA SARS-CoV-2 vaccines [17, 37] or following adeno-vectorised vaccine [16] are reported, whereas painless thyroiditis with thyrotoxic periodic paralysis is described following inactivated virus vaccine in one patient [15]. Thyrotoxicosis (n = 5) is observed after the first dose.
| No. | Author (Ref) | Gender | Age | Type of vaccine | Dose | Time (days) | TSH  | FT4 | TPO-Ab | Tg-Ab | TSHr-Ab | Thyroid ultrasound, Colour flow Doppler | Thyroid scintigraphy | Treatment                                                                 | Follow-up                           |
|-----|--------------|--------|-----|-----------------|------|-------------|------|-----|--------|--------|---------|--------------------------------------|----------------|--------------------------------------------------------------------------------|-------------------------------------|
| 1   | Vera Lasta [24] | F      | 40  | mRNA            | 1st  | 2           | <0.001 | 45.95 | Y       | Y       | Y       | Enlarged thyroid gland, hypervascularity | NA                      | Propanolol, diltiazem, ivabradine, thiamazole | Good response                          |
| 2   | Vera Lasta [24] | F      | 28  | mRNA            | 1st  | 3           | <0.001 | 23.68 | Y       | N       | Y       | Multiple anechoic areas, increased vascularisation | Diffuse toxic goiter, Patchy inhomogenous tracer distribution, mildly increased uptake | Propanolol, thiamazole | Thyrostatic treatment, Normal thyroid function |
| 3   | Zettinig [25] | F      | 71  | mRNA            | 2nd  | 35          | 45.82  | Y    | Y       | Y       | Y       | Slightly enlarged, hypo and anechoic areas, increased vascularisation | Patchy inhomogenous tracer distribution, normal uptake | Thyrostatic treatment | Normal thyroid function |
| 4   | Zettinig [25] | M      | 46  | mRNA            | 1st  | 15          | 20.98  | Y    | Y       | Y       | Y       | Enlarged thyroid gland, hypervascularity | NA                      | Propanolol, diltiazem, ivabradine, thiamazole | Good response                          |
| 5   | Lee [15]      | F      | 46  | Adenovirus vectored | 1st  | 1           | 0.01   | 33.92 | Y       | Y       | Y       | Increased vascularity | Increased uptake (38.6%) | Methimazole | Hyperfunctioning diffuse goiter | Methimazole |
| 6   | Lee [15]      | F      | 73  | Adenovirus vectored | 2nd  | 14          | <0.008 | 73.8  | Y       | NA      | Y       | Increased vascularity | Increased uptake (54.2%) | Methimazole | Propanolol, prednisone (7 days) | Euthyroidism at 8 weeks |
| 7   | Lee [15]      | M      | 34  | Adenovirus vectored | 1st  | 14          | 26.61  | NA   | NA      | Y       | Y       | Increased vascularity | Increased uptake (13.8%) | Methimazole | Propanolol | Euthyroidism in 3 months, decreased anti-TSHr antibodies |
| 8   | Lee [15]      | M      | 39  | Adenovirus vectored | 1st  | 14          | <0.01  | 36.98 | NA      | NA      | Y       | Diffuse goiter, ill-defined, hypoechoic lesion in left lobe | Increased uptake | Methimazole | Propanolol | Euthyroidism in 3 months, decreased anti-TSHr antibodies |
| 9   | Sriphrapradang [26] | F      | 70  | Adenovirus vectored | 2nd  | 2           | 0.003  | 41.06 | NA      | NA      | Y       | Increased uptake | Increased uptake | Methimazole | Propanolol | Euthyroidism in 3 months, decreased anti-TSHr antibodies |
| 10  | Pujol [17]    | F      | 38  | mRNA            | 1st  | 12          | 0.008  | 25.87 | Y       | Y       | Y       | Diffuse hypoechogenicity, increased vascularity | Methimazole | Propanolol, diltiazem, ivabradine, thiamazole | Good response                          |
| 11  | Goblirsch [27] | F      | 71  | mRNA            | 2nd  | <0.01       | 92.68  | N     | N       | Y       | Y       | Multinodular goiter | Increased uptake (38.6%) | Methimazole | Propanolol, prednisone (7 days) | Euthyroidism at 8 weeks |
| 12  | Hamoache [28] | M      | 32  | mRNA            | 1st  | 22          | <0.005 | 69.63 | Y       | Y       | Y       | Heterogenous thyrois | Increased uptake (72%) | Methimazole, thiamazole | Propanolol, diltiazem, ivabradine, thiamazole | Good response                          |
| 13  | Lai [29]      | F      | 40  | mRNA            | 2nd  | 39          | <0.02  | 66.6  | Y       | Y       | Y       | Heterogenous echogenicity, increased vascularity | Diffuse markedly increased uptake | Methimazole, thiamazole | Propanolol | Improvement of thyroid function |
| 14  | Patrizio [30] | M      | 52  | mRNA            | 2nd  | 28          | <0.004 | 71.57 | Y       | ±       | Y       | Enlarged thyroid, heterogenous echotexture, increased vascularisation | Methimazole | Propanolol | Euthyroidism in 3 months, decreased anti-TSHr antibodies |
| 15  | Sriphrapradang [31] | F      | 30  | Adenovirus vectored | 3rd  | 4           | 0.006  | 16.6  | Y       | Y       | Y       | Methimazole | Methimazole | Hyperfunctioning diffuse goiter | Methimazole |
