Safety of an Inactivated SARS-CoV-2 Vaccine Among Healthcare Workers in Turkey: An Online Survey

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Background: As vaccination against coronavirus disease-19 (COVID-19) evolves, hesitancy has become a problematic issue that has gradually spread worldwide. The main reason for vaccine hesitancy is uncertainties about vaccine side effects.

Aims: To evaluate the safety of an inactivated COVID-19 vaccine, CoronaVac, and determine the risk factors of emergence of side effects.

Study Design: Cross-sectional study.

Methods: An online questionnaire was administered via the internet to healthcare workers who received one or two doses of CoronaVac. The online survey consisted of three sections detailing sociodemographic data, COVID-19 history, and post-vaccine side effects. Side effects that occurred in the period starting from immediately after the first vaccination to the end of the 14th day after the second vaccination were recorded.

Results: A total of 1628 healthcare workers responded to the online survey. Of these, 24.3% had a side effect either after the first or second dose of CoronaVac. Redness and/or pain at the inoculation site, headache, muscle and joint pains, palpitations, and dizziness were the most common side effects. Female sex, age <50 years, and thyroid disorder in the pre-vaccine period were found to be risk factors for the emergence of side effects. Blood pressure control could not be achieved in 2.2% of participants despite medication use, and permanent medication was needed in 2.5% of participants for blood pressure control.

Conclusion: Almost a quarter of healthcare workers have at least one side effect after the first or second dose of CoronaVac. Female gender, age <50 years, and thyroid disorder appear to be risk factors for the occurrence of side effects.
vaccine usefulness and safety, started to be observed.\textsuperscript{3} Vaccine hesitancy remains a barrier to full population inoculation against highly infectious diseases. Coincident with the rapid developments of COVID-19 vaccines globally, concerns about the safety of such a vaccine could contribute to this problem. Perhaps, the most important factor in vaccine hesitancy is speculated side effects, defined as any adverse medical event that occurs after vaccination, which is thought to be due to the vaccine.

Even though there are few publications on inactivated vaccines, current data shows that they are tolerably safe.\textsuperscript{4} The reported side effects are usually local or mild–moderate such as fever, fatigue, headache, and pain/redness at the injection site. Moreover, various vaccine-related side effects that were not reported in phase trials appeared in real life.

Therefore, this study aimed to describe the side effects of CoronaVac and to determine potential risk factors for side effects in order to prevent vaccine hesitancy with reliable real-world data.

**MATERIALS AND METHOD**

**Study Design and Participants**

This is a cross-sectional study, approved by the local institutional ethics committee (2021/112). An online questionnaire was administered via internet to healthcare workers. An informed consent statement was required to be checked in at the beginning of the questionnaire. All procedures performed involving human participants were in accordance with ethical standards of the hospital, national research committee, and the 1964 Helsinki Declaration. A restriction was set in the online survey link such that an IP address could only be used to fill out the questionnaire once to avoid repeating questionnaire. We performed a logic check and corrected any non-logical data.

Healthcare workers who are familiar with the recognition of side effects and more willing to contribute to scientific literature, aged over 18 years, and received one or two doses of CoronaVac voluntarily responded to the online questionnaire between June and August 2021. The respondents came from seven geographical regions of Turkey and the Turkish Republic of Northern Cyprus and were categorized due to NUTS-1: the first level of Nomenclature of the Territorial Units for the Statistics system. The participants received no financial incentive.

Booster vaccination with an mRNA vaccine was not an exclusion criterion; however, only side effects that occurred after CoronaVac administration were asked for evaluation. Side effects that occurred from the time of the first vaccination until 14 days after the second dose were recorded.

