Original Article

HEALTH SCIENCES
MEDICINE

DOI: 10.32322/jhsm.1326088
J Health Sci Med. 2023;6(5):948-953

The effect of COVID-19 vaccines on thyroid function and thyroid autoimmunity

Işılay Taşkaldıran[1], Feride Pınar Altay[1], Yusuf Bozkuş[1], Özlem Turhan İyidir[1], Aslı Nar[1], Nilüfer Bayraktar[2], Neslihan Başçıl Tütüncü[1]

[1]Department of Endocrinology and Metabolism, Faculty of Medicine, Başkent University, Ankara, Turkey
[2]Department of Medical Biochemistry, Faculty of Medicine, Başkent University, Ankara, Turkey

Cite this article as: Taşkaldıran I, Altay FP, Bozkuş Y, et al. The effect of COVID-19 vaccines on thyroid function and thyroid autoimmunity. *J Health Sci Med.* 2023;6(5):948-953.

Received: 13.07.2023 ◆ **Accepted**: 21.08.2023 ◆ **Published**: 28.09.2023

ABSTRACT

Aims: There have been reports about various thyroid autoimmune events after SARS-CoV-2 vaccinations. There is limited data on the extent to which vaccines for COVID-19 are effective on thyroid autoimmunity. This study investigates how COVID-19 vaccination affects thyroid antibodies and functions in individuals without any thyroid disease history.

Methods: The study evaluated individuals aged 18-65 with no previous COVID-19 history or thyroid disease who had at least two COVID-19 vaccine doses (CoronaVac + Pfizer-BioNTech or Pfizer-BioNTech alone) between October 2021 and October 2022. All participants' thyroid hormone (free triiodothyronine, thyroid-stimulating hormone, and free thyroxine) and thyroid autoantibody (anti-thyroglobulin, antithyroid peroxidase, and TSH receptor antibody) levels were measured.

Results: The study included 92 individuals in total. Thyroid functions and antithyroid antibody levels were found to be in the normal range before the implementation of the SARS-CoV-2 vaccine. Of the study participants, 42 received the Sinovac + BioNTech vaccine, and 50 received the BioNTech vaccine alone. While a decrease in st4 value was observed only in the BioNTech group after vaccination (p=0.007), thyroid dysfunction was not observed in any participant. After vaccination, TRAB positivity was observed in one participant, ANTI-TPO positivity in six participants, and ANTI-TG positivity in eight participants. No statistically significant antibody positivity was detected. No participants with antibody positivity displayed thyroid dysfunction.

Conclusion: Although some positivity in terms of antithyroid antibodies was observed after COVID-19 vaccination, this antibody positivity did not have a statistically significant level, and thyroid dysfunction was not detected in any participant. The COVID-19 vaccine is safe for thyroid function and autoimmunity.

Keywords: COVID-19, Sinovac, BioNTech, anti-thyroid peroxidase, anti-thyroglobulin, TSH receptor antibody

INTRODUCTION

The COVID-19 pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has severely impacted the entire world. With the COVID-19 pandemic causing serious mortality and morbidity, various types of vaccines were developed in a relatively brief period to protect against the disease.[1]

The rapid development of SARS-CoV-2 vaccines and rapid community vaccination has led to a decrease in the severity and spread of the disease. In addition to the tremendous social benefits offered by vaccination, some inflammatory and autoimmune side effects were also observed with vaccination, and these side effects were followed closely.[2]

Some cases reported following SARS-CoV-2 vaccination include various thyroid disorders related to autoimmune and inflammatory mechanisms, like Graves' disease, autoimmune hypothyroidism, and subacute thyroiditis.[3] In order to increase vaccine response, most vaccines contain adjuvants. They can also trigger autoimmune and inflammatory adverse effects in genetically predisposed individuals by activating autoimmune cascades.[4]

Currently, inactivated virus vaccine (CoronaVac) and the mRNA vaccine (BNT162b2) are administered in Turkey. However, there is limited data as to the effects of vaccines against COVID-19 on thyroid autoimmunity. To increase our knowledge on this subject, we evaluated

Corresponding Author: Işılay Taşkaldıran, dr.isilaymenekse@hotmail.com

thyroid antibodies and thyroid functioning following the implementation of COVID-19 vaccines in individuals without a previous history of autoimmune thyroid disease.

METHODS

The study was carried out with the permission of by Başkent University Non-interventional Clinical Researches Ethics Committee (Date: 17.11.2021, Decision No: 21/439). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. All the participants gave their written informed consent.

