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ORIGINAL ARTICLE / ARAŞTIRMA YAZISI

Infectious Diseases / Bulaşıcı Hastalıklar

Comparison of Adverse Effects of COVID-19 Vaccines Among Elderly: Pfizer/BioNTech Versus CoronaVac

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ABSTRACT

Purpose: The SARS-CoV-2 infection has triggered the COVID-19 pandemic with enormous public health and economic consequences. The safety and efficacy of currently available COVID-19 vaccines have been demonstrated in few studies; however, further information on specific high-risk groups like the elderly with comorbidities is needed. In this cross-sectional study, we aimed to compare the adverse side effects of two different COVID-19 vaccines (RNA-based Pfizer/BioNTech and inactivated CoronaVac) among the elderly with comorbidities.

Methods: We selected a total of 800 participants 65 years or older from Turkish Republic of Northern Cyprus who received either one of the vaccines. We collected data on the possible side effects that have been previously attributed to coronavirus vaccination via quantitative telephone interviews.

Results: We found that both CoronaVac and Pfizer/BioNTech were safe in adults over 65 years old, even with comorbidities. The most common side effects were pain on the injection site and fatigue. Adverse effects, particularly allergic reactions, were higher in Pfizer/BioNTech vaccinated group compared with the CoronaVac group.

Conclusion: In conclusion, both vaccines were well tolerated and safe among the elderly even with comorbidities, As this specific group was largely excluded from the previous trials, we believe that this study may have a contributing impact on vaccine acceptance and health policy decision-making.

Keywords: adverse effects, COVID-19, SARS-CoV-2, elderly, vaccination

İleri Yaş Grubunda Uygulanan Pfizer/Biontech Ve Coronavac Aşılarının Yan Etkilerinin Karşılaştırılması

Amaç: SARS-CoV-2'nin neden olduğu COVID-19 pandemisi tüm dünyada çok büyük bir halk sağlığı sorunu olmaya devam etmektedir. Mevcut COVID-19 aşılarının spesifik gruplardaki güvenliği ve etkinliği ile ilgili çok az sayıda çalışma mevcuttur. Özellikle ileri yaşta ve ek hastalığı olanlarda bu tür çalışmalara ihtiyaç vardır. Biz bu kesitsel çalışmada RNA bazlı Pfizer/BioNTech ile CoronaVac inaktif virus aşılarının ek hastalığı olan yaşlı popülasyondaki yan etkilerini karşılaştırmayı amaçladık.

Metodlar: Kuzey Kıbrıs Türk Cumhuriyeti'nde aşılanmış olan 65 yaş üstü toplam 800 gönüllü kişi çalışmamıza dahil edildi. Telefon yoluyla katılımcılara ulaşıldı ve COVID-19 aşılarının yol açabileceği olası yan etkiler açısından sorgulandı.

Bulgular: Çalışmamızın sonuçlarına göre hem CoronaVac hem de Pfizer/BioNTech 65 yaş üstü kişilerde ek hastalık varlığında bile güvenli olduğu görüldü. En sık görülen yan etkiler aşı uygulanan bölgede ağrı ve halsizlik olarak raporlandı. Yan etkilerden biri olan allerjik reaksiyonlar Pfizer/BioNTech grubunda CoronaVac grubuna göre daha yüksek oranda saptandı.

Sonuç: Sonuç olarak yaşlı ve kronik hastalığı olan kişilerde her iki aşının da tolere edildiği ve güvenli olduğu görüldü. Spesifik bir grup üzerinde yapılmış bu çalışmanın sonuçları COVID-19 aşılama programlarına ve geliştirilecek sağlık politikasına katkıda bulunabileceğini düşünüyoruz.

Anahtar Kelimeler: ileri yaş, yan etki, SARS-CoV-2, COVID-19, aşılama

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection triggered a coronavirus disease (COVID-19) pandemic with an unprecedented burden to healthcare and the global economy (1). Although containment strategies of isolation, quarantine, and physical distancing have been effective in limiting the spread of infection in the short term in many countries, the absence of population immunity and the absence of an effective treatment has left the global population susceptible to continuing waves of the infection. Furthermore, the initial expectations of wide population herd immunity or probable less virulent virus variants have not been materialized. Therefore, global mass vaccination appears to be the key to fighting against COVID -19 pandemic.