**Variables and Measurement**

The online survey consisted of three sections detailing sociodemographic data, COVID-19 history, and post-vaccine side effects. Sociodemographic data included age, sex, and occupational and medical history. In the second part of the questionnaire, questions such as whether the participants had COVID-19, defined as either polymerase chain reaction (PCR) positivity or a negative PCR result with appropriate radiological findings in the pre-vaccine period, and the severity were recorded. In the third part, we collected information about side effects that occurred in the period starting from immediately after the first vaccination to the end of the 14th day after the second vaccination. In addition, detailed data were collected on blood pressure changes that were observed after and thought to be related to the vaccination, and interventions to control blood pressure were administered.

**Outcomes**

The participants were asked to respond to appropriate questions according to their real situation. All side effects from the first hour to 14 days after each dose of CoronaVac were recorded. The responses were considered as the primary outcome of the study. It was also planned to identify potential risk factors for the development of vaccine-related side effects as a secondary outcome.

**Data Analysis**

Safety analyses were expressed as counts and percentages for side effects. Descriptive statistics are presented as mean (standard deviation) for continuous variables and frequency and percentages for categorical variables. Due to the cross-sectional design of this study and the fact that there is no similar study, it was aimed to reach as many health workers as possible; thus, a sample size was not calculated. To determine significant variables for side effect status, logistic regression analysis was applied. First, univariate logistic regression was conducted, and variables with $P$ value $\leq 0.25$ were specified as candidate variables. Using the candidate variables, multiple logistic regression analysis was implemented with backward elimination to determine the final model. Statistical significance was considered as $P < 0.05$. All analysis was performed by using IBM SPSS version 23.

**RESULTS**

**Sociodemographic Characteristics**

A total of 1,628 healthcare workers participated in the study, 1039 (64%) women and 589 men (36%), and 369 (22%) stated that they were current smokers. Mean age of the population was 47.6 ± 12.2 years.

Among the participants, 727 (44.7%) were specialist physicians, 274 (16.8%) primary care physicians, 175 (10.8%) general practitioners, 81 (5%) research assistants, 79 (4.9%) nurses, 67 (4.1%) dentists, 23 (1.4%) pharmacists, and the remaining 202 (12.3%) consisted of other healthcare personnel (Table 1).

Five hundred and sixty-nine (35%) participants had at least one comorbidity. The most common comorbidities were hypertension ($n = 265/16.2\%$), thyroid disorders ($n = 146/9\%$), diabetes mellitus ($n = 102/6.3\%$), asthma ($n = 58/3.6\%$), coronary artery disease ($n = 52/3\%$), rheumatological diseases ($n = 44/2.7\%$), and a history of previous malignancy ($n = 42/2.6\%$). Five hundred and sixty-one (34.5%) people were treated with at least one drug for their chronic diseases (Table 2).
Pre-vaccine Period

Three-hundred and twenty (19.7%) of the participants declared that they had COVID-19 (288 PCR positive, 32 PCR negative) in the pre-vaccine period. Of these, 19 (5.9%) were asymptomatic, 154 (48.1%) had mild and 138 (43.1%) had moderate acute COVID-19 infection, and 9 (2.8%) had a severe clinical deterioration requiring respiratory support. Respiratory system involvement was observed in 177 (10.9%) of the whole survey population, 55.3% of the COVID-19 positive group of participants (Table 2).

Side Effects

Three-hundred and ninety-six (24.3%) healthcare workers had at least one side effect after either the first or second dose of CoronaVac. After the first dose of CoronaVac, 300 (18.4%) participants reported side effects, whereas 254 (15.6%) participants reported side effect after the second dose. Redness/pain at the inoculation site, headache, muscle/joint pain, palpitations, dizziness, and sleep disturbances were the most common side effects, and these varied in frequency in the post-vaccination period. Vaccine-induced side effects were most common after the first dose and within 24 h of administration. After the first and second doses, side effects persisted after two weeks in 4.3% and 4.6% of participants, respectively. There were 3 (0.2%) episodes of syncope/loss of consciousness after the first dose of CoronaVac.