Volunteers aged 18-65 years who were admitted to Başkent University Faculty of Medicine Endocrinology and Metabolic Diseases Clinic between 01.10.2021 and 01.10.2022 were included in our study. The inclusion criteria in our study were the following: having serum thyroid autoantibodies tested before and obtaining a negative result, having been vaccinated against COVID-19, and having had the vaccination at least one and at most six months ago. The exclusion criteria included having a history of COVID-19 infection and a history of autoimmune thyroid disease, being currently on or having previously used thyroid hormone replacement or antithyroid medication, having pregnancy, having an active malignancy, receiving active chemotherapy, taking immunomodulatory drugs or tyrosine kinase inhibitors that may affect the thyroid function test, having another vaccination (such as human papillomavirus, influenza, pneumonia, and hepatitis B vaccination) in the last 6 months, serious active infection, radiation therapy to the neck and being on drugs that can alter thyroid function tests like amiodarone and steroids.

All the participants were tested for any of the thyroid autoantibodies before administering the first COVID-19 vaccine dose, and they were found to be negative. Moreover, they all displayed normal thyroid functioning in tests. The participants' demographic data and any information about their diseases, if any, were recorded. All the participants completed at least two COVID-19 vaccine doses as per the recommendations. Vaccines were administered to participants as CoronaVac (Sinovac) + Pfizer-BioNTech or simply Pfizer-BioNTech.

Blood was collected from all participants in order to measure the levels of free thyroxine (fT4), serum thyroid stimulating hormone (TSH), thyroid peroxidase antibody (anti-TPO), free triiodothyronine (fT3), TSH receptor antibody (TRAB), and thyroglobulin antibody (anti-TG). The levels of serum TSH, TRAB, fT3, and fT4 were measured using a chemiluminescent immunoassay using Abbott Alinity I (Abbott Diagnostic, IL, USA). Serum anti-TG and anti-TPO levels were detected using a chemiluminescent immunoassay with a Beckman Coulter Access 2 analyzer (Beckman Coulter Inc., CA, USA). The reference ranges were 0.35-4.94 mU/L, 0.7-1.48 ng/dl, and 1.58-3.91 ng/dl for TSH, fT4, and fT3, respectively. An anti-TPO level > 5.61 IU/ml, an anti-TG level >4 IU/ml, and a TRAB level >1.5 IU/L were considered positive.

Statistical Analysis

The study data were analyzed using IBM SPSS Statistics 25.0 package software (IBM Corporation, Armonk, NY, USA). The Kolmogorov-Smirnov test was implemented in order to determine whether continuous numerical variables had a normal distribution, and the Levene test was used to assess the homogeneity of variances. Continuous numerical variables were given as median (25^{th} percentile-75^{th} percentile) or mean±standard deviation. On the other hand, categorical variables were stated as the number of cases and as a percentage. Student's t-test was used to assess the significance of the variance between the groups with regard to mean values. In terms of continuous numerical variables for which the assumptions of parametric test statistics were not met, the significance of inter-group variance was investigated by the Mann-Whitney U test. When analyzing categorical data, the data analyzed were evaluated through Fisher's exact probability test in cases where at least 25% of the cells had an expected frequency of less than 5 in 2 × 2 cross tables. Furthermore, the $\chi 2$ test with continuity correction was implemented if the expected frequency was between 5-25. The Wilcoxon Sign test was implemented in order to find out whether the groups displayed statistically significant differences with regard to biochemical measurements before and after vaccination. Multivariate linear regression analysis was applied in order to ascertain whether the type of vaccine administered had a statistically significant modifying effect on post-vaccine anti-TPO measurements when adjusted for age, gender, and pre-vaccine anti-TPO measurements. For each variable, 95% confidence intervals and regression coefficients were calculated. A p-value of <0.05 was accepted as statistically significant unless stated otherwise. On the other hand, the Bonferroni correction was applied to inspect Type I errors in all possible multiple comparisons.

RESULTS

The study sample included 92 participants. Prior to the implementation of the SARS-CoV-2 vaccine, thyroid functions, and antithyroid antibody levels were found to be in the normal range. Among the sample, 42 received Sinovac + BioNTech, and 50 received BioNTech alone. The participants with Sinovac + BioNTech had a statistically significantly higher mean age than those with BioNTech

alone (p=0.009). The percentage of males was statistically significantly higher, and the percentage of females was statistically significantly lower in the Sinovac + BioNTech group than those with BioNTech alone (p=0.024). However, no statistically significant difference was detected between the groups concerning smoking history, obesity, concomitant diseases, autoimmune disease, and thyroid disease in the family (p >0.05) (Table 1).

