Subacute thyroiditis at the time of SARS-CoV-2 pandemic

Alessandro Brancatella\textsuperscript{1}, M.D., Nicola Viola\textsuperscript{1}, M.D., Grazia Rutigliano\textsuperscript{2}, M.D. PhD, Daniele Sgrò\textsuperscript{1}, M.D., Ferruccio Santini\textsuperscript{1}, M.D., Francesco Latrofa\textsuperscript{1}, M.D.

\textsuperscript{1}Endocrinology Unit, Department of Clinical and Experimental Medicine, University Hospital of Pisa, Pisa, Italy

\textsuperscript{2}Department of pathology, University of Pisa, Pisa, Italy

Corresponding Author:
Francesco Latrofa, M.D.
Endocrinology Unit I, Department of Clinical and Experimental Medicine, University Hospital of Pisa, Pisa, Italy. Phone +39050995001; Fax +39050996551; e-mail: francesco.latrofa@unipi.it

Disclosure summary
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Abstract

**Context.** Acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been related to subacute thyroiditis (SAT).

**Objectives.** To compare SAT cases at the time of SARS-CoV-2 pandemic to those observed in the previous years.

**Methods.** A cross-sectional, retrospective study was conducted at the Endocrinology Unit of University-Hospital of Pisa, Italy. We included all patients observed from January 2016 to December 2020 because of an untreated SAT, who had developed the disease within 15 days prior to the visit. SAT cases from 2016 to 2019 (N=152) are referred as “pre-SARS-CoV-2”, while 2020 SAT patients are classified as “pos-SARS-CoV-2” (N=18) or “neg-SARS-CoV-2” (N=28), according to positive or negative test for SARS-CoV-2 performed up to 45 days from SAT onset.

**Results.** While during the years 2016-2019 most SAT cases were observed in the 3rd quarter, in 2020 two peaks, superimposable to the outbreaks of SARS-CoV-2 pandemic of the 2nd and the 4th quarters, were seen. In the 2nd and the 4th quarters of 2020 we observed higher levels of free thyroxine (FT4), C-reactive protein (CRP) and thyroglobulin (Tg) compared to the same quarters of the years 2016-2019. Pos-SARS-CoV-2 had higher FT4 (28.4 vs 24.1 nmol/L), CRP (8.5 vs 3.6 mg/L) and Tg (155 vs 60 μg/L) (P<0.05 for all) and resulted more frequently in hypothyroidism (13/15 vs 30/152 at 3 months) (P<0.001) than to pre-SARS-CoV-2 patients. Neg-SARS-CoV-2 patients showed a clinical picture intermediate between the other two groups.

**Conclusions.** SARS-CoV-2 pandemic has caused a shift in the annual timing and severity of SAT cases.

**Key words:** SAT, thyroid dysfunction, viruses, thyroid, thyroiditis
Introduction

The viral or post viral origin of subacute thyroiditis (SAT) is suggested by direct evidence (i.e. identification of viruses in thyroid tissues) and mainly by epidemiological studies (i.e. the association between SAT and positive antibodies to specific viruses) (1). Most cases of SAT are reported in summer and fall, concomitantly with the spread of enteroviruses, coxsackieviruses and echoviruses (1–3). Given the self-limited course of the disease and the good response to anti-inflammatory treatment, the search for etiological viruses is not performed in clinical practice. The American Thyroid Association guidelines on the management of thyrotoxicosis and hyperthyroidism recommend that SAT treatment should be guided by its degree of severity, steroids being advised in patients with moderate to severe and NSAIDs in those with mild forms (4). In clinical practice the severity of SAT is established on symptoms and the levels of inflammatory markers as well as of FT4 and Tg. Furthermore, no study has ever evaluated whether the causative virus influence the severity of clinical presentation of SAT (1,2). In 2020, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged as a respiratory virus with a pandemic spread and millions people worldwide experienced coronavirus disease 2019 (COVID-19) (5,6). After our first report in May 2020 (7), several outpatients affected by SAT associated with SARS-CoV-2 infection have been described worldwide (8–10). In addition some studies showed a destructive, painless thyroiditis in patients hospitalized for severe COVID-19 (11,12).