| 16  | Pierman [32]  | F      | 34  | mRNA            | 1st  | 10          | 0.01   | 32.69 | NA      | NA      | Y       | Goiter, increased vascularity | Methimazole | Thiamazole | Propanolol, potassium iodine, corticosteroid, furosemide, carvedilol | Euthyroidism in 3 months, decreased anti-TSHr antibodies |
| 17  | Yamamoto [33] | F      | 64  | mRNA            | 1st  | 4           | <0.008 | 42.73 | NA      | NA      | Y       | Goiter, increased vascularity | Methimazole | Thiamazole | Propanolol, potassium iodine, corticosteroid, furosemide, carvedilol | Euthyroidism in 3 months, decreased anti-TSHr antibodies |
| 18  | Di Filippo [34] | M      | 32  | Adenovirus vectored | 2nd  | 10          | 0.005  | 38.1  | Y       | Y       | Y       | Enlarged thyroid gland, hypervascularisation | Methimazole | Thiamazole | Propanolol, potassium iodine, corticosteroid, furosemide, carvedilol | Good clinical and hormonal response, normal anti-TSHr antibodies |
| 19  | Di Filippo [34] | M      | 35  | Adenovirus vectored | 1st  | 5           | <0.004 | 63.84 | Y       | Y       | Y       | Enlarged thyroid gland, hypervascularisation | Methimazole | Thiamazole | Propanolol, thiamazole | Good clinical and hormonal response, normal anti-TSHr antibodies |
| N° | Author (Ref) | Gender | AGE  | Type of vaccine | Dose | Time (days) | TSH  | FT4  | TPO-Ab | Tg-Ab | TSHr-Ab | Thyroid ultrasound, Colour flow Doppler | Thyroid scintigraphy | Treatment | Follow-up                        |
|----|-------------|--------|------|-----------------|------|-------------|------|------|--------|-------|---------|--------------------------------------|---------------------|-----------|----------------------------------|
| 20 | Pla Peris [19] | F | 71 | mRNA           | 2nd  | 60          | <0.005 | 29.6 | Y      | N      | Y      | Enlarged thyroid, increased vascularity | Diffuse markedly increased uptake | Methimazole | Decreased Ac anti-TSHr after 2 months |
| 21 | Pla Peris [19] | F | 42 | mRNA           | 1st  | <14         | <0.005 | 37.32 | N      | NA     | Y      | Enlarged thyroid, increased vascularity | Diffuse markedly increased uptake | Methimazole | Decreased Ac anti-TSHr after 2 months |
| 22 | Pla Peris [19] | F | 54 | mRNA           | 2nd  | <14         | <0.005 | 60.5  | Y      | Y      | Y      | Enlarged thyroid, increased vascularity | NA                             | Methimazole |                                     |
| 23 | Pla Peris [19] | F | 46 | mRNA           | 1st  | 50          | <0.005 | 41.19 | Y      | Y      | y      | Enlarged thyroid, increased vascularity | NA                             | Methimazole |                                     |
| 24 | Pla Peris [19] | F | 69 | mRNA           | 1st  | <14         | <0.005 | 23.17 | N      | N      | Y      | Enlarged thyroid gland, heterogeneous echogenicity, diffuse hypoechoic pattern | NA | Methimazole, non-steroidal antiinflammatory drugs |
| 25 | Raven [21]    | F | 35 | Adenovirus vectored | 1st  | 5           | <0.02  | 64    | Y      | Y      | Y      | Diffuse heterogeneous thyroid, marked increased vascularity | Carthimazole |                                     |
| 26 | Weintraub [35] | F | 38 | mRNA           | 1st  | 5           | <0.008 | 108   | Y      | NA     | Y      | Diffusely enlarged gland, heterogeneous echogenicity, increased vascularity | Methimazole, propanolol | Normal FT4 at 3 months |
| 27 | Weintraub [35] | F | 63 | mRNA           | 2nd  | 4           | 0.011  | 30.9  | Y      | NA     | Y      | Heterogeneous hypervascular thyroid gland | At 6 months: high radiotracer activity in both lobes, uptake at 24 h: 41% | No treatment |                                     |
| 28 | Weintraub [35] | M | 30 | mRNA           | 2nd  | 28          | <0.005 | 22.9  | N      | N      | Y      | Diffuse hyperplasia, increased vascularisation | Methimazole, atenolol | At 6 weeks, normal FT4, improvement of irritability and restless sleep |
| 29 | Oguz [23]     | F | 40 | mRNA           | 1st  | 2           | <0.015 | 27.92 | Y      | Y      | Y      | Diffuse hyperplasia, increased vascularisation | Diffusely increase radiotracer uptake | Methimazole | Not in remission                  |
| 30 | Oguz [23]     | M | 29 | mRNA           | 1st  | 15          | <0.015 | 12.15 | N      | N      | N      | Diffuse hyperplasia, increased vascularisation | 24-h RAIU: 27% | No treatment | Remission 10 weeks                |
| 31 | Oguz [23]     | F | 43 | mRNA           | 1st  | 9           | 0.015  | 33.1  | N      | N      | N      | Diffuse hyperplasia, increased vascularisation | 24-h RAIU: 61% | Methimazole | Not in remission                  |
| 32 | Oguz [23]     | F | 43 | mRNA           | 1st  | 14          | 0.01   | 25.5  | Y      | Y      | Y      | Diffuse hyperplasia, increased vascularisation | 24-h RAIU: 23% | Stop levothyroxine | Hypothyroidism at 20th week |