Researchers worldwide have taken quick action in developing vaccines for COVID-19 with more than 198 vaccine candidates in preclinical and clinical trials (2). Based on the current literature, there is reasonable evidence that COVID-19 vaccines may be the key to combating the pandemic; however, there have been concerns about vaccine side effects. Public perception of vaccine effectiveness and the possible side effects are leading challenges in accepting the vaccination (3). Data about the side effects of vaccination in specific groups such as the elderly and those with comorbidities remains lacking (4-6). In addition, the safety of different vaccines, such as mRNA-based and inactivated vaccines, has not been compared previously.

Mass vaccination is the safest way to reach population-based immunity (7). As the vaccines are administered to millions of people in the upcoming months, more data will become available to analyze the vaccine side effects more accurately. As of January 2021, both mRNA-based Pfizer/BioNTech and inactivated virus CoronaVac vaccines are available for healthcare workers and the elderly in the Turkish Republic of Northern Cyprus (TRNC). This study aimed to compare the adverse side effects of these vaccines among the elderly with comorbidities.

MATERIAL AND METHODS

In this cross-sectional study, 800 elderly individuals, 65-year-old or older, who received Pfizer/BioNTech or CoronaVac vaccines were invited to participate. Individuals were identified from the Ministry of Health of the Turkish Republic of Northern Cyprus vaccine registry. In addition to demographic information and comorbidities, the questionnaire was designed to inquire about the self-identified common side effects, such as fever, chills, pain at the injection site, swelling and redness, lymphadenopathy, fatigue, headaches, muscle and joint pain, diarrhea, nausea, and vomiting, that have been previously attributed to coronavirus vaccinations.

The Study Sample and Data Collection

Using WinPepi statistical calculator (ver. 11.65; http://www.brixtonhealth.com), we estimated the minimum sample size with the expected prevalence of 10% for side effects and the confidence interval of 95%. With the 10% loss to follow-up, the minimum estimated sample size was 396 for each vaccine group. Accordingly, we decided to include a total of 800 consenting participants (400 mRNA +400 inactive vaccine groups) for the study. We called eligible participants by phone and collected their informed consent before requesting their response to the questionnaire.

Statistical Analyses

Statistical analyses were performed on IBM SPSS, ver. 20.0 (Chicago, IL, USA). The categorical variables were expressed as counts (percentages), and the continuous variables were expressed as median, mean ± 2 standard deviation (SD). Comparisons of categorical variables between the groups were performed using Yates's corrected chi-square test and the continuous variables were compared using student-t test. A two-sided p-value of 0.05 was considered as the cut-off value for statistical significance.

RESULTS

Of the 800 participants, 423 (52.9%) were female, and 377 (47.1%) were male. The mean age of the CoronaVac group was significantly higher than the Pfizer/BioNTech group (71.7 ± 6.1 years vs 70.85 ± 5.5 years; p=0.002). There were 398 patients (49.8%) with at least one comorbidity in the general study population. Of these, 208 (52.3%) were in the CoronaVac group, and 190 (47.7%) were in the Pfizer/BioNTech group. There was no statistically significant difference between the groups in terms of presence of a comorbidity. Chronic heart diseases (37.0%), diabetes mellitus (16.0%), and chronic lung diseases (9.0%) were the most common comorbidities. The demographic characteristics of participants were presented in Table 1.

The prevalence of chronic heart disease in women was higher than in men (40.4% vs. 33.2%, p=0.03); frequencies of other comorbidities were similar between male and female participants.

Table 1: Demographic characteristics of the individuals according to vaccine groups			
	CoronaVac n=400	Pfizer/ BioNTech n=400	P
Age, years (mean ± standart deviation)	71.7 ± 6.1	70.85 ± 5.5	0.002
Sex (%)			
Woman (n=423)	57.5	48.2	0.009
Male (n=377)	42.5	51.8	
Presence of at least one comorbidity (%)			
No	48	52.5	0.203
Yes	52	47.5	
Comorbidities (%)			
Chronic heart diseases (n=296)	41.2	32.8	0.013
Chronic lung diseases (n= 72)	9.0	9.0	1
Chronic liver diseases (n=6)	0.5	1.0	0.4
Chronic kidney diseases (n=24)	2.8	3.3	0.7
Diabetes mellitus (n=128)	17.5	14.5	0.2
Rheumatic diseases (n=10)	0.8	1.8	0.2
Cancer (n=22)	2.2	3.2	0.4