Table 1. Demographic and clinical characteristics of the participants by groups

	Total (n=92)	Sinovac + BioNTech (n=42)	BioNTech (n=50)	p value
Age (years)	43.6±12.3	47.2±12.2	40.6±11.6	0.009†
Sex				0.024‡
Female	74 (80.4%)	29 (69.0%)	45 (90.0%)	
Male	18 (19.6%)	13 (31.0%)	5 (10.0%)	
Smoking	33 (35.9%)	16 (38.1%)	17 (34.0%)	0.850‡
Obesity	15 (16.3%)	8 (19.0%)	7 (14.0%)	0.712‡
Comorbidities				
Diabetes mellitus	20 (21.7%)	12 (28.6%)	8 (16.0%)	0.229‡
Hypertension	16 (17.4%)	10 (23.8%)	6 (12.0%)	0.225‡
Hyperlipidemia	6 (6.5%)	4 (9.5%)	2 (4.0%)	0.406¶
Coronary artery disease	2 (2.2%)	2 (4.8%)	0 (0.0%)	0.206¶
Chronic kidney disease	2 (2.2%)	1 (2.4%)	1 (2.0%)	>0.999¶
Family history of thyroid disease	31 (33.7%)	15 (35.7%)	16 (32.0%)	0.878‡
Autoimmune disease	12 (13.0%)	8 (19.0%)	4 (8.0%)	0.209‡

† Student's t-test, ‡ Continuity corrected $\chi 2$ test, ¶ Fisher's exact probability test.

The groups did not show any statistically significant difference with regard to TSH levels before and after vaccination (p=0.459, p=0.743, respectively). Pre-vaccine and post-vaccine TSH levels were similar in participants that had BioNTech alone and Sinovac + BioNTech (p=0.576, p=0.923, respectively). Finally, compared to pre-vaccination, the groups did not have any statistically significant difference regarding changes in the TSH level after vaccination (p=0.815) (Table 2).

The ST4 levels in the groups were not statistically significantly different before and after vaccination (respectively; p=0.377, p=0.952). The ST4 levels showed a statistically significant decrease after vaccination in participants with BioNTech alone (p=0.007). In participants who had Sinovac + BioNTech, pre- and post-vaccination ST4 levels were close (p=0.197). Finally, the study did not reveal any statistically significant difference between the study groups with regard to the change in ST4 levels following vaccination (p=0.490) (Table 2).

Regarding the pre-and post-vaccination anti-TPO levels, the groups showed no statistically significant differences (p=0.469, p=0.909, respectively). There was a statistically significant increase in anti-TPO levels following vaccination in participants who had BioNTech alone (p=0.010). In patients who had Sinovac + BioNTech, pre- and post-vaccination anti-TPO levels were statistically similar (p=0.993). Finally, no statistically significant differences were detected between the groups with regard to the change in anti-TPO levels following vaccination (p=0.153). When adjustments were made for age, gender, and pre-vaccination ANTI-TPO measurements, post-vaccination Anti-TPO levels remained higher in participants who had BioNTech alone compared to those with Sinovac + BioNTech (B=2.835, 95% CI: 0.034 - 5.635, p=0.047).

Table 2. Biochemical measurements according to groups and follow-up times

	Before vaccination	After vaccination	p value†	Changing
TSH				
Sinovac+Biontech	1.73 (0.912.48)	1.66 (0.89-2.74)	0.923	-0.03 (-0.36-0.42)
Biontech	1.85 (1.14-2.56)	1.44 (0.93-2.90)	0.576	-0.07 (-0.79-0.46)
p-value ‡	0.459	0.743		0.815
fT4				
Sinovac+Biontech	0.93 (0.78-1.03)	0.88 (0.82-0.93)	0.197	0.00 (-0.10-0.01)
Biontech	0.95 (0.87-1.04)	0.90 (0.81-0.93)	0.007	-0.05 (-0.14-0.04)
p-value ‡	0.377	0.952		0.490
Anti-TPO				
Sinovac+Biontech	0.69 (0.07-1.30)	0.55 (0.30-0.90)	0.993	0.00 (-0.63-0.50)
Biontech	0.40 (0.20-1.00)	0.60 (0.30-1.00)	0.010	0.01 (-0.10-0.52)
p-value ‡	0.469	0.909		0.153
Anti-TG				
Sinovac+Biontech	0.90 (0.90-0.90)	0.90 (0.90-0.90)	0.892	0.00 (0.00-0.00)
Biontech	0.90 (0.90-0.90)	0.90 (0.90-0.90)	0.225	0.00 (0.00-0.00)
p-value ‡	0.714	0.389		0.512

