



Could increased thiamazole sales among children in Belgium during the pandemic indicate a surge in Graves' disease cases?

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Abstract

Purpose This study aimed to assess the thiamazole sales in the paediatric population in Belgium from 2016 to 2023 in Belgium using the data provided by The National Institute for Health and Disability Insurance (NIHDI). It also assessed during the same period the number of pediatric patients diagnosed with pediatric AITD in a single-center setting.

Materials and methods We retrospectively analyzed data from the NIHDI national database, collecting the daily defined dose (DDD) and the number of pediatric patients treated with thiamazole. Additionally, a single-center study was conducted including children newly diagnosed HT or GD between January 1, 2016, and December 31, 2023. Patients were categorized into three groups: pre-pandemic (2016–2019), pandemic (2020–2022), and post-pandemic (2023).

Results An increase in thiamazole prescriptions was observed, peaking in 2022 (88,500 DDD/year for Group 2 vs. 77,295 DDD/year for Group 1, $p=0.001$). At our center, among the 43 newly diagnosed patients with GD, a significant rise in GD diagnoses was noted during the pandemic (10 cases/year) compared to the pre- and post-pandemic periods (3 cases/year, $p=0.037$). In contrast, the number of HT cases remained stable across all three periods, with a total of 141 patients. No significant differences in disease severity were found between patients diagnosed before or during the pandemic.

Conclusion Pediatric thiamazole prescriptions at the national level and GD diagnoses at the local level increased during the COVID-19 pandemic, while HT incidence remained unchanged. Although a direct causal link with SARS-CoV-2 cannot be confirmed, these findings suggest that the pandemic may have influenced GD incidence, warranting further investigation. Disease severity did not differ between patients diagnosed before and during the pandemic.

Keywords Graves' disease · Hashimoto thyroiditis · SARS-CoV-2 · Thiamazole · Children

Introduction

Hashimoto's Thyroiditis (HT) and Graves' Disease (GD) are the most common autoimmune thyroid diseases (AITD) in children [1], both showing a female predominance [2, 3]. The prevalence of HT varies between 1.0% and 2% [4, 5]. The overall incidence of GD in children and adolescents is around 4.58/100,000 per year, with a lower incidence of 1 to 2.91/100,000 per year in children before the age of 15 years

[6]. The etiopathogenesis of AITD is not fully understood, but it is known that these diseases result from a complex interaction between genetic background, environmental factors (e.g., iodine status, stress, gut microbiota), and the immune system [7]. Viral infections are considered the most significant trigger leading to autoimmune diseases in individuals with genetic susceptibility [8].

Since March 2020, the world has faced a pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). According to Sciensano, the seroprevalence of SARS-CoV-2 for adults donating blood in Belgium was 100% by the end of 2022 [9]. Similar seropositivity rates were reported in individuals under 18 years old.

The role of SARS-CoV-2 and its global spread in the development of autoimmune diseases has garnered significant attention within the scientific community [10–13]. Several cases of autoimmune endocrine diseases (such as type

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1 diabetes, HT and GD) have been described following a SARS-CoV-2 infection in adults.

Various mechanisms have been proposed to explain this potential association, including an increased production of inflammatory cytokines, which may damage the thyroid gland and expose thyroid antigens to the immune system; a cross-reaction between SARS-CoV-2 proteins (including the spike protein) and thyroid antigens such as TPO, triggering an autoimmune response; and the overexpression of angiotensin-converting enzyme 2 (ACE2) on thyroid follicular cells, a well-documented entry point for SARS-CoV-2 [14, 15].

In adults, several literature reviews have described cases of autoimmune thyroiditis, mainly Graves' disease, diagnosed after SARS-CoV-2 infection and an increased risk of Graves' disease and Graves' orbitopathy have been described following Covid-19 vaccination [16–18]. However, no study has been found describing the prevalence of AITD in adults during the pandemic. Furthermore, no study demonstrated a causal link between SARS-CoV-2 and the development of AITD, and no prospective studies on this subject have been carried out. A population-based registry study of the Austrian health insurance database showed that SARS-CoV-2 has no clinically significant impact on thyroid function, with stable prescription rate of thiamazole and levo-thyroxine over the period 2017–2021 [19].