Aim of the present study was to compare the features of SAT cases observed during the SARS-CoV-2 pandemic to those of SAT patients reported in previous years.
Methods

Study design and population

This was a retrospective, cross-sectional, observational study. From January 2016 to December 2020, 312 subjects were referred to the outpatient clinic of the Endocrinology Unit of University Hospital of Pisa, Italy, because of SAT. The diagnosis of SAT was based on clinical features (neck pain and systemic symptoms), laboratory tests (increased levels of free thyroxine - FT4, associated with decreased levels of thyroid stimulating hormone - TSH and inflammatory markers, i.e. C-reactive protein - CRP and erythrocyte sedimentation rate – ESR) and imaging features (diffuse hypoechoic areas and absent vascularization at neck ultrasound along with a reduced uptake at thyroid scintigraphy). We reviewed the charts of all patients with an untreated SAT who had developed the disease within 15 days prior to the visit and who had been evaluated at the Endocrinology Unit. Of the 312 SAT patients evaluated, some were excluded because lacking a full evaluation (n. 37), others because referred to us more than 15 days after the onset of SAT (n. 45), and others because already on anti-inflammatory drug (n. 32), leaving 198 patients included in the study. The results of laboratory tests and the findings of neck ultrasound were available in the whole cohort while those of thyroid scintigraphy in 54 patients only. During the follow-up thyroid function was tested every 15 to 90 days, according to the patient’s clinical status. The finding of TSH levels > 10 mIU/L with normal or low FT4 levels 3 months after the onset of SAT established the diagnosis of hypothyroidism. Data publication was approved by the local institutional review committee (Comitato Etico di Area Vasta Nord Ovest – CEAVNO). Patients gave their informed consent to participate in the study.

Classification of SAT according to SARS-CoV-2 status

Patients of the period January 2016 to December 2019 are referred as “pre-SARS-CoV-2”. Patients of 2020 are classified as “pos-SARS-CoV-2” or “neg-SARS-CoV-2”, according to the finding of a positive or negative test for SARS-CoV-2 infection within 45 days prior to the onset of SAT. SARS-CoV-2 diagnosis was based on nucleic acid amplification tests obtained on nasopharyngeal swab or measurement of class M and class G antibodies to SARS-CoV-2 by highly specific assays.

Data on deaths related to SARS-CoV-2 infection were obtained from the public records of the “Istituto Superiore di Sanità, Rome, Italy” (https://www.iss.it/coronavirus, accessed on February 2nd).
Laboratory exams

Thyroid hormones and TSH were tested using immunoenzymatic assays (Ortho-clinical diagnostic Inc., Rochester, NY). Reference ranges were 6-16 nmol/L for FT4, 2.3-4.2 pmol/L for free-triiodothyronine (FT3) and 0.4-4.5 mIU/L for TSH, respectively. Thyroglobulin (Tg) was measured by an immunometric assay (IMA) (Access Thyroglobulin assay; Beckman Coulter, Inc., Fullerton CA) (functional sensitivity 0.1 ng/ml) only in subjects showing thyroglobulin antibodies (TgAbs) below the interfering cut-off (see below). TgAbs were measured by a non-competitive IMA, Access Thyroglobulin Antibody (Tosoh Corporation, Tokyo, Japan); analytic, functional and positive cut-off were 6, 8 and 30 IU/mL respectively. In this assay TgAbs interfere with Tg measurement when their levels are ≥ 9.3 IU/mL (13). Thyroid peroxdyase antibodies (TPOAbs) were checked by AIA-Pack 2000 TPOAb (Tosoh Corporation, Tokyo, Japan) (positive cutoff > 10 IU/mL). TSH-receptor antibodies (TRAbs) were tested by ELISA (ElisaRSR™ TRAb 3rd generation, Cardiff, UK) (positive cutoff > 1.5 IU/mL). ESR and CRP were measured using standard methods (reference range < 15 mm/h and < 1.5 mg/L, respectively). IgM to SARS-CoV-2 were measured by anti-SARS-CoV-2 kit (CLIA, Roche) (positive cut-off > 0.1 AU/mL); IgG to SARS-CoV-2 were assessed by anti-SARS-CoV-2 kit (CLIA, Roche) (positive cut-off > 1.4 AU/mL) or by Liaison® SARS-CoV-2 S1/S2 IgG (Diasorin- Saluggia, Varese, Italy) (positive cut-off > 15 AU/mL).

