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Higher antibody responses after mRNA-based vaccine compared to inactivated vaccine against SARS-CoV-2 in Behcet's syndrome

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Abstract

There are limited data about humoral response to vaccine in Behçet's syndrome (BS). We compared SARS-CoV-2 antibody response after two doses of inactivated (Sinovac/CoronaVac) or mRNA (Pfizer/BioNTech) vaccines in patients with BS and healthy controls (HCs). We studied 166 (92M/74F) patients with BS (mean age: 42.9 ± 9.6 years) and 165 (75M/90F) healthy controls (mean age: 42.4 ± 10.4 years), in a single-center cross-sectional design between April 2021 and October 2021. A total of 80 patients with BS and 89 HCs received two doses of CoronaVac, while 86 patients with BS and 76 HCs were vaccinated with BioNTech. All study subjects had a negative history for COVID-19. Serum samples were collected at least 21 days after the second dose of the vaccine. Anti-spike IgG antibody titers were measured quantitatively using a commercially available immunoassay method. We found that the great majority in both patient and HC groups had detectable antibodies after either CoronaVac (96.3% vs 100%) or BioNTech (98.8% vs 100%). Among those vaccinated with CoronaVac, BS patients had significantly lower median (IQR) titers compared to HCs [36.5 (12.5–128.5) vs 102 (59–180), $p < 0.001$]. On the other hand, antibody titers did not differ among patients with BS and HCs who were vaccinated with BioNTech [1648.5 (527.0–3693.8) vs 1516.0 (836.3–2599.5), $p = 0.512$). Among different treatment regimen subgroups in both vaccine groups, those who were using anti-TNF-based treatment had the lowest antibody titers. However, the difference was statistically significant only among those vaccinated with CoronaVac. Among patients vaccinated with BioNTech, there was no statistically significant difference between different treatment regimen groups. Compared to inactivated COVID-19 vaccine, mRNA-based vaccine elicited higher antibody titers among BS patients. Only in the CoronaVac group, patients especially those using anti-TNF agents were found to have low titers compared to healthy subjects. BS patients vaccinated with BioNTech were found to have similar seroconversion rates and antibody levels compared to healthy controls. Further studies should assess whether the low antibody titers are associated with diminished protection against COVID-19 in both vaccine groups.

Keywords Immunity · Humoral · COVID-19 · Vaccine · Behcet's syndrome · BioNTech · CoronaVac

Introduction

Harmless and effective vaccines are crucial for terminating the COVID-19 pandemic, which has caused more than six million deaths globally as of June 6, 2022 [1]. Among the several potential vaccines against SARS-CoV-2, the mRNA-based vaccine (BNT162b2) of Pfizer-BioNTech [2] and the inactivated vaccine of Sinovac-CoronaVac [3] were found to be effective without an unexpected adverse event profile in phase-3 randomized, placebo-controlled trials, which included healthy individuals. Side effects were mostly mild to moderate and transient and included arm pain, arthralgia and fever. Soon after worldwide mass vaccination has started, it has become clear that vaccines may cause some rare adverse events such as transverse myelitis in otherwise healthy people [4]. It has become also evident that immune-compromised individuals, particularly transplant recipients, may not succeed in mounting a satisfactory immune response to a primary series of COVID-19 vaccines [5–9].

Throughout the pandemic, several observational studies gathered a large body of evidence related to the efficacy of SARS-CoV-2 vaccines among patients with autoimmune or inflammatory rheumatic diseases (AIIRD). As revealed in a recent review, satisfactory rates of seroconversion are

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obtained after vaccination in the majority of the patients with AIIRD; however, neutralizing and anti-spike antibodies were lower than in healthy controls [10]. Moreover, evidence indicates that humoral response is significantly blunted by B cell-depleting agents and glucocorticoids [10]. It has to be noted that the majority of the published data are associated with classical forms of AIIRD, while information with rare inflammatory disorders such as Behçet's syndrome (BS) is very limited. Similarly, data associated with mRNA-based vaccines outweigh considerably that related to inactivated vaccine.

BS, a complex inflammatory disorder of unknown etiology, is rather common in Turkey, with a prevalence rate of 0.4% [11]. Recurrent oro-genital aphthous ulcerations and panuveitis are most characteristic lesions of BS; however, it may also involve joints, all types of venous or arterial vessels, central nervous and gastrointestinal systems [11–13]. While both genders are affected almost equally, young male patients have a considerably more severe disease course compared to females [11–13]. Although BS cannot be considered as a classical autoimmune disease, patients are usually treated with immunosuppressive drugs with or without colchicine [11].