Currently, limited pediatric data are available on AITD in the context of SARS-CoV-2, highlighting a significant gap in the literature [20].

The objective of the present study was to assess trends in the number of pediatric patients receiving thiamazole prescriptions before and during the SARS-CoV-2 pandemic, using data from the Belgian National Institute for Health and Disability Insurance (NIHDI). In parallel, we assessed the number of pediatric patients diagnosed with GD and with HT at our center during the same period.

Materials and methods

The study was conducted after approval by the Ethics Committee of Hôpital Universitaire des Enfants Reine Fabiola (CEH n° 101/23).

National data analysis

At the national level, we analyzed the Pharmanet data provided by the National Institute for Health and Disability Insurance from 2016 to 2023, focusing on the number of pediatric patients who received thiamazole per year. In Belgium, the NIHDI employs the WHO- Defined Daily Dose (DDD) to monitor and analyze medication consumptions,

including thiamazole. For thiamazole, the DDD is set at 10 mg per day. Data on the number of pediatric patients receiving thiamazole specifically became available as since 2018.

Single-center cohort

We included all patients aged 0 to 18 years newly diagnosed with GD or HT in the Pediatric Endocrinology Unit of HUDERF between January 1, 2016, and December 31, 2023.

The diagnosis of GD included:

- a suppressed or very low thyroid-stimulating hormone (TSH) level.
- an elevated free T₄ (fT₄) and/or free T₃ (fT₃) values.
- the presence of thyroid-stimulating immunoglobulins (TSI).

The diagnosis of HT was defined by the presence of anti-thyroid peroxidase (TPO) and/or anti-thyroglobulin (TG) antibodies, along with one of the following criteria:

- Elevated TSH levels (HT with hypothyroidism),
- The presence of a goiter on ultrasound despite normal TSH levels (euthyroidism),
- Suppressed TSH levels with elevated fT₄ and/or fT₃ levels (thyrotoxicosis).

Demographic data as well as clinical, biological, and ultrasound characteristics, the treatment and the disease progression were extracted from the electronic medical record.

Grouping and comparative analysis

Initially patients were classified into three groups based on the date of diagnosis, in order to analyze the number of cases per year.

- Group 1 (pre-pandemic): Patients diagnosed during the pre-pandemic period from 01/01/2016 to 31/12/2019;
- Group 2 (pandemic): Patients diagnosed during the pandemic period from 01/01/2020 to 31/12/2022;
- Group 3 (post-pandemic): Patients diagnosed during the post-pandemic period from 01/01/2023 to 31/12/2023;

All patients were included to describe the overall GD and HT cohorts. However, Group 3 was excluded from the comparative analysis, as it covered only one year, whereas Group 1 and Group 2 spanned four and three years, respectively.

Since HT patients were subdivided into three categories (hypothyroidism, euthyroidism, and thyrotoxicosis) and the

Fig. 1 The distribution of defined daily dose of thiamazole and the number paediatric patients receiving thiamazole in Belgium (data from Pharmanet NIHDI)