| Variable                  | Category                  | n (%)   |
|---------------------------|---------------------------|---------|
| Gender                    | Female                    | 1039 (63.82) |
|                           | Male                      | 589 (36.18) |
| Profession                | Specialist physician      | 727 (44.66) |
|                           | Primary care physician    | 274 (16.83) |
|                           | General practitioners     | 175 (10.75) |
|                           | Research assistants       | 81 (4.98) |
|                           | Nurse                     | 79 (4.85) |
|                           | Dentist                   | 67 (4.12) |
|                           | Pharmacist                | 23 (1.41) |
|                           | Other and unemployed      | 202 (12.41) |
| Region                    | İstanbul (TR1)            | 291 (17.87) |
|                           | West Marmara (TR2)        | 60 (3.69) |
|                           | Aegean (TR3)              | 345 (21.19) |
|                           | East Marmara (TR4)        | 172 (10.57) |
|                           | West Anatolia (TR5)       | 332 (20.39) |
|                           | Mediterranean (TR6)       | 192 (11.79) |
|                           | Central Anatolia (TR7)    | 36 (2.21) |
|                           | West Black Sea (TR8)      | 51 (3.13) |
|                           | East Black Sea (TR9)      | 25 (1.54) |
|                           | Northeast Anatolia (TRA)  | 7 (0.43) |
|                           | Central East Anatolia (TRB)| 13 (0.8)  |
|                           | Southeast Anatolia (TRC)  | 56 (3.44) |
|                           | Unknown                   | 41 (2.52) |
|                           | Turkish Republic of Northern Cyprus | 7 (0.43) |
| Age (years)               | < 50                      | 820 (50.59) |
|                           | ≥ 50                      | 801 (49.41) |
| Age (mean)                |                           | 47.80 ± 11.78 |

| Variable                  | Category                  | Descriptive statistics n (%) |
|---------------------------|---------------------------|-------------------------------|
| Chronic diseases          | Hypertension              | 265 (16.28) |
|                           | Thyroid disorder          | 146 (8.97) |
|                           | Diabetes mellitus         | 102 (6.27) |
|                           | Asthma                    | 58 (3.56) |
|                           | Coronary artery disease   | 52 (3.19) |
|                           | Rheumatology disease      | 44 (2.70) |
|                           | A history of previous malignancy | 42 (2.58) |
| Chronic diseases present  | Yes                       | 568 (34.89) |
|                           | No                        | 1060 (65.11) |
| Having at least 2 chronic diseases | Yes            | 193 (11.86) |
|                           | No                        | 1435 (88.14) |
| No of people on chronic medicine | Yes            | 561 (35.42) |
|                           | No                        | 1023 (64.58) |
| COVID-19 before CoronaVac | Yes                       | 320 (19.66) |
|                           | No                        | 1308 (80.34) |
| Smoking                   | Yes                       | 369 (22.89) |
|                           | No                        | 1243 (77.11) |

TABLE 1. Basic Characteristics of Participants

TABLE 2. The Medical History of the Participants in the Pre-Vaccine Period
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(n = 1/0.1%). No syncope/loss of consciousness was observed after the second dose (Figure 1).

Sudden Blood Pressure Change
One-hundred and fifteen (9.5%) of the healthcare workers stated that they had blood pressure control problems at any time after vaccination. Hypertension persisted in 35 (2.1%) of the participants without a previous diagnosis of hypertension. Blood pressure irregularity was controlled in 98 (6%) participants, whereas 27 (1.7%) participants had to be started on permanent medication. Eight (0.5%) of the participants previously diagnosed with hypertension and 6 (0.4%) healthy participants reported that blood pressure control could not be achieved despite additional medication.