Age in years, Time in days, TSH in mU/L, and FT4 in pmol/l
Gender F female, M male, Y yes, N not present, TPO-Ab TPO antibody, Tg-Ab Tg antibody, TSHr-Ab TSH receptor antibody, NA not available
and hypothyroidism \((n = 1)\) after the second dose of vaccine. In thyrotoxic patients, mean free \(T4\) concentration is \(33.2 \pm 1.3\) pmol/L, lower than in patients with Graves’ disease or subacute thyroiditis \((p < 0.01)\). Four patients have anti-TPO or anti-thyroglobulin antibodies, and markedly decreased thyroid uptake at the thyroid scan is observed in all thyrotoxic patients. Thyrotoxic patients are followed with no medical treatment and euthyroid state is restored after 4 to 8 weeks, with transient subclinical hypothyroidism in one patient.

**Comments**

(a) Post-vaccination Graves’ disease was associated with mRNA or adenovirus-vectored type vaccines, while inactivated vaccine seems to be safe to induce Graves’ hyperthyroidism. Among several explanations (variable used doses, humoral-mediated and cell-mediated immunity response), one may be that mRNA and adenovirus-vectored type vaccines have higher immunogenicity than inactivated SARS-CoV-2 vaccine [38], and induce stimulatory anti-TSH receptor antibodies.

(b) The overall prevalence of thyroid-eye disease among patients with Graves’ disease is up to 40\% [39], but signs of thyroid-eye disease after Covid-19 vaccination are rare: one patient presents with a swelling of the eyelids [32], an active thyroid-eye disease is reported in a patient on chronic levothyroxine treatment for post-radioiodine hypothyroidism [40], and one patient develops moderate to severe ophthalmopathy after 10 weeks of medical treatment [27].

(c) Development of Graves’ disease and subacute thyroiditis may occur within a few days of the vaccination, suggesting that the patient had mild or subclinical autoimmune or inflammatory diseases that were aggravated by SARS-CoV-2 vaccines. On the other hand, rapid onset of symptoms is the time when the viral protein concentration reaches its peak in one or two days triggering an autoimmune response.

(d) Clinical course of focal painful thyroiditis may be mild [21], and symptoms related to subacute thyroiditis may be identified as being post-vaccination symptoms, and consequently the diagnosis of subacute thyroiditis may be overlooked.

(e) Co-occurrence of subacute thyroiditis and Graves’ disease is rare in the literature, but is observed in some patients following Covid-19 vaccination. Subacute thyroiditis at the inflammatory phase may release thyroid antigens with subsequent development of stimulatory TSH-receptor antibodies, promoting consequently the thyrotoxicosis of autoimmune hyperthyroidism [41, 42].