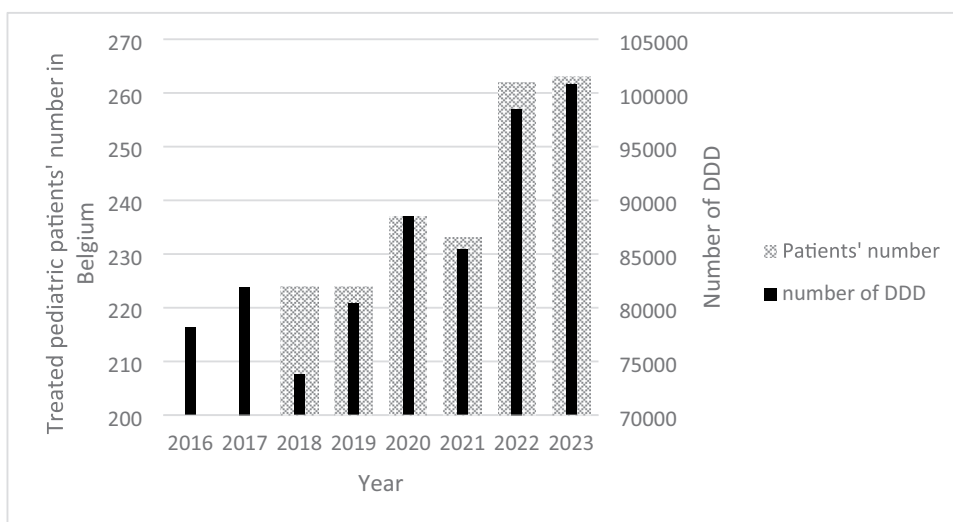


Table 1 Distribution of the number of paediatric patients treated with thiamazole and the daily defined dose (DDD) (data from the National Institute for health and disability insurance Data) by groups and the distribution of patients with AITD by diagnosis and groups at HUDERF

	Pre-pandemic (Group 1)	Pandemic (Group 2)	Post-pandemic (-Group 3)	P*
The National Institute for Health and Disability Insurance Data				
Median DDD/year (minimum-maximum)	79,295 (73,800–81,933)	88,500 (85,400–98,300)	100,800	0.001
Median Patients number/year** (minimum-maximum)	224 (224–224)	237 (233–262)	263	0.001
Graves-Basedow disease (GT), n	12	28	3	
Median GD diagnosis/year (minimum-maximum)	3 (2–4)	10 (6–12)	3	0.037
Hashimoto Thyroiditis (HT)	70	55	16	
Hashitoxicosis, n (%)	6 (8.5%)	4 (7.3%)	0	0.400
Euthyroid, n (%)	11 (15.7%)	14 (25.5%)	2	
Hypothyroidism, n (%)	53 (75.8%)	37 (67.2%)	14	
Median HT diagnosis /year (minimum-maximum)	18.5 (12–21)	18 (17–20)	16	0.583

*p between Group1 and Group 2; **data available from 2018 only

majority had hypothyroidism, comparisons between Group 1 (pre-pandemic) and Group 2 (pandemic) were restricted to hypothyroid patients.

Statistical analysis

The data were assessed for normality using the Shapiro-Wilk test. For normally distributed data, comparisons were made using the Student’s t-test, reporting the mean and standard deviation (SD). For non-normally distributed data, the median and interquartile range (IQR) were used, with comparisons conducted using the Wilcoxon test. For categorical variables, comparisons were made using the Chi-square test or Fisher’s exact test, as appropriate. A p-value < 0.05 was used as the threshold for statistical significance.

Results

National thiamazole prescription trends

The number of paediatric patients and the number of Defined Daily Doses (DDD) of thiamazole were higher in Group 2 (pandemic years: 2020–2022) compared to Group 1 (pre-pandemic years: 2016–2019), as shown in Fig. 1; Table 1. Specifically, 88,500 DDDs were recorded in Group 2 versus 79,295 in Group 1 (p=0.001). This increase peaked in 2022. These findings are illustrated in Fig. 1.

AITD diagnoses at the Single-Center level

Over the eight-year study period, a total of 182 pediatric patients were newly diagnosed with autoimmune thyroid disease (AITD) at our center. This cohort included 141 patients with Hashimoto’s thyroiditis (HT) and 43 patients

with Graves' disease (GD). Notably, two patients were diagnosed with both HT and GD (see Table 1).

The annual number of newly diagnosed HT cases remained relatively stable throughout the study period. In contrast, a noticeable increase in new GD diagnoses was observed during the pandemic years, with the highest number recorded in 2022 (Fig. 2).

When comparing across study periods, the median annual number of new GD diagnoses was significantly higher in Group 2 (pandemic period) compared to Group 1 (pre-pandemic period) ($p=0.037$). Additionally, the number of new GD diagnoses in Group 2 exceeded those in Group 3 (post-pandemic, 2023). In contrast, the number of new HT diagnoses did not differ significantly between the groups.

Graves' disease: comparative characteristics (Group 1 vs. Group 2)

The demographic, clinical, biochemical, ultrasound, and therapeutic characteristics of patients diagnosed with GD in Groups 1 and 2 are presented in Table 2. A statistically significant difference in median age at diagnosis was observed between the two groups. However, there were no significant differences in: presence of goiter or orbitopathy at diagnosis, free thyroxine (fT4) and free triiodothyronine (fT3) levels at diagnosis, the number of patients with markedly elevated fT4 levels (>75 pmol/L) and median thyroid-stimulating immunoglobulin (TSI) levels.