Risk Factors for the Emergence of Side Effects
Sex (female), drug use for comorbidities, age (<50), history of previous malignancy, asthma, coronary artery disease, and thyroid disorders, or having a chronic disease in the pre-vaccine period were selected as potential independent variables for logistic regression analysis. Hypertension, diabetes mellitus, rheumatologic disease, and COVID-19 in pre-vaccine period could not achieve statistical significance. The binary logistic regression revealed female gender [odds ratio (OR) (95% confidence interval (CI); 2.399 (1.816–3.171)] (P < 0.001), age < 50 [(OR (95% CI); 1.372 (1.080–1.743)] (P = 0.01), and having thyroid disorder [(OR (95% CI); 1.841 (1.282–2.644)] (P = 0.001) in pre-vaccine period were found to be risk factors for the occurrence of side effects after vaccination (Table 3).

DISCUSSION
In this study, 24.3% of the healthcare workers had at least one side effect either after the first or the second dose of CoronaVac. Moreover, 18.4% and 15.6% of the participants had side effects after the first and second dose of vaccination, respectively. Almost all the side effects were mild–moderate and tolerable. A total of 95% of the healthcare workers stated that they had blood pressure control problems at any time after vaccination. Female sex, age < 50 years, and having thyroid disorders in the pre-vaccine period were risk factors for the emergence of side effects after CoronaVac.

Three-hundred and ninety-six (24.3%) healthcare workers had at least one side effect either after the first or second dose of CoronaVac. A study through which the largest reliable data for Turkey obtained showed that the incidence of post-vaccine side effects was 18.9%, claiming ours' (Based on the results of a Phase I inactivated COVID-19 vaccine study from India in which three different vaccination regimens were applied, the incidence of side effects was found to be in the range of 14%–21%). In a phase II randomized, placebo–controlled trial of an inactivated SARS-CoV-2 vaccine in China, the overall side effect emergence rates during 28 days after immunization were 27.3%, 19.3%, and 12%

FIG. 1. The side effects of Coronavac

| Redness/pain at the inoculation site | Headache | Muscle/joint pain | Palpitation | Sudden blood pressure elevation | Dizziness | Sleep disturbances | Diarrhea/abdominal pain | Sudden decrease in blood pressure | Sudden shortness of breath | Skin rash | Runny nose | Fever | Hormonal irregularities | Syncope/loss of consciousness |
|-------------------------------------|---------|------------------|-------------|--------------------------------|-----------|-------------------|------------------------|-----------------------------|----------------------------|-----------|-----------|-------|----------------------|-----------------------------|
|                                    | 229 (14.07%) | 129 (7.92%)     | 67 (4.12%)  | 53 (3.26%)                    | 48 (2.95%)| 25 (1.54%)        | 23 (1.42%)             | 14 (0.86%)                  | 21 (1.32%)                | 17 (1.04%)| 13 (0.8%)    | 11 (0.68%)| 10 (0.65%) | 3 (0.18%)       |
| First Dose | 336 (20.64%) | 336 (20.64%)     | 336 (20.64%)| 336 (20.64%)                  | 336 (20.64%)| 336 (20.64%)      | 336 (20.64%)            | 336 (20.64%)               | 336 (20.64%)              | 336 (20.64%)| 336 (20.64%)| 336 (20.64%)| 336 (20.64%)| 336 (20.64%) | 336 (20.64%)           |
in the medium-dose, high-dose, and placebo groups, respectively.\textsuperscript{9} Although common data in the literature are compatible with our data, another study conducted among healthcare workers in Turkey reported the frequency of side effects as 62.5%.\textsuperscript{10}

After the first and second doses, 18.4% and 15.6% of healthcare workers had side effects, respectively. In a relatively small study from China that found similar results after enrolling healthcare workers, 15.6% recipients of the first dose and 14.6% of the second dose had side effects; of these, 7.5% of participants reported at least one side effect after both inoculations.\textsuperscript{11}