Thyroid imaging

Neck ultrasound was performed by Technos (Esaote Biomedica, Genova, Italy), with a 7.5-MHz linear transducer. Thyroid volume was calculated using the ellipsoid volume formula.

Statistical analysis

Statistical data analysis was performed using SPSS 21 (IBM Corp., Armonk, NY). Data are presented as mean±SD or median with interquartile range (IQR), as indicated. The Shapiro-Wilk test was used to assess normality of data distribution of continuous variables. Statistical tests used to compare groups included Student’s t-test for normally distributed variables and Mann-Whitney U tests for variables with skewed distribution. The Kruskal-Wallis test or one-way analysis of variance (ANOVA) with post-hoc correction were also applied, depending on the distribution of variables. The
Chi-squared test or the Fisher exact test were used to compare counts and frequencies between groups for categorical variables, as appropriate.

Results

Features of study population

Features of the 198 patients included in the present study are summarized in Table 1. Most patients were female; mean age was 44.6 years. Neck pain was referred by all subjects and was bilateral in 48 patients, while fever was reported by 145 subjects. Fifty-six patients reported respiratory symptoms in the month preceding the onset of SAT. All subjects showed thyrotoxicosis, a high FT4/FT3 ratio and high levels of ESR, PCR and Tg. TgAbs and TPOAbs were positive, at low levels, in few patients whereas TRAbs were undetectable in the entire cohort. At neck ultrasound, most patients had an increased thyroid volume. All patients (n. 54) undergoing thyroid scintigraphy showed an absent or reduced uptake. Of 182 patients who were followed for at least 3 months, 57 developed hypothyroidism. Of the 46 patients evaluated in 2020, 18 were classified as pos-SARS-CoV-2 and 28 as neg-SARS-CoV-2. None of the 2020 patients had been previously hospitalized because of COVID-19.

Seasonal distribution of SAT and SARS-CoV-2 incidence

We observed a comparable number of SAT patients per year throughout the period 2016-2020 (40 in 2016, 34 in 2017, 43 in 2018, 35 in 2019 and 46 in 2020). However, seasonal distribution of SAT cases was different in the 2nd, 3rd and 4th quarters. Indeed, while in the 3rd quarter of the year they were more common in the years 2016-2019 compared to 2020 (68/152 vs. 6/46) (P=.01), both in the 2nd and the 4th quarters they were less frequent in the period 2016-2019 than in 2020 (31/152 vs. 16/46 in the 2nd, [P=.01] and 21/152 vs. 17/46 in the 4th [P=.03]) (Figure 1).

The two waves of SAT of 2020 were superimposable to the two peaks of SARS-CoV-2 deaths observed in Tuscany (Figure 1). It is worth noting that the number of SARS-CoV-2 deaths from January to March is probably underestimated because of the poor awareness of the disease during the initial phase of the pandemic.
Severity of SAT according to the quarters

The levels of FT4, CRP and Tg were similar across the quarters in the period 2016-2019 (Figure 2, Panels A-C).

Higher levels of FT4 were observed in SAT 2020 patients compared to SAT 2016-2019 patients in the 2nd (28.3 vs 23.7 nmol/L) (P<.001) and in 4th (31.6 vs 24.1 nmol/L) (P=.007) quarters but not in the 3rd quarters (23.9 vs 24.8 nmol/L) (P=0.1) (Figure 2, Panel A). The levels of CRP were higher in SAT 2020 patients in comparison to SAT 2016-2019 patients in the 2nd (7.9 vs 3.2 mg/L) (P<.001) and in the 4th (7.9 vs 3.6 mg/L) (P=.006) quarters and similar in 3rd quarter (4.1 vs 3.4 mg/L) (P=.63) (Figure 2, Panel B). Higher levels of Tg were retrieved in SAT 2020 patients as compared to SAT 2016-2019 patients in the 2nd (141 vs 90 μg/L) (P=.002) and in the 4th (153 vs 65 μg/L) (P=.01) quarters and similar in the 3rd quarter (78 vs 52 μg/L) (P=.12) (Figure 2, Panel C). The values of ESR in the 2nd quarter were also higher in SAT 2020 compared to SAT 2016-2019 (94 mm/h vs 48 mm/h, P<.001).