Side Effects

The most common side effect for both vaccine groups was pain on the injection site. All side effects except headache were lower after the second dose of the vaccine (Figure 1). The incidence of side effects of swelling and redness (5.1% vs. 0.63%; p<0.001), chills (1.13% vs. 0.25%; p=0.034), allergic reaction (3.38% vs. 0.75; p<0.001), and fatigue (12.0% vs. 6.63; p<0.001) was higher after the first dose compared to the second dose. Only one recipient of the Pfizer/BioNTech vaccine complained of post-vaccination axillary lymphadenopathy. There was no statistical difference in side effects after the first and second doses of vaccination between the sex groups.

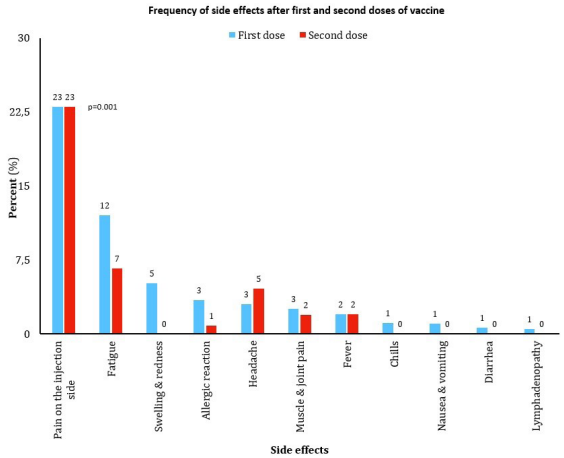

Figure 1: *Frequency of side effects after first and second doses of vaccine in the general population*

After the first dose, pain on the injection site (23.3% vs. 19.2%, p=0.007), and fever (3.0 % vs. 1%, p=0.043) were significantly higher in those who received Pfizer/BioNTech vaccine (Figure 2). After the second dose, pain on the injection site (27.3% vs. 17.8%, p=0.001) and fatigue (8.5% vs. 4.8%, p=0.03) were significantly higher in the same group (Figure 3).

When we re-examined the study population as ≤ 70 years (n=384, 48%), and >70 years of age (n=416, 52%), where sex and vaccine distributions were similar, we observed other differences. Pain on the injection site (p=0.014), was higher after the first (27.1% vs 19.7%, p=0.014) and the second dose (28.4% vs 17.1%, p=0.000) of vaccination among the ≤70 age group. Fatigue was also higher in the same age group (8.6% vs 4.8%, p=0.03). However, swelling and redness (2.6% vs 7.5%, p=0.002) were significantly higher in the >70 age group (Figure 4).

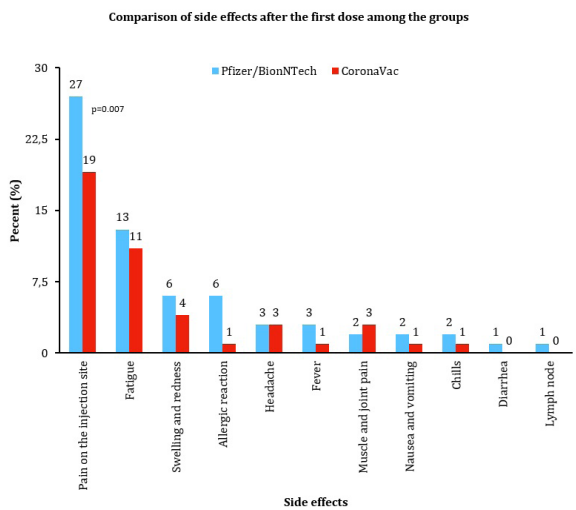

Figure 2: *Comparison of side effects after the first dose among the Pfizer/BioNTech and Coronovac groups*

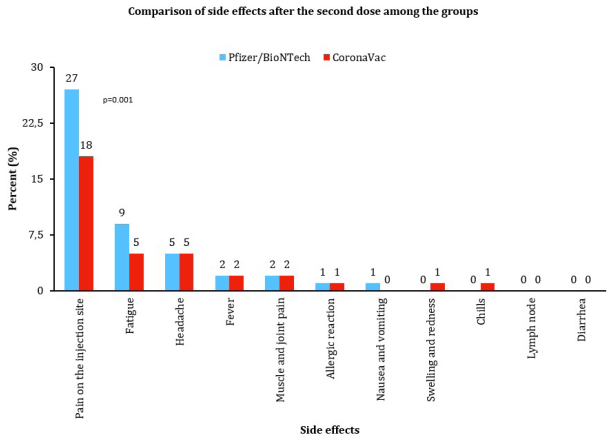

Figure 3: *Comparison of side effects after the second dose among the groups Pfizer/BioNTech and Coronovac groups*