Hashimoto's thyroiditis with hypothyroidism: comparative characteristics (Group 1 vs. Group 2)

Among patients with HT presenting with hypothyroidism at diagnosis, clinical and biochemical characteristics from

Groups 1 and 2 are summarized in Table 3. As with GD, a significant difference was noted in the median age at diagnosis between the two groups, with a younger age at diagnosis in Group 1. However, other parameters were comparable across both groups.

Discussion

This is the first study to analyze health insurance data to assess thiamazole prescriptions specifically in the pediatric population during and around the pandemic years. Our findings demonstrate a significant increase in thiamazole prescriptions highlighting a unique trend that has not been previously reported in this age group. Additionally, we show that, in a single center, despite a stable number of total outpatient visits, there was an increase in the frequency of new GD diagnoses during the pandemic, whereas the incidence of new HT diagnoses remained unchanged. Potential diagnostic delay during the pandemic may have contributed to more advanced GD at presentation, potentially leading to higher thiamazole requirements or more severe laboratory findings at diagnosis. Nevertheless, in our cohort, we did not observe significant differences in fT4, fT3, markedly elevated fT4, or TSI levels between groups, suggesting that disease severity at presentation was not greater during the pandemic.

The annual number of pediatric patients receiving thiamazole peaked in 2022, coinciding with the pandemic. A similar number of patients were treated in 2023, likely reflecting the cumulative nature of prescription data, which does not distinguish newly diagnosed cases from those receiving ongoing treatment.

Fig. 2 Annual Distribution of new cases of Graves' Disease (GD), Hashimoto Thyroiditis (HT) and the number of consultations over the studied period at HUDERF, endocrinology department

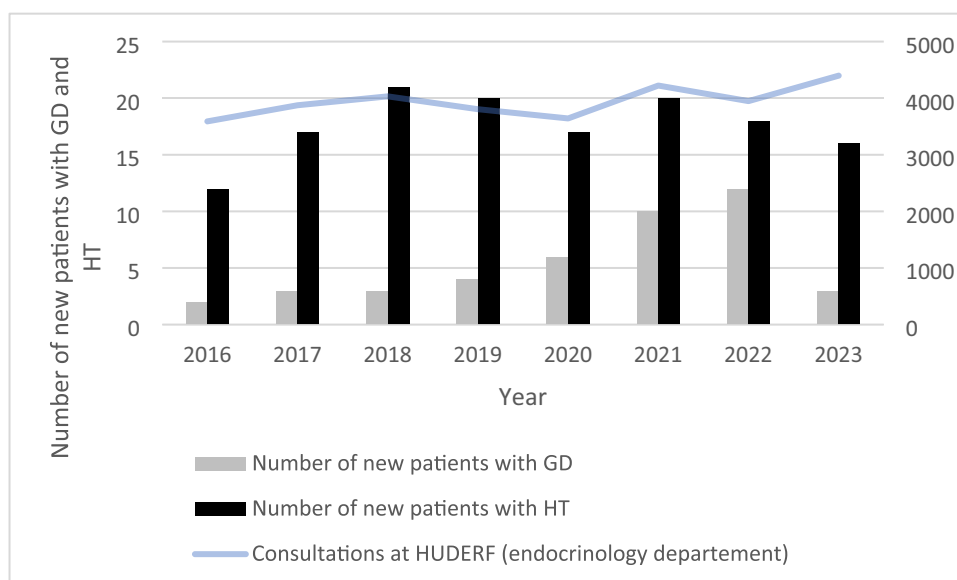


Table 2 Comparison of graves' disease patients: pre-pandemic and during the pandemic