Clinical and laboratory features of pre-SARS-CoV-2, neg-SARS-CoV-2 and pos-SARS-CoV-2 patients

Comparisons between pre-SARS-CoV-2, neg-SARS-CoV-2 and pos-SARS-CoV-2 cohorts are reported in Table 2. Sex distribution was similar in the three groups, whereas mean age was lower in pos-SARS-CoV-2 than in pre-SARS-CoV-2 patients. Previous respiratory symptoms as well as bilateral (as opposite to unilateral) neck pain were more common in pos-SARS-CoV-2 patients compared to pre-SARS-CoV-2 and neg-SARS-CoV-2. Fever was more common in pos-SARS-CoV-2 compared to pre-SARS-CoV-2. FT4, FT3, ESR and Tg were higher in neg-SARS-CoV-2 than in pre-SARS-CoV-2 subjects. Pos-SARS-CoV-2 showed higher levels of FT4, FT3, ESR, CRP and Tg and lower levels of TSH compared to pre-SARS-CoV-2 subjects. Finally, compared to neg-SARS-CoV-2, pos-SARS-CoV-2 had higher CRP levels. Hypothyroidism at 3 months was more frequently diagnosed in pos-SARS-CoV-2 than in pre-SARS-CoV-2 and in neg-SARS-CoV-2 patients. At the end of follow-up (median 28 months), 92% of 2016-2019 SAT patients who developed hypothyroidism at 3 months were still hypothyroid. Twenty (9 pos-SARS-CoV-2 and 11 neg-SARS-CoV-2) of the 27 patients who were hypothyroid at 3 months were checked at 6 months and were all hypothyroid.
Discussion

Subacute thyroiditis, a thyroid disease of viral or post-viral origin, is characterized by neck pain and systemic symptoms, namely fever, asthenia and malaise, high levels of inflammatory markers and thyrotoxicosis (2,14). Many respiratory viruses, i.e. coxsackievirus, echovirus, rhinovirus and adenovirus have been associated with SAT by means of high titers of virus-specific antibodies or positive virus swabs, whereas studies based on virus culture from thyroid tissue yielded conflicting results (1). Furthermore, the association of SAT with viral outbreaks has been occasionally reported (3,15). The course of SAT is usually self-limited and responds excellently to anti-inflammatory treatment. Because specific antiviral treatment is not required, diagnostic tools aimed at identifying the etiological viruses are not routinely employed (1,2). In 2020 SARS-CoV-2, originated in Wuhan, China, spread quickly worldwide, emerging as the cause of a respiratory disease (COVID-19) of various severity degree (5,6). Other tissues may be also involved in SARS-CoV-2 infection (16,17). After our first report in May 2020 (7), several cases of SAT associated with SARS-CoV-2 infection have been described by our and additional groups (8–10,18–22). In order to investigate the effect of SARS-CoV-2 pandemic on the clinical picture of SAT, we performed a cross-sectional study which included the cases of SAT observed in the year 2020 and those observed in the years 2016-2019, prior to the SARS-CoV-2 pandemic.

The overall number of SAT cases referred to our Institution in 2020 was similar to that observed in each year of the period 2016-2019. Patients’ age and the female-to-male ratio of the 2020 cohort was also comparable to patients observed at our institution in the years 2016-2019 as well as to those described in previous studies (2,23). While, similarly to previous reports, most cases of SAT in years 2016-2019 occurred in the 3rd quarter (2,3), in 2020 most cases were recorded in the 2nd and 4th quarters, within a month from the two main SARS-CoV-2 outbreaks in Tuscany. It is likely that, in 2020, both social distancing and the face masks used in order to prevent SARS-CoV-2 pandemic had reduced the spread of other viruses.