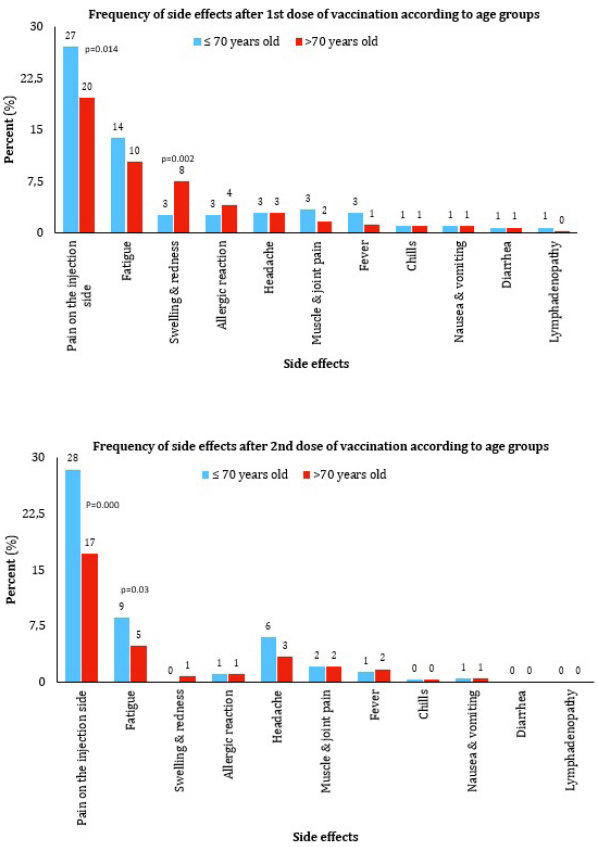

Figure 4: *Comparison of side effects after 1st and 2nd dose of vaccination among the study populations ≤ 70 and >70 years of age*

The pain on the injection site (p=0.002), swelling and redness (p=0.001), fever (p=0.04), and allergic reaction (p=0.000) after first dose of vaccination were higher in patients with any comorbidity. The pain on the injection site (p=0.009) were also high in these patients after second dose of vaccination . Side effects after the 1st and 2nd dose vaccine according to the presence of at least one comorbidity were shown in Figure 5. Some of the post-vaccination side effects demonstrated significant differences by the distribution of comorbidities such as chronic heart and liver diseases, diabetes mellitus, and cancer. Side effects after both the first and the second dose vaccines based on the distribution of comorbidities were presented in Table 2. While sex and age distribution did not pose a risk, the type of vaccine and presence of some comorbidities were found to be related to allergic reactions. Allergic reactions were significantly higher in Pfizer/BioNTech group compared to the CoronaVac group (p=0.000). The frequency of allergic reactions after the first dose in patients with chronic kidney disease was found to be significantly higher than those without chronic kidney disease (29.2% vs. 2.6%; p = 0.000). Although the frequency of allergic reactions after the second vaccine doses was lower than the first vaccine doses, allergic reactions were higher in patients with chronic kidney disease than those without chronic kidney disease (4.2% vs. 0.6%; p = 0.049). However, the frequency of allergic reactions after the second vaccination was higher in patients with malignancy compared to those without it (4.5% vs 0.6%; p = 0.04).