Descriptive statistics were expressed as the median (25th percentile-75th percentile). † These results were considered statistically significant for $p < 0.025$, according to the Wilcoxon sign test, the Bonferroni correction, and between pre- and post-vaccination comparisons within the groups. ‡ For comparisons made within each follow-up time, the results were considered statistically significant for $p < 0.025$, according to the Mann-Whitney U test and the Bonferroni correction. For comparisons of changes following vaccination, the result was considered statistically significant if $p < 0.05$.

The pre- and post-vaccination anti-TG levels were not statistically significantly different in the groups (p=0.714, p=0.389, respectively). The pre- and post-vaccination anti-TG levels were statistically similar in participants who had BioNTech alone and participants who had Sinovac + BioNTech (p=0.225, p=0.892, respectively). Finally, as shown in Table 2, there were no statistically significant differences between the groups regarding the change in anti-TG levels following vaccination (p=0.512).

According to Table 3, the BioNTech group and Sinovac + BioNTech group did not show any statistically significant difference with respect to the percentage of individuals positive for Anti-TG, TRAB, and Anti-TPO after vaccination (p > 0.999, p=0.457, and p=0.684, respectively).

Table 3. Comparison of the two groups in terms of post-vaccination Anti-TPO, Anti-TG, and TRAB positivity

	Sinovac+Biontech (n=42)	Biontech (n=50)	p value†
Anti-TPO positivity	2 (4.8%)	4 (8.0%)	0.684
Anti-TG positivity	4 (9.5%)	4 (8.0%)	>0.999
TRAB positivity	1 (2.4%)	0 (0.0%)	0.457

† Fisher's exact probability test.

DISCUSSION

There have been numerous reports of the development of case-base autoimmune thyroid disease after COVID-19 vaccination. However, there are a minimal number of studies on the risk of developing autoimmune thyroid disease following vaccination against COVID-19. This study investigated the changes observed in thyroid function and antithyroid antibodies after COVID-19 vaccination in people without a history of thyroid disease.

Our study observed no overt thyroid dysfunctions following either type of COVID-19 vaccine (BNT162b2 and CoronaVac). There were no significant changes in post-vaccination TSH levels. While the group that received BioNTech alone showed a statistically significant decrease in the st4 levels, in general, the st4 levels did not differ statistically significantly following vaccination across the groups. Although TRAB positivity was observed in one participant, anti-TG positivity in four participants, and anti-TPO positivity in six participants following vaccination, all the patients were euthyroid. In addition, thyroid antibody positivity was not found to be statistically significant. Our results showed no clinically significant thyroid autoimmune disease due to COVID-19 vaccination.

In a recent study conducted on 72 healthy people in Greece, although a slight decrease was observed in values of TSH, total triiodothyronine (T3), and total thyroxine (T4) after vaccination with BioNTech for COVID-19, all values were within normal limits, and no thyroid dysfunction was observed.[5] In another study involving 215 people in China, after COVID-19 vaccination (60% BNT162b2; 40% CoronaVac), TSH values did not change, but fT4 slightly increased and fT3 slightly decreased. Abnormal thyroid function was observed in only three patients after vaccination, and none of these were clinically overt.[6] Also, in a prospective study conducted in China, 36 (6.38%) of 564 individuals who participated in the study with normal thyroid function at baseline developed thyroid dysfunction following the implementation of the COVID-19 vaccine (BBIBP-CorV and CoronaVac).[7] As a result, our study is concordant with the literature, and we can state that no clinically significant thyroid dysfunction developed after vaccination with both CoronaVac and BioNTech.