By evaluating the severity of SAT, we observed that the levels of FT4, CRP, Tg and ESR in the period 2016-2019 were similar across the quarters and comparable to those reported in previous studies (2,23,24). The observation that the levels of FT4, CRP, Tg and ESR were significantly higher in SAT occurring in the 2nd and 4th quarters of 2020 suggests that the clinical picture of SAT induced by SARS-CoV-2 is more severe compared to that related to other viruses. In addition, compared to pre-SARS-CoV-2 patients, more pos-SARS-CoV-2 patients had experienced respiratory symptoms in the previous month and had bilateral (in comparison to unilateral) neck pain. Furthermore, compared to pre-SARS-CoV-2, pos-SARS-CoV-2 patients present with a more severe thyrotoxicosis and higher levels of inflammatory markers. Finally, more pos-SARS-CoV-2 patients than pre-SARS-CoV-2
patients experienced hypothyroidism. All these findings point to a higher severity of SAT cases induced by SARS-CoV-2 as compared to those previously observed, caused by other viruses.

Particularly noteworthy is the observation that, as pos-SARS-CoV-2, most neg-SARS-CoV-2 cases occurred in the 2nd and the 4th quarters of 2020. The clinical and biochemical features and the rate of evolution to hypothyroidism of these patients were intermediate between pre-SARS-CoV-2 and pos-SARS-CoV-2 subjects. Although not conclusive, some of these evidences suggest that these SAT cases were likely due to SARS-CoV-2 infections which had gone undiagnosed.

We did not observe a rise in total number of SAT in 2020 compared to the previous years, even though a large part of Tuscan population has been affected by SARS-CoV-2 infection. This indicates that only a small portion of subjects infected by SARS-CoV-2 experienced SAT and supports the notion that only predisposed people develop this disease (25). Moreover, our findings suggest that the severity of SAT and the risk of developing hypothyroidism is correlated with the causative virus.

In conclusion, our study demonstrates that SARS-CoV-2 pandemic, although not associated with a rise in the total number of SAT cases, has influenced the severity of the disease, leading to more severe forms of the disease.
Compliance with ethical standards

Conflict of interest

This research was supported by “Fondi di Ateneo 2019”, University of Pisa to Francesco Latrofa.

Informed consent

Written informed consent was obtained from the patients for publication of this study.

Contributorship statement

A.B. and F.L planned the study. A.B., N.V. and D.S. extracted the data. A.B. and G.R. performed the statistical analysis. A.B., F.S., and F.L wrote the manuscript. All authors discussed the results of the study.

Data availability statement

Some or all data generated or analyzed during this study are included in this published article or in the data repositories listed in References.
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Figure captions

Figure 1. Percentage distribution of cases of SAT in years 2016-2019 (white columns) and in 2020 (black columns) (Panel A). The absolute number of cases of deaths for SARS-COV-2 in 2020 in Tuscany is reported as solid gray curve. The dashed vertical line identifies each quarter. Data on deaths related to SARS-CoV-2 infection were obtained from the public records of the “Istituto Superiore di Sanità, Rome, Italy” (https://www.iss.it/coronavirus, access on February 2nd) *P<.05 between the two groups in the quarter.

Figure 2. Comparison of the median levels of FT4 (Panel A), CRP (Panel B) and Tg (Panel C) at the onset of SAT in the years 2016-2019 (N=152) and in the year 2020 (N=46). The dashed vertical line identifies each quarter. *P<.05 between the two groups in the quarter.
Table 1. Clinical, laboratory and imaging features of the entire cohort of SAT patients (n.198) evaluated in the years 2016-2020.