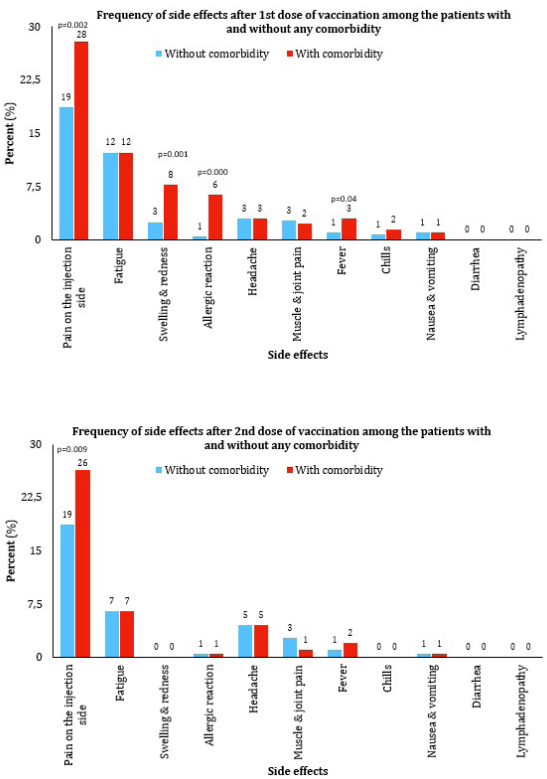

Figure 5: *Comparison of side effects after 1st and 2nd dose of vaccination among the patients with and without any comorbidity*

Table 2: Comparison of vaccine-related side effects in the distribution of comorbidities

Vaccine-related side effects		After the first dose				After the second dose			
		Pain on the injection site (n=186)	p	Fever (n=16)	p	Pain on the injection site (n=180)	p	Fever after (n=12)	p
Chronic Heart Diseases (n=296)	(-) (+)	94 (18.7%) 92 (31.1%)	0.000	5 (1%) 11 (3.7%)	0.008	101 (20.1%) 79 (26.7%)	0.03	5 (1%) 7 (2.4%)	0.1
Chronic Lung Diseases (n=72)	(-) (+)	167 (22.9%) 19 (26.4%)	0.51	15 (2.1%) 1 (1.4%)	0.7	165 (22.7%) 15 (20.8%)	0.7	8 (1.1%) 4 (5.6%)	0.003
Chronic liver disease (n=6)	(-) (+)	186 (23.4%) 0 (0%)	0.2	13 (1.6%) 3 (50%)	0.000	179 (22.6%) 1 (16.7%)	0.7	12 (1.5%) 0 (0%)	0.8
Chronic kidney disease (n=24)	(-) (+)	181 (23.4%) 5 (20.8%)	0.8	16 (2.1%) 0 (0%)	0.5	171 (22.2%) 9 (37.5%)	0.07	12 (1.6%) 0 (%)	0.5
DM (n=128)	(-) (+)	151 (22.5%) 35 (27.3%)	0.2	15 (2.2%) 1 (0.8%)	0.3	140 (20.9%) 40 (31.2%)	0.01	11 (1.6%) 1 (0.8%)	0.5
Rheumatic diseases (n=10)	(-) (+)	184 (23.3%) 2 (20%)	0.8	16 (2%) 0 (0%)	0.7	177 (22.4%) 3 (30%)	0.6	12 (1.5%) 0 (0%)	0.7
Cancer (n=22)	(-) (+)	182 (23.4%) 4 (18.2%)	0.6	6 (2.1%) 0 (0%)	0.5	171 (22%) 9 (40.9%)	0.04	12 (1.5%) 0 (0%)	0.6

DM : Diabetes Mellitus
(-) : absent (+) : Present

DISCUSSION

In this study, we found that two doses of both CoronaVac and Pfizer/BioNTech vaccines had mild and similar adverse effects which were tolerated in adults over 65 years and older, even with certain comorbidities. The most common side effects of both vaccines were pain on the injection site and fatigue. While there was no significant difference between the male and female participants, age distribution, presence of comorbidities, and the type of vaccination was related to some adverse effects. The incidence of adverse side effects, especially allergic reactions, in the Pfizer/BioNTech group was higher than that of the CoronaVac group.

COVID-19 vaccines are among the most remarkable achievements in modern medical history. The vaccine gave real hope for ending the fight against the COVID-19 pandemic. The FDA has authorized the mRNA-based Pfizer/BioNTech vaccines on December 11, 2020 (7); an inactivated virus vaccine CoronaVac was approved for emergency use in China and phase three clinical trials that are ongoing in Brazil, Turkey, and Indonesia (2). Both vaccines were available in TRNC in mid-January. Healthcare professionals and individuals ≥ 65 years old were the first to be vaccinated. We aimed to evaluate and compare the side effects of these vaccines, especially in the presence of age and age-related comorbidities.