	<i>n</i>	Pre-pandemic (group 1) 12	<i>n</i>	Pandemic (group 2) 28	<i>p</i> -value
<i>Demographical and clinical characteristics at diagnosis</i>					
Age, years (SD)	12	10.9 (2.9)	28	12.2 (2.7)	0.036
Sex F, n (%)	12	10 (83.3%)	28	25 (89.2%)	0.622
BMI SDS, (IQR)	11	0.3 (1.7)	26	0.0 (1.5)	0.500
Goiter at diagnosis, n (%)	11	9 (81.8%)	26	20 (76.9%)	0.900
Exophthalmia at diagnosis, n (%)	12	4 (33.3%)	28	10 (35.7%)	0.108
<i>Personal and familial history</i>					
Personal history of autoimmunity, n (%)	12	1 (0%)	28	1 (3.6%)	0.900
Familial history of autoimmunity, n (%)	12	1 (11.1%)	28	4 (14.2%)	0.900
Familial history of thyroid disease, n (%)	12	4 (33.3%)	28	17 (60.7%)	0.213
<i>Biology and ultrasound at diagnosis</i>					
fT ₄ , pmol/l (IQR)	12	53.2 (21.9)	28	45.5 (27.9)	0.500
fT ₃ , pmol/l (IQR)	7	27.5 (21.3)	24	23.3 (19.6)	0.500
T4I > 75, pmol, n (%)	12	1/12 (8.3%)	28	9/28 (32.1%)	0.230
TSI, U/L (IQR)	18	5.5 (4.0)	28	6.1 (10.9)	0.500
Goiter at ultrasound, n (%)	9	7 (84.6%)	23	18 (78.2%)	0.999
<i>Treatment and evolution</i>					
Dose of thiamazole at start, mg/kg/j (SD)	7	0.4 (0.1)	15	0.4 (0.2)	0.345
Use of beta-blockers, n (%)	12	4 (33.3%)	28	12 (42.8%)	0.729
Other treatment, n (%)	12	0 (0%)	28	2 (7.1%)	0.513
Block and replace therapy, n (%)	12	3 (25%)	28	5 (17.8%)	0.676
Dose of thiamazol when euthyroidism (mg/kg/j) (IQR)	14	0.1 (0.2)	17	0.1 (0)	0.500
Time to euthyroidism, months (SD)	14	4.0 (1.8)	17	6.2 (5.2)	0.134

Abbreviations: BMI- Body mass index; fT₄- Free thyroxine, fT₃- free triiodothyronine TSI- Thyroid stimulating immunoglobulin

Table 3 Comparison of Hashimoto thyroiditis patients with hypothyroidism: Pre-Pandemic and during the pandemic

	<i>n</i>	Group 1 (pre-pandemic) 53	<i>n</i>	Group 2 (pandemic) 37	<i>p</i> -value
<i>Clinical and demographical characteristics at diagnosis</i>					
Age, years (SD)	53	11.3 (2.8)	37	12.1 (2.3)	0.019
Sex F, n (%)	53	43 (81.1%)	37	29 (78.4%)	0.631
BMI SD (SD)	48	1.0 (1.1)	16	1.2 (1.1)	0.066
Goiter, n (%)	51	27 (52.9%)	36	23 (63.8%)	0.425
<i>Personal and familial history</i>					
Personal history of autoimmunity, n (%)	52	7 (13.5%)	37	6 (16.2%)	0.651
Familial history of autoimmunity, n (%)	52	8 (15.4%)	37	5 (13.5%)	1.000
Familial history of thyroid disease, n(%)	52	30 (57.7%)	37	21 (56.7%)	0.897
<i>Biology and ultrasound at diagnosis</i>					
Goiter at ultrasound, n (%)	41	25 (60.9%)	28	20 (71.4%)	0.425
TSH, mUI/l (IQR)	53	24.0 (63.8)	32	13.8 (116.4)	0.500
TSH > 100mUI/l, n(%)	53	9 (17.0%)	37	10 (27.1%)	0.439
fT ₄ , pmol/l (SD)	53	10.2 (3.9)	32	9.9 (4.2)	0.007
fT ₃ , pmol/l (SD)	17	5.1 (2.1)	13	5.2 (1.8)	0.168
anti-TPO antibodies, kUI/L (IQR)	31	379.5 (543.8)	23	491.5 (785.7)	0.500
anti-TG antibodies, kUI/L (IQR)	27	316.5 (457.7)	23	250.5 (897.5)	0.500
<i>Treatment and evolution</i>					
Levothyroxine dose at diagnosis, µg/kg (IQR)	48	1.0 (0.6)	34	1.0 (0.5)	0.900
Levothyroxine dose at euthyroidism, µg/kg (IQR)	26	1.40 (0.6)	16	1.30 (0.8)	0.680
Time until euthyroidism, months (IQR)	26	2.7 (3.2)	16	2.3 (2.3)	0.051