Redness/pain at the inoculation site, headache, muscle/joint pain, palpitations, dizziness, and sleep problems were the most common side effects in this study. Our study corroborates the report of the Food and Health Bureau indicating that the common side effects (≥ 10%) were injection site pain, headache, and fatigue.\textsuperscript{12} In another similar study enrolling healthcare workers, inoculation site pain (41.5%), fatigue (23.6%), headache (18.7%), muscle pain (11.2%), and joint pain (5.9%) were the most side effects.\textsuperscript{13} In a large cohort conducted in Turkey, the most common side effect was inoculation site pain (2.4%), fatigue (8.2%), myalgia (4%), chill (2.5%), and nausea (0.7%).\textsuperscript{7} A phase 1 clinical trial with the inactivated vaccine showed that the most common side effects were injection site pain (5%), headache (3%), fatigue (3%), fever (2%), and nausea or vomiting (2%).\textsuperscript{4} An online questionnaire survey among healthcare workers in China found that the most common side effects were localized pain at the injection site, fatigue, muscle soreness, and headache.\textsuperscript{11} In Turkey, a survey conducted among healthcare workers reported that the most common side effects were arm pain, fever, weakness, muscle aches, nausea, headache, and swelling of the lymph node on the grafted side.\textsuperscript{13}

Almost every study evaluating CoronaVac found similar side effects at the same frequency and severity. Interestingly, in this study, 9.5% of the participants answered yes to the question “Did you have any problems with blood pressure control in any period after vaccination?”. To our current knowledge, blood pressure dysregulation has been reported as an inactivated vaccine side effect for the first time in this report. In the acute COVID-19 period, laboratory results showed that angiotensin-II (Ang II) level was elevated in most patients without prior hypertension, and Ang II levels were significantly higher in elevated blood pressure groups compared with normal blood pressure and healthy control groups. It is hypothesized that the binding of SARS-CoV-2 to ACE-2, inhibiting Ang II degradation and increasing blood pressure or over activation of the renin-angiotensin system, promotes an inflammatory response and cytokine storm, which stimulates the NADH/NADPH oxidase system and triggers cell contraction and vasoconstriction.\textsuperscript{14} In a case series on hypertension observed immediately after mRNA vaccine inoculation, nine patients showed elevated blood pressure, and all patients recovered to normal with monitoring and speculated that a stress response is likely in view of public debate, in addition to pain response and white coat effect.\textsuperscript{15} Theoretically, components of the vaccines such as polyethylenglycol may cause hypertension, but it is unlikely due to low dosage as patients reacted within minutes of the injection. The average percentage of members with high blood pressure was 62% in the US in the pre-pandemic period; however, by the end of January, when the first confirmed case of COVID-19 was announced, the average percentage of members with high blood pressure was 15.6% recipients of the first dose and 14.6% of the second dose had side effects; of these, 7.5% of participants reported at least one side effect after both inoculations.\textsuperscript{11}

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### TABLE 3. Risk Factors for the Emergence of Side Effects after CoronaVac

| Variables                        | OR (95% CI) | p-value | OR (95% CI) | p-value |
|----------------------------------|-------------|---------|-------------|---------|
| Sex (female/male)                | 2.766 (2.114–3.620) | <0.001  | 2.399 (1.816–3.171) | <0.001  |
| Smoking (present)                | 0.893 (0.679–1.175) | 0.419   | -           | -       |
| Drug usage (present)             | 1.264 (0.998–1.601) | 0.052   | -           | -       |
| Age (<50/≥50)                    | 1.616 (1.285–2.033) | <0.001  | 1.572 (1.080–1.743) | 0.010   |
| Chronic illnesses                |             |         |             |         |
| Hypertension                     | 1.026 (0.756–1.391) | 0.870   | -           | -       |
| Thyroid disorder                 | 2.205 (1.550–3.139) | <0.001  | 1.841 (1.282–2.644) | 0.001   |
| Diabetes                         | 0.944 (0.589–1.514) | 0.812   | -           | -       |
| Asthma                           | 1.654 (0.951–2.877) | 0.075   | -           | -       |
| Coronary artery disease          | 0.636 (0.308–1.317) | 0.224   | -           | -       |
| Rheumatology disease             | 1.453 (0.763–2.769) | 0.256   | -           | -       |
| History of previous malignancy   | 0.609 (0.268–1.382) | 0.236   | -           | -       |
| Chronic disease (present)        | 1.237 (0.980–1.563) | 0.074   | -           | -       |
| Having at least 2 chronic diseases (present) | 1.192 (0.849–1.671) | 0.310 | - | - |
| COVID-19 before CoronaVac (present) | 1.077 (0.813–1.427) | 0.605 | - | - |