Previous clinical data showed that vaccine-induced immune responses and side effects were different by age groups and sex (8-10). It has been reported that both antibody response and also side effects after vaccination are higher in women (9, 10). In this study, the mean age and the presence of comorbidities other than chronic heart disease were similar in both sexes. Unlike the previous literature, there was no statistically significant difference between the male and female participants in terms of side effects after both the first and the second vaccination doses. Since we included only the elderly population, we also wanted to evaluate the effect of age categories on side effects. We observed that pain on the injection site and fatigue were higher in the ≤70 age group. However, swelling and redness were significantly higher in the >70 age group.

Both CoronaVac and Pfizer/BioNTech vaccines were tolerated by elderly patients with comorbidities. No severe, life-threatening side effects were observed. The most common side effects for both vaccines were local reactions such as pain on injection site, and fatigue which were similar to the previous study of another inactivated COVID-19 vaccine from Sinopharm (Beijing China) (11). The incidence of adverse reactions in the Pfizer/BioNTech group was significantly higher compared to the CoronaVac group.

Allergic reactions, which have a broad spectrum from local reactions to anaphylaxis, are among the most serious side effects of the vaccines(12). Clinical signs of allergic reactions linked to antigen, animal proteins, preservatives, stabilizers, egg proteins, gelatin, and other additives tend to be more severe in the elderly. The Pfizer/BioNTech vaccine is an mRNA-based vaccine, which was produced with new technology; the mRNA is surrounded by lipid nanoparticles to allow it to be delivered to cells. These lipid nanoparticles and additive polyethylene glycol are suspected to be responsible for allergic reactions; however, The anaphylactic reaction to the mRNA-based vaccine is extremely rare (12). It is recommended to inform patients about the possible allergic reactions before vaccination with Pfizer/BioNTech and to administer for those with a history of anaphylaxis or serious allergic reactions with necessary clinical precautions (12). There were no reported serious allergic side effects with the inactivated vaccine (13). Although there is no previous study comparing Pfizer/BioNTech and CoronaVac in terms of side effects and allergic reactions, as we observed, the data in the literature suggests that the risk of allergic reactions is likely to be higher with Pfizer/BioNTech (12, 13).

The fear of side effects, particularly among the elderly and patients with comorbidities and prior history of allergic reactions, may lead to unnecessary vaccine hesitancy. As older age people and people with comorbidities were largely excluded from the previous vaccine trials, the efficacy of vaccines and possible side effects in this population has not been fully assessed. For the first time, this study demonstrates a significant association between preexisting comorbidities and a higher incidence of self-reported, non-life-threatening, side effects after two types of vaccinations. From this aspect, people over 65 years old with comorbidities are no different from healthy and younger participants who reported similar incidences of adverse reactions in previous studies (2, 7). We believe that the findings of our study will contribute to the selection of appropriate vaccines and evidence-informed health policy decision-making (7, 14).

The main strength of our study was the study population of people 65 years or older, with preexisting diseases. To our knowledge, this is the first study to examine and compare the adverse side effects from Pfizer/BioNTech and CoronaVac vaccines in this specific group. Given that older people may have reported side effects less frequently, potential selection bias due to the specific age bracket of the participants is the main limitation of the study.

In conclusion, both CoronaVac and Pfizer/BioNTech vaccines were safe in the elderly, even with comorbidities. The most common side effects of both vaccines were pain on the injection site and fatigue. There was no significant difference in side effects between the male and female participants. Although the age distribution, presence of comorbidities, and the type of vaccine were related to some adverse effects, all of them were mild to moderate local reactions. The side effects, especially allergic reactions, were more frequent in Pfizer/BioNTech group compared to the CoronaVac group.

DECLARATIONS

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The authors declared that this study had received no financial support.

Conflicts of Interest/Competing Interests

The authors declared no potential conflicts of interest concerning the research, authorship, and publication of this article.

Ethics Approval

The study was approved by the Ministry of Health, Dr. Burhan Nalbantoglu State Hospital, Institutional Ethics Committee (ref no:12/21).

Availability of Data and Material

We can provide all the original data.

Authors' Contributions

HE: Study design, literature search, writing of the manuscript; EUE: Study design, data collection, literature search; SAB: Data collection, writing of the manuscript FGI: Data collection; literature search CS: Analysis of data, writing of the manuscript; OCE: Analysis of data, writing of the manuscript FY: Design of the study, writing of the manuscript

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