Abbreviations: BMI – Body mass index; anti-TG antibodies – Thyroglobulin antibodies; anti-TPO antibodies – Thyroid peroxidase antibodies; TSH – Thyroid-stimulating hormone

While previous studies have investigated the impact of the COVID-19 pandemic on thyroid function in the general population, our study is the first to focus on pediatric patients using health insurance data. Austrian authors analyzed similar data to assess the pandemic's effect on thyroid function but reported stable prescription rates for thyroid medications across all age groups [19]. Other studies also found no significant impact of the pandemic on the incidence of autoimmune thyroiditis in the general population [21]. In contrast, a single-center study in the general population reported that the annual number of GD cases remained stable between 2017 and 2020 but doubled in 2021 [22]. Additionally, Beiglböck et al. found that despite stable prescription rates of thyroid medications, there was an increase in patients experiencing thyroid storm during the pandemic years, while the incidence of myxedema coma remained unchanged [19].

Similarly, a population-based study in 22 million individuals in UK analyzing data from 2000 to 2019 (before the COVID-19 pandemic) reported an increase in GD incidence, particularly among older adults, while the incidence of HT remained stable [23]. This study provides robust evidence of socioeconomic, seasonal, and regional disparities for several autoimmune diseases (and specifically GD), implicating environmental factors in disease pathogenesis.

In adults, literature reviews, including those by Tatal et al. (covering cases published between December 2019 and October 2021) [16] and by Shinzato et al. (focusing on adult cases published between 2020 and early 2024) [18], documented cases of autoimmune thyroid diseases, mostly GD, diagnosed either concomitantly or within 7–90 days after SARS-CoV-2 infection. Interestingly, in this second review, some patients with known HT, developed GD after a SARS-CoV-2 infection. In our cohort, we also observed a patient with a HT diagnosed prior to pandemic, who developed GD during the pandemic.

A study conducted by Lui et al. on adult patients hospitalized for COVID-19 reported an increase in anti-thyroid antibodies (anti-TPO and anti-TG) three months after the infection [24]. We observed no difference in the anti-TPO and anti-TG antibodies (showed by the similar IQR in the groups) between the two groups (Group 1 and Group 2) (Table 3), but the distribution of TSI levels shows that several patients from Group 2 exhibit elevated TSI values compared to Group 1 (Table 2).

Few pediatric data are available in the literature. One study on the incidence of GD during the COVID-19 pandemic in pediatric patients has been published and shows an increase from 1.2% of newly diagnosed GD patients attending endocrinology consultations before the pandemic to 2.6% during the pandemic [25]. Our report also shows an increase in newly diagnosed GD cases during the pandemic,

although the total number of consultations at our clinic remained stable over the years.

Munarin et al. describes a higher rate of severe HT in pediatric patients during the pandemic, even if overall HT diagnoses were lower [5]. In our cohort 27.1% of patients in the pandemic group (Group 2) compared to 17.0% in the pre-pandemic group (Group 1) had TSH levels more than 100 mUI/l, but this difference was not significant. A delay in diagnosis could explain a more severe clinical picture at presentation.