CI: confidence interval
pressure increased to 67\%. With confusing and discrete data, the relationship between SARS-CoV-2 and hypertension and the underlying mechanism, if any, have not been fully elucidated. For the first time in this publication, the problem of blood pressure control was directly associated with the vaccine by the participants. This data absolutely needs detailed evaluation and verification.

Only 0.2% of the participants had a syncop/loss of consciousness after the first dose. No severe side effect was observed after the second dose. In a phase I trial of an inactivated vaccine, only one serious side effect of viral pneumonitis (unrelated to the vaccine) was reported.8 The interim results of a double-blind, randomized, placebo–controlled, phase 3 trial in Turkey showed a satisfactory safety profile, with no severe side effects or deaths during the study period.7 In the phase II trial of inactivated SARS-CoV-2 vaccine enrolling 750 healthy adults, no serious side effects were reported.9 No alarming side effects have been observed with these vaccines, which have been administered to more than two and a half billion people in the field in Turkey.13

Female sex, age < 50, and the presence of thyroid disorders in the pre-vaccine period were the risk factors for the emergence of side effects after CoronaVac. Methodologically, a similar study of healthcare workers in China showed that professional titles, knowledge about inactivated vaccine, worry about the side effects, health status, side effects after other vaccines, allergic history, and sleep quality were significantly related to the side effects.10 In a study conducted on healthcare workers in Turkey investigating inactive-vaccine side effects, females, older age group (≤ 32 years old), people with chronic illnesses, and taking regular medications were at a higher risk of vaccine side effects.15 Female sex was the consociate side effect factor for the occurrence of side effects after vaccination in healthcare workers. In some case reports or case series, it has been shown that there are thyroiditis attacks in the acute or post–COVID period; however, the data did not go beyond this, and no causal hypothesis could be established.17,20

This study is a large and widely attended study that includes data of healthcare workers from all geographic regions of Turkey. Although there is participation from all the provinces of Turkey, it still does not represent the whole country and the entire population. Due to the nature of online questionnaire surveys, it is not possible to be certain that the data is completely accurate; the causality between the symptoms mentioned as side effects in the study and the vaccine cannot be established.

The study found that inactivated SARS-CoV-2 vaccine, CoronaVac, has an accepted favorable safety profile with limited mild–moderate side effects. Blood pressure dysregulation should be kept in mind as a side effect. Females, young people, and the participants with thyroid disorders are at increased risk of the side effects. Given that these results show that CoronaVac has a good safety profile, we have obtained reliable and comprehensive data against vaccine hesitancy.

**Patient Consent for Publication:** An informed consent statement was required to be checked in at the beginning of the questionnaire.

**Data Sharing Statement:** The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

**Author Contributions:** Design- S.O., N.K.; Data Collection or Processing- O.B., S.O., N.K., M.K.; Critically Reviewed the Paper- N.K., S.O., M.K., B.S.; Writing- O.B., N.K.