| Study Population (N=198)                          | Results                  |
|--------------------------------------------------|--------------------------|
| Sex                                              |                          |
| - Female (%)                                     | 167 (84)                |
| - Male (%)                                       | 31 (16)                 |
| Mean age (SD)                                    | 44.6 (± 12)             |
| Patients with respiratory symptoms prior to SAT onset (%) | 56 (28)                |
| Median time from respiratory symptoms to SAT (IQR) | 30 (28-45)              |
| Patients with bilateral neck pain (%)            | 48 (24)                 |
| Patients with fever (%)                          | 145 (73)                |
| Laboratory and imaging findings                  |                          |
| FT4 (IQR)                                        | 24.3 (4.6)              |
| FT3 (IQR)                                        | 5.8 (1.7)               |
| FT4/FT3 (IQR)                                    | 4.3 (1.2)               |
| TSH (IQR)                                        | 0.1 (0.2)               |
| ESR (IQR)                                        | 43 (45)                 |
| CRP (IQR)                                        | 3.8 (2.2)               |
| Tg (IQR)                                         | 69 (70)                 |
| Patients with positive TgAbs (%)                 | 62 (31)                 |
| - Median titer (IQR)                             | 65 (52)                 |
| Patients with positive TPOAbs (%)                | 27 (14)                 |
| - Median titer (IQR)                             | 35 (65)                 |
| Thyroid volume (IQR)                             | 22.3 (6)                |
| Scintigraphy                                     |                          |
| Activity                                | Count |
|----------------------------------------|-------|
| Absent/reduced uptake                  | 54    |
| Normal uptake                          | 0     |
| Not available                          | 144   |

### Treatment and follow-up

| Type of treatment (%)                 | Count (%)   |
|---------------------------------------|-------------|
| Steroids                              | 175 (89)    |
| NSAIDs                                | 15 (7)      |
| None                                  | 8 (4)       |

| Median duration of steroid treatment (days) (IQR) | Count (IQR) |
|--------------------------------------------------|-------------|
| Hypothyroidism at 3 months‡ (%)                  | 57 (29)     |

### SARS-CoV-2 status (Year 2020)

| Status                  | Count (%) |
|-------------------------|-----------|
| pos-SARS-CoV-2 (%)      | 18 (39)   |
| neg-SARS-CoV-2 (%)      | 28 (61)   |