(f) At the thyrotoxic phase, free \(T4\) concentrations are higher in patients with Graves’ disease than in subacute thyroiditis, and hypothyroidism \((n = 1)\) after the second dose of vaccine.

Table 3: Clinical characteristics, laboratory results and imaging findings of patients with SARS-CoV-2 vaccine-induced chronic autoimmune thyroiditis

| N° | Author (Ref) | Gender | Age (yrs) | Type of vaccine | Dose | Time (days) | Neck pain | TSH (mU/L) | FT4 (pmol/L) | TPO-Ab | Tg-Ab | ESR (mm/h) | CRP (mg/L) | Thyroid ultrasound, Colour Doppler | Thyroid scintigraphy | Treatment | Follow-up |
|----|--------------|--------|-----------|----------------|------|-------------|-----------|------------|-------------|--------|--------|------------|------------|--------------------------------|----------------------|-----------|-----------|
| 1  | Leber [36]   | F      | 32        | Inactivated   | 2nd  | 1           | Y         | 13.2       | Normal      | Y         | Y      | 17         | 1          | Normal volume, mild hypoechogenicity, decreased vascularity | Markedly decreased thyroid uptake | Methylprednisolone for 5 days | Normal TSH after corticosteroid treatment |
| 2  | Lee [15]     | M      | 33        | Inactivated   | 1st  | 10          | N         | 0.012      | 37.4        | Y        | Y      | NA         | NA         | Heterogenous echogenicity, decreased vascularity | Decreased thyroid uptake | No treatment | No treatment |
| 3  | Pujol [17]   | M      | 32        | mRNA vectored | 1st  | 10          | NA        | 0.01       | 30.5        | Y        | Y      | NA         | NA         | Inflammatory process | Absence of uptake | No treatment | At 8 weeks: TSH = 116 mU/L Levelthyroxine |
| 4  | Siolos [16]  | F      | 39        | Adenovirus vectored | 1st  | 21          | N         | <0.03      | 20.47       | Y        | Y      | 17         | 1          | Markedly decreased thyroid uptake | Decreased thyroid uptake | No treatment | Euthyroid state at 8 weeks |
| 5  | Capezzone [37] | M      | 34        | mRNA         | 1st  | 7           | N         | 0.01       | 24          | Y        | Y      | 10         | 0.6        | Normal volume, mild hypoechogenicity, decreased vascularity | Decreased thyroid uptake | No treatment | Normal TSH after 4 weeks |
| 6  | Capezzone [37] | F      | 29        | mRNA         | 1st  | 7           | N         | 0.003      | 21.7        | Y        | Y      | NA         | NA         | Markedly decreased thyroid uptake | Decreased thyroid uptake | No treatment | Normal TSH after 4 weeks |

Age in years, Time in days, TSH in mU/L, and FT4 in pmol/L
thyroiditis \((p = 0.001)\) and in thyrotoxic patients after silent or painless autoimmune thyroiditis \((p < 0.001)\).

(g) In patients with autoimmune thyroiditis, the appearance of an episode of thyrotoxicosis within a few days of the first dose of vaccination may suggest that the patient had a (chronic) autoimmune thyroiditis which was aggravated by the SARS-CoV-2 vaccines, or that thyroid dysfunction may be mild or moderate, and consequently this diagnosis of painless or autoimmune thyroiditis may be overlooked.

(h) No relapses or exacerbation of symptoms or signs of thyrotoxicosis are observed in the majority of the patients with Graves’ disease or subacute thyroiditis after a repeated or a booster dose of SARS-CoV-2 vaccination [23].

Pathophysiological mechanisms of thyroid diseases after SARS-CoV-2 vaccines

SARS-CoV-2 vaccination may induce autoimmune and inflammatory thyroid dysfunctions, and may precipitate different forms of thyrotoxicosis (autoimmune hyperthyroidism or Graves’ disease, overt subacute thyroiditis and atypical autoimmune thyroiditis, or concurrence of subacute thyroiditis and Graves’ disease). Investigation is needed to clarify the etiology of the thyrotoxicosis in order to start adapted treatment or management. The underlying pathogenic mechanisms of SARS-CoV-2 vaccine-induced thyroid disorders are as yet unclear and are a subject of discussion:

(a) Molecular mimicry: Adenoviral-vectored and mRNA vaccines encode and inactivated whole-virus vaccines contain the SARS-CoV-2 spike protein, and various SARS-CoV-2 proteins (spike protein, nucleoprotein and membrane proteins) share a genetic similarity or homology with a large heptapeptide human protein including thyroid peroxidase peptide sequences [43]. Therefore, SARS-CoV-2 proteins in vaccines can cross-react with thyroid target proteins and cause autoimmune thyroid diseases. After polyclonal activation of B lymphocytes by vaccination, antibodies directed against SARS-CoV-2 proteins might cross-react with thyroid antigens located on the follicular cells of the thyroid, and may promote mitochondrial damage and cause thyroid dysfunctions. Therefore, molecular mimicry is a potential mechanism underlying the autoimmune reactions after SARS-CoV-2 vaccination, and has been proposed to cause autoimmune thyroid disorders such as Graves’ hyperthyroidism after SARS-CoV-2 vaccination.

(b) Autoimmune/inflammatory syndrome induced by adjuvants (ASIA): ASIA, described in 2011 by Shoenfeld and Agmon-Levin [44], is the consequence of the dysregulation of immune system following exposure to adjuvants. Adjuvants enhance the immunogenicity of vaccines, increase both innate and adaptive immune response, and can induce the formation of autoantibodies or localised/systemic inflammation. The SARS-CoV-2 vaccines contain several excipients such as aluminium hydroxide or aluminium salts (Coronavac vaccine), polysorbate 80 (Astra-Zeneca vaccine) or polyethylene glycol (PEG) lipid conjugates that stabilise the lipid nanoparticles and may act as adjuvants in mRNA vaccine (Pfizer BioNTech) and oil-in-water emulsion type that may trigger autoimmune or allergic reaction following SARS-CoV-2 vaccines. Autoimmune endocrine diseases such as type 1 diabetes mellitus, primary ovarian failure, adrenal insufficiency and autoimmune thyroid diseases have been reported to be related to ASIA syndrome after human papillomavirus, influenza, hepatitis B vaccination [45–50] and recently after Covid-19 vaccines.

(c) Genetic predisposition or susceptibility: despite a mass immunisation campaign against Covid-19 infection, thyroid adverse effects such as subacute thyroiditis, Graves’ disease and silent autoimmune thyroiditis appear to be rare, suggesting they are probably under-reported adverse effects of Covid-19 vaccines or are usually occurring with individual predisposition or genetic susceptibility. In genetically susceptible individuals, T lymphocytes are excessively sensitised to the TSH receptor antigen and vaccines, activating B lymphocytes, may produce and secrete autoantibodies against the TSH receptor and cause Graves’ hyperthyroidism [51, 52]. Moreover, molecular mimicry between human leucocytes antigen (HLA) genes and SARS-CoV-2 antigens can predispose individuals to Graves’ disease as SARS-CoV-2 products altering the HLA structure and function. On the other hand, certain types of HLA (HLA-B35) are considered for susceptibility to subacute thyroiditis, activation of the antigen-HLAB35 complex, leading to immune-mediated destruction of the thyroid follicular cells [53]. Interestingly, a report on two sisters who present subacute thyroiditis a few days after receiving a Covid-19 mRNA vaccine has been recently described [22], and the potential role of genetic predisposition remains to be investigated further. However, no potential risk factors (personal or familial autoimmune disease, pregnancy, postpartum) or predictors (smoking, stress, drugs, hypovitaminosis D) have been reported to have an influence on the occurrence of the majority of autoimmune or inflammatory thyroid diseases following SARS-CoV-2 vaccination.

Conclusion

Although the benefits of SARS-CoV-2 vaccination are undeniable and far outweigh the potential side effects, clinicians should be aware of possible autoimmune and inflammatory thyroid adverse effects following Covid-19 vaccination. Vaccination against SARS-CoV-2 should be
highly recommended, and it is the priority in the fight against Covid-19.

During this massive vaccination campaign, autoimmune and inflammatory thyroid diseases following vaccination with SARS-CoV-2 vaccines appear to be rare, but the potential cases are being reported more frequently. Clinicians can advise patients to seek medical assistance if they are experiencing anterior neck pain, fever or palpitations so that they are treated properly and in a timely fashion. Patients with prior personal or family history of autoimmune thyroid and non-thyroidal diseases may require post-vaccine monitoring and management.

Further clinical studies are warranted to clarify the clinical features, predisposing factors, clinical management and prevention of autoimmune and inflammatory thyroid diseases after SARS-CoV-2 vaccination. At the same time, further research is needed to investigate the etiopathogenesis of thyroid dysfunctions following vaccination against SARS-CoV-2.

Compliance with ethical standards
Conflict of interest The author declares no competing interests.

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