In a recent prospective study conducted in China, none of the 545 recipients who were negative for antithyroid antibodies before vaccination developed an abnormal antibody result following COVID-19 vaccination.[7] In another study in China, after BNT162b2 and CoronaVac vaccines were administered to 215 participants, anti-Tg and anti-TPO titers moderately increased following vaccination, but anti-TPO/Tg positivity did not show any statistically significant difference. A greater increase in anti-TPO titer was observed after BNT162b2.[6] Another study evaluated the TRAB levels of 231 Graves' patients after administering the inactivated COVID-19 vaccine. Increasing TRAB levels were detected following vaccination.[8] In our study, some participants were positive for some of the thyroid autoantibodies, but this antibody positivity was not statistically significant, and thyroid dysfunction was not detected in any participants.

Although at least 5 billion people were vaccinated against COVID-19 until Dec 21, 2022,[9] post-vaccine thyroid-related autoimmune and inflammatory diseases have only been reported on a case-by-case basis. Since vaccination is widespread worldwide, the possibility of coincidental occurrence of these detected thyroid cases within a period should not be ignored.

In a review of COVID-19 post-vaccination thyroid autoimmune inflammatory diseases, 52 cases of subacute thyroiditis, 22 cases of Graves', and six cases of silent thyroiditis were reported after vaccination. The mean age was 45-46 years, and the symptoms started in an average of 9-15 days. Most of the patients were women.[10] Similarly, another case series presentation reported one subacute thyroiditis, one Graves' disease, and one silent thyroiditis case after COVID-19 vaccination.[3] Two cases of Graves' disease and one case of hypothyroidism were reported in another case series after the COVID-19 vaccination. It was stated here that these patients had a family history of thyroid disease, and it was reported that the family

history could be a sign of genetic predisposition.[11] Similarly, in the case series of 51 patients evaluated for post-COVID-19 thyroid autoimmune conditions, the majority of the cases were Graves' patients, female, and did not have a pre-existing thyroid disease.[11]

Among our participants, when those with positive post-vaccination antibody titers were examined individually, it was found that one participant with TRAB positivity was a female with a family history of thyroid disease, and anti-TPO positivity was found in a total of six participants who were all female. Moreover, four of them had a history of thyroid disease in their families. Of the eight participants who were found to be anti-TG positive, seven were female, and half had a family history of thyroid disease. Based on these findings, it can be suggested that females and those with a family history of thyroid disease may be at a higher risk for post-vaccination thyroid autoimmunity.

It is thought that the adjuvants in the vaccines affect thyroid autoimmune and inflammatory events that develop after COVID-19 vaccination.[11,12] It is possible to find adjuvants in various types of vaccines, and they are utilized to augment the vaccination response. Events involving various autoimmune conditions due to adjuvants were defined as autoimmune/inflammatory syndrome (ASIA) by Shoenfeld and Agmon-Levin in 2011.[13] Aluminum is one of the most commonly used adjuvants in vaccines. Aluminum increases proinflammatory cytokines by affecting the immune system itself.[14] In addition, adjuvants can cause ASIA by affecting the immune balance and triggering the activation of B lymphocytes in genetically predisposed individuals, leading to a wide variety of autoimmune events, including autoimmune thyroid disease.[14,15]

Previous studies have obtained data showing that vaccines other than those against COVID-19 also affect thyroid autoimmunity. Among the studies performed, thyroid autoimmune events have also been reported following vaccinations against human papillomavirus (HPV), Hepatitis B, influenza, and Bacille Calmette-Guerin (BCG). However, these reported cases did not hinder the benefit of vaccination, and whether these side effects developed purely by chance over time has been an issue of debate.[16-19]

Our study had certain limitations. One of these was that the pre-vaccination anti-TPO levels of all the participants were measured, but this was not the case for anti-TG and TRAB levels. In addition, long-term thyroid function tests of participants with positive antibody titers were unavailable. In addition, only those without pre-existing thyroid disease were included in the study. How vaccination affects people with a history of thyroid disease and those who use thyroid medication could not be evaluated. Finally, COVID-19 PCR or IgG testing was not performed to exclude asymptomatic COVID-19 cases before the study was included in the study.

CONCLUSION

COVID-19 vaccination resulted in a statistically insignificant rate of positivity in antithyroid antibodies. However, there was no clinical reflection of this positivity, and none of the participants showed any clinically significant thyroid dysfunction. Our results demonstrate that COVID-19 vaccination does not have a severe clinical side effect on the thyroid. COVID-19 vaccination can proceed safely concerning thyroid autoimmunity.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of by Başkent University Non-interventional Clinical Researches Ethics Committee (Date: 17.11.2021, Decision No: 21/439).

Informed consent: All patients signed and free and informed consent form.

Referee Evaluation Process: Externally peer reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study was funded by the Başkent University Faculty of Medicine, Ankara, Turkey.