We observed a higher median age at diagnosis for both GD and HT during the pandemic. This may reflect delayed presentation due to reduced access to care, although the total number of consultations in our clinic did not decrease during the pandemic. Changes in health-seeking behavior and chance variation cannot be excluded as alternative explanations. The increase in GD incidence during the pandemic is likely multifactorial. Stress is a well-recognized risk factor for GD, and children and adolescents were particularly exposed to unprecedented stress levels due to strict quarantine measures, school closures, and social isolation [28]. In addition, SARS-CoV-2 infection itself may have acted as a trigger for thyroid autoimmunity, as suggested in the literature [21]. Mechanistic evidence supporting this hypothesis was provided by Poma et al., who demonstrated activation of type I and type II interferon signaling pathways in thyroid tissue from patients dying of COVID-19 [26]. Finally, although pediatric vaccination was introduced late and only a small fraction of our patients were vaccinated, immune responses to vaccination may also contribute to thyroid dysfunction, as reported in systematic reviews and retrospective studies of post-vaccination thyroiditis [27–29]. Since vaccination coverage in Belgium reached 24.6% among 5–11-year-olds, 71.6% in 12–15-year-olds, and 82.3% in 16–17-year-olds by October 2022 (compared to more than 80% in adults) [9], SARS-CoV-2 vaccination cannot be excluded as a potential contributing factor in our cohort. The temporal peak of GD cases in 2022, as well as the older age at diagnosis observed in the pandemic group compared with the pre-pandemic group, could therefore be influenced not only by natural SARS-CoV-2 infection but also by the higher vaccination coverage in adolescents. In our study, however, vaccination status was only available for a minority of patients: 6 children had a documented SARS-CoV-2 infection prior to diagnosis and 2 had received vaccination. These numbers are insufficient to establish any causal relationship, but they highlight the difficulty of disentangling the respective roles of infection, vaccination, and indirect pandemic-related factors (e.g., stress, environmental changes, lifestyle modifications). Taken together, these observations support the interpretation that the increase in GD incidence likely arises from a multifactorial context

rather than from a single trigger. Our study highlights an increase in thiamazole sales in the pediatric population during the COVID-19 pandemic period. Concomitantly, we observed an increase in newly diagnosed cases of pediatric GD in our center, whereas the number of HT cases remained stable. These findings suggest a rise in new cases of GD, but not HT, during the pandemic. A strength of our study is the independent analysis of HT and GD, with GD data further supported by national health insurance records. However, its retrospective design limits the ability to establish a causal link between SARS-CoV-2 infection and the development of GD. Other pandemic-related factors, such as increased psychological stress, may also have contributed to this observed rise in GD incidence. Another limitation is that the number of patients was only available from 2018 onwards, while DDD data covered the entire period (2016–2023). Importantly, for DDD we observed statistically significant differences across the pre-pandemic, pandemic, and post-pandemic periods, supporting the robustness of this finding.

Future analyses extending the post-pandemic period over several years will be essential to determine whether the observed increase in GD persists beyond the immediate pandemic context. Such long-term follow-up will also help to disentangle the potential influence of COVID-19 vaccination, which was introduced late in children but may play a role in more recent years.

Our study provides the first pediatric-focused analysis of health insurance data, demonstrating an increase in thiamazole prescriptions in children in Belgium during the pandemic and a rise in GD diagnoses in our pediatric endocrinology unit during the same period. These findings emphasize the need for further research into the underlying factors contributing to this trend in the pediatric population. While a direct causal relationship between SARS-CoV-2 infection and the development of GD cannot be confirmed, pandemic-related factors such as increased psychological stress, delayed diagnosis, or environmental influences may have played a role and warrant further investigation.

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Author contributions All authors meet the ICMJE criteria for authorship, have approved the final version of the manuscript, and agree to be accountable for all aspects of the work. Fiorenza Ulgiati: conceptualization, data curation, formal analysis, investigation, methodology, validation, writing - original draft, and writing - review and editing; Alfredo Vicinanza: data curation, methodology, validation, and writing - review and editing; Claudine Heinrichs: data curation, methodology, validation, and writing - review and editing; Noha Diouri: data curation, investigation and formal analysis, validation; Sylvie Tenoutasse:

data curation, methodology, validation, and writing - review and editing; Cecile Brachet: conceptualization, data curation, formal analysis, investigation, methodology, validation, writing - original draft, and writing - review and editing; Emese Boros: conceptualization, data curation, formal analysis, investigation, methodology, validation, writing - original draft, and writing - review and editing.

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Data availability All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

Ethics approval This study protocol was reviewed and approved by the Ethics Committee of Hôpital Universitaire des Enfants Reine Fabiola, approval number 101/23. Given the retrospective nature of the study, written informed consent was not required.

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