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**REFERENCES**

1. https://www.worldometers.info/coronavirus/worldometer
2. Weiss P, Murdoch DR. Clinical course and mortality risk of severe COVID-19. Lancet. 2020;395:1014-1015. [CrossRef]
3. Pulendran B, Ahmed R. Immunological mechanisms of vaccination. Nat Immunol. 2011;12:509-517. [CrossRef]
4. Mallapaty S. China COVID vaccine reports mixed results - what does that mean for the pandemic? Nature. 2021. Epub ahead of print. PMID: 33452510. [CrossRef]
5. Dubé E, Gagnon D, MacDonald NE; SAGE Working Group on Vaccine Hesitancy. Strategies intended to address vaccine hesitancy: review of published reviews. Vaccine. 2015:33:4191-4203. [CrossRef]
6. Doroftei B, Ciobica A, Ilie OD, Maftei R, Ilea C. Mini-Review discussing the Reliability and Efficiency of COVID-19 Vaccines. Diagnostics (Basel). 2021;11:579. [CrossRef]
7. Tanriover MD, Doğanay HL, Akova M, et al. Efficacy and safety of an inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac): interim results of a double-blind, randomised, placebo-controlled, phase 3 trial in Turkey. Lancet. 2021;398:213-222. [CrossRef]
8. Ellis R, Varefu KM, Jogland H, et al. Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBV152: a double-blind, randomised, phase 1 trial. Lancet Infect Dis. 2021;21:637-645. Erratum in: Lancet Infect Dis. 2021;21:e81. [CrossRef]
9. Che Y, Liu X, Pu Y, et al. Randomized, Double-Blinded, Placebo-Controlled Phase 2 Trial of an Inactivated Severe Acute Respiratory Syndrome Coronavirus 2 Vaccine in Healthy Adults. Clin Infect Dis. 2021;73:3949-3955. [CrossRef]
10. Ricci D, Viola N, Sgrò D, Santini F, Latrofa F. Subacute Thyroiditis Manifestation of SARS-CoV-2 Infection? Insights From a Case Series. J Clin Med. 2021;10:2629. [CrossRef]
11. Zhang MX, Zhang TT, Shi GF, et al. Safety of an inactivated SARS-CoV-2 vaccine among healthcare workers in China. Expert Rev Vaccines. 2021:20:891-898. [CrossRef]
12. Food and Health Bureau (FHB). Report on Evaluation of Safety, Efficacy and Quality of CoronaVac COVID-19 Vaccine (Vero Cell) Inactivated. 2021. Available online: https://www.fhb.gov.hk/download/our_work/health/2021/08/evaluation_report_CoronaVac.pdf (accessed on 1 April 2021)
13. (https://www.ttb.org.tr/makale_goster.php?Guid=6dc46898-d802-11eb-9450-8a979bfc4eda.)
14. Chen G, Li X, Gong Z, et al. Hypertension as a sequela in patients of SARS-CoV-2 infection. PLoS One. 2021;16:e0250815. [CrossRef]
15. Meylan S, Livio F, Foerster M, et al. Stage III Hypertension in Patients After mRNA-Based SARS-CoV-2 Vaccination. Hypertension. 2021;77:56-57. [CrossRef]
16. https://www.mobilhealthnews.com/news/covid-19-pandemic-leads-more-people-high-blood-pressure-research-suggests
17. Brancatella A, Ricci D, Cappellani D, et al. Is Subacute Thyroiditis an Underestimated Manifestation of SARS-CoV-2 Infection? Insights From a Case Series. J Clin Endocrinol Metab. 2020:105.dgaa537. [CrossRef]
18. Brancatella A, Ricci D, Viola N, Sgrò D, Santini F, Latrofa F. Subacute Thyroiditis After Sars-COV-2 Infection. J Clin Endocrinol Metab. 2020:105.dgaa276. [CrossRef]
19. Ippolito S, Dentali F, Tanda ML. SARS-CoV-2: a potential trigger for subacute thyroiditis? Insights from a case report. J Endocrinol Invest. 2020:43:1171-1172. [CrossRef]
20. Asfuroğlu Kalkan E, Ates I. A case of subacute thyroiditis associated with Covid-19 infection. J Endocrinol Invest. 2020:43:1173-1174. [CrossRef]