Author Contributions: All the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Yan ZP, Yang M, Lai CL. COVID-19 Vaccines: a review of the safety and efficacy of current clinical trials. *Pharmaceuticals (Basel).* 2021;14(5):406.
2. Akinosoglou K, Tzivaki I, Marangos M. Covid-19 vaccine and autoimmunity: awakening the sleeping dragon. *Clin Immunol.* 2021;226:108721.
3. Pujol A, Gómez LA, Gallegos C, et al. Thyroid as a target of adjuvant autoimmunity/inflammatory syndrome due to mRNA-based SARS-CoV2 vaccination: from Graves' disease to silent thyroiditis. *J Endocrinol Invest.* 2022;45(4):875-882.
4. Shoenfeld Y, Agmon-Levin N.' ASIA' - autoimmune/inflammatory syndrome induced by adjuvants. *J Autoimmun.* 2011;36(1):4-8.
5. Paschou SA, Karalis V, Psaltopoulou T, et al. Patients with autoimmune thyroiditis present similar immunological response to COVID-19 BNT162b2 mRNA vaccine with healthy subjects, while vaccination may affect thyroid function: a clinical study. *Front Endocrinol (Lausanne).* 2022;13:840668.
6. Lui DTW, Lee CH, Cheung CYY, et al. Effect of COVID-19 vaccines on thyroid function and autoimmunity and effect of thyroid autoimmunity on antibody response. *J Clin Endocrinol Metab.* 2022;107(9):e3781-e3789.

7. Li L, Chen X, Li B, et al. Effect of inactivated SARS-CoV-2 vaccine on thyroid function and autoimmunity within 28 days after the second dose. *Thyroid.* 2022;32(9):1051-1058.
8. Huang L, Jiang Z, Zhou J, Chen Y, Huang H. The effect of inactivated SARS-CoV-2 vaccines on TRAB in Graves' disease. *Front Endocrinol (Lausanne).* 2022;13:835880.
9. WHO. Coronavirus (COVID-19) Dashboard. Available online: https://covid19.who.int/
10. Caron P. Autoimmune and inflammatory thyroid diseases following vaccination with SARS-CoV-2 vaccines: from etiopathogenesis to clinical management. *Endocrine.* 2022;78(3):406-417.
11. Ruggeri RM, Giovanellla L, Campennì A. SARS-CoV-2 vaccine may trigger thyroid autoimmunity: real-life experience and review of the literature. *J Endocrinol Invest.* 2022;45(12):2283-2289.
12. Huang L, Jiang Z, Zhou J, Chen Y, Huang H. The Effect of inactivated SARS-CoV-2 vaccines on TRAB in Graves' disease. *Front Endocrinol (Lausanne).* 2022;13:835880.
13. Watad A, David P, Brown S, Shoenfeld Y. Autoimmune/inflammatory syndrome induced by adjuvants and thyroid autoimmunity. *Front Endocrinol (Lausanne).* 2017;7:150.
14. Ruiz JT, Lujan L, Blank M, Shoenfeld Y. Adjuvants- and vaccines-induced autoimmunity: animal models. *Immunol Res.* 2017;65(1):55-65.
15. Bragazzi NL, Hejly A, Watad A, Adawi M, Amital H, Shoenfeld Y. ASIA syndrome and endocrine autoimmune disorders. *Best Pract Res Clin Endocrinol Metab.* 2020;34(1):101412.
16. Siegrist CA, Lewis EM, Eskola J, Evans SJ, Black SB. Human papilloma virus immunization in adolescent and young adults: a cohort study to illustrate what events might be mistaken for adverse reactions. *Pediatr Infect Dis J.* 2007;26(11):979-984.
17. Yu O, Bohlke K, Hanson CA, et al. Hepatitis B vaccine and risk of autoimmune thyroid disease: a vaccine safety datalink study. *Pharmacoepidemiol Drug Saf.* 2007;16(7):736-745.
18. Hernán Martinez J, Corder E, Uzcategui M, Garcia M, Sostre S, Garcia A. Subacute thyroiditis and dyserythropoesis after influenza vaccination suggesting immune dysregulation. *Bol Asoc Med P R.* 2011;103(2):48-52.
19. Dow CT. Proposing BCG Vaccination for *Mycobacterium avium* ss. paratuberculosis (MAP) associated autoimmune diseases. *Microorganisms.* 2020;8(2):212.