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1 Measured in patients with TgAbs < 9.3 IU/mL (interfering cut-off); ‡ Evaluated in 182 subjects with a minimum follow-up of 3 months; SD=standard deviation; IQR=interquartile range; SAT=subacute thyroiditis; FT4= free thyroxine; FT3= free triiodothyronine; TSH= Thyroid-stimulating hormone; ESR= erythrocyte sedimentation rate; CRP=C-reactive protein; Tg= thyroglobulin; TgAbs= thyroglobulin antibodies; TPOAbs=thyroid peroxidase antibodies; NSAIDs= nonsteroidal anti-inflammatory drugs; SARS-CoV-2: severe acute respiratory syndrome virus 2. Normal ranges: FT4 6-16 nmol/L; FT3 2.3-4.2 pmol/L; TSH 0.4-4.5 mIU/L; ESR < 15 mm/h; CRP < 1.5 mg/L; Tg < 35 μg/L; TgAbs < 30 IU/mL (positive cut-off); TPOAbs < 10 IU/mL (positive cut-off).
|                          | Pre-SARS-CoV-2 N=152 | Neg-SARS-CoV-2 N=28 | Pos-SARS-CoV-2 N=18 | Overall P value | Pre-SARS-CoV-2 vs Neg-SARS-CoV-2 P value | Pre-SARS-CoV-2 vs Pos-SARS-CoV-2 P value | Neg-SARS-CoV-2 vs Pos-SARS-CoV-2 P value |
|--------------------------|----------------------|---------------------|---------------------|----------------|----------------------------------------|----------------------------------------|----------------------------------------|
| Sex                      |                      |                     |                     |                |                                        |                                        |                                        |
| Female (%)               | 130 (86)             | 19 (68)             | 18 (100)            | .11            | .38                                    | .12                                    | .43                                    |
| Male (%)                 | 22 (14)              | 9 (32)              | 0 (0)               |                |                                        |                                        |                                        |
| Mean age – (SD)          | 46 (± 9)             | 43 (± 14)           | 34 (± 14)           | .006           | .32                                    | <.001                                  | .08                                    |
| Respiratory symptoms    | 30 (20)              | 12 (43)             | 14 (78)             | <.001          | .008                                   | .01                                    | .01                                    |
| preceding SAT onset (%) |                     |                     |                     |                |                                        |                                        |                                        |
| Median time from         | 30 (15)              | 30 (18)             | 29 (12)             | .08            | .86                                    | .06                                    | .33                                    |
| respiratory symptoms to  |                     |                     |                     |                |                                        |                                        |                                        |
| SAT (IQR)                |                     |                     |                     |                |                                        |                                        |                                        |
| Bilateral neck pain (%)  | 21 (14)              | 11 (39)             | 16 (89)             | <.001          | .0025                                  | <.001                                  | .016                                   |
| Fever (%)                | 105 (69)             | 23 (82)             | 17 (94)             | .005           | .12                                    | .002                                  | .34                                    |
| FT4 (IQR)                | 24.1 (3.8)           | 26.9 (8.9)          | 28.4 (5.6)          | <.001          | .001                                  | <.001                                  | .29                                    |
| FT3 (IQR)                | 5.8 (1.88)           | 7.0 (2)             | 8.2 (1.6)           | <.001          | <.001                                  | <.001                                  | .13                                    |
| TSH (IQR)                | 0.1 (0.23)           | 0.02 (0.29)         | 0.01 (0.19)         | <.001          | .11                                    | .004                                  | .25                                    |
| ESR (IQR)                | 43.5 (29)            | 71.5 (49.8)         | 91 (25)             | <.001          | <.001                                  | <.001                                  | .06                                    |
| CRP (IQR)                | 3.6 (1.2)            | 5.3 (5.3)           | 8.5 (1.1)           | <.001          | .13                                    | <.001                                  | .005                                   |
| *Tg (IQR)                | 60 (40)              | 94.5 (27)           | 155 (150)           | <.001          | <.001                                  | <.001                                  | .45                                    |
| Thyroid volume (IQR)     | 22 (6)               | 23.3 (5.4)          | 22 (5)              | .37            | .45                                    | .58                                    | .39                                    |
| Treatment – (%)          |                      |                     |                     |                |                                        |                                        |                                        |
| Steroids                 | 135 (89)             | 24 (86)             | 16 (92)             | .54            | .61                                    | .39                                    | .53                                    |
| NSAIDs                   | 12 (8)               | 2 (7)               | 1 (0)               |                |                                        |                                        |                                        |
| None                     | 5 (3)                | 2 (7)               | 1 (8)               |                |                                        |                                        |                                        |
| Median duration (days)   | 90 (40)              | 90 (40)             | 85 (13)             | .28            | .43                                    | .29                                    | .54                                    |
| of steroid treatment     |                     |                     |                     |                |                                        |                                        |                                        |
| (IQR)                    |                     |                     |                     |                |                                        |                                        |                                        |
| Hypothyroidism at 3 months – (%) |       |                     |                     | <.001          | <.001                                  | <.001                                  | .01                                    |
Table 2. Comparison of clinical, laboratory and imaging features between pre-SARS-CoV-2, neg-SARS-CoV-2 and pos-SARS-CoV-2 cohorts

*Measured in patients with TgAbs < 9.3 IU/mL (interfering cut-off); ‡Established in the 21 subjects with a follow-up of 3 months; †Established in the 15 subjects with a follow-up of 3 months; SD=standard deviation; IQR=interquartile range; SAT=subacute thyroiditis; FT4= free thyroxine; FT3= free triiodothyronine; TSH= Thyroid-stimulating hormone; ESR= erythrocyte sedimentation rate; CRP= C-reactive protein; Tg= thyroglobulin; NSAIDs= nonsteroidal anti-inflammatory drugs; SARS-CoV-2: severe acute respiratory syndrome virus 2; NAATs= nucleic acid amplification tests; NS=not significative; NA=not applicable. Normal ranges: FT4 6-16 nmol/L; FT3 2.3-4.2 pmol/L; TSH 0.4-4.5 mIU/L; ESR < 15 mm/h; CRP < 1.5 mg/L; Tg < 35 µg/L.
Figure 2

A

B

C

FT4 (mmol/L)

CRP (mg/L)

Tg (mcg/L)

1st Quarter

2nd Quarter

3rd Quarter

4th Quarter

SAT 2016-2019

SAT 2020

*