In this study, we aimed to evaluate the antibody response induced after two doses of mRNA (Pfizer/BioNTech) or inactivated (Sinovac/CoronaVac) vaccines in a BS cohort followed by a single tertiary medical center. We studied age- and gender-matched immunocompetent individuals as well to compare with BS cohort.

Patients and methods

Study design and description of study population

This cross-sectional study was conducted at Cerrahpasa Medical Faculty of Istanbul University-Cerrahpasa between April and October 2021. We studied patients with BS who were seen consecutively at the Rheumatology outpatient clinic. All those who got two shots of either CoronaVac or BioNTech and volunteered to participate were included in the study. Information about disease duration, clinical type of involvement and current drug use was obtained from the patient's charts. We categorized treatment regimens as: solo colchicine, conventional disease-modifying anti-rheumatic drug (DMARD)-based treatment, anti-tumor necrosis factor (anti-TNF)-based treatment and no treatment.

As healthy controls, we studied healthcare workers and their relatives who did not have an immunocompromised condition or a history of immunosuppressive drug use. All HCs were age- and gender-matched to BS patients and received two shots of either CoronaVac or BioNTech. Those BS patients or HCs who have been diagnosed with COVID-19 verified with positive PCR test or those had been symptomatic for COVID-19 infection but having negative PCR test were not included in the study. Blood collection was done at least 3 weeks after the second dose of vaccination.

Vaccination program in Turkey

The vaccination campaign in Turkey started first with healthcare workers and then continued with the elderly on January 14, 2021. As of April 2, 2021, the country entered the second stage of campaign beginning immunizations for immunocompromised individuals as well as individuals aged 60 and above and other prioritized groups [7, 14]. CoronaVac was the first available vaccine in Turkey for the first 14 weeks; by the first week of April 2021 both vaccines were made available to the general population in Turkey [7, 14]. Second dose was done 28 days after the first inoculation. By July 1, 2021, "booster" vaccines, or third doses were started to be given to healthcare workers and elderly and to other prioritized groups.

Antibody quantification

All venous blood samples were aliquoted after centrifugation at 5000 rpm for 5 min. Serum samples were stored at -20 degrees until the day of the study. For detection of antibodies to SARS-CoV-2 spike protein receptor binding domain (RBD), we used the commercially available Elecsys Anti-SARS-CoV-2 S assay (Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim, Germany) [15]. Antibodies to the RBD of the spike protein of SARS-CoV-2 are recognized as correlates of neutralizing antibodies and hence are frequently used to evaluate the immune response after vaccination [16–19].

The test uses the double-antigen sandwich principle. The antigen within the reagent captures predominantly anti-SARS-CoV-2 IgG, but also anti-SARS-CoV-2 IgA and IgM. The analytical measuring interval is 0.40–25,000 U/mL. Numeric values are interpreted as "negative" (<0.8 U/mL) and as "positive" (≥ 0.80 U/mL) Samples with anti-SARS-CoV-2-S concentrations above the measuring range were diluted 1:100. Titers were expressed in antibody units (AU/ml).

Ethical statement

The study protocol was approved by the Ministry of Health (2021-01-25T14_17_28) and by the Ethics Committee of Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty (10.03.2021-49045). Written informed consent was obtained from each enrolled participant. All study procedures were

carried out in accordance with the ethical standards of the Helsinki Declaration.

Statistical methods

Descriptive statistics were presented as mean and standard or median [interquartile range (IQR)] based on distribution of continuous variables. Categorical variables were presented as frequencies and percentages (%). Continuous variables were evaluated for normality distribution using the Shapiro–Wilk test. Categorical variables were compared by using Chi-square or Fisher's exact test for proportion. Patients with BS and healthy controls were compared using independent-sample *t* test for normally distributed variables and Mann–Whitney *U* test for non-normally distributed variables.

We did not do a sample size analysis due to the lack of information while we were designing the study. However, we performed a post hoc power analysis with G*power version 3.9.12 to determine the required sample size for the comparison of BS and healthy controls (Sinovac/CoronaVac: patients $n=80$ vs HCs $n=89$; Pfizer/BioNTech: 86 patients vs HCs: 76). With 0.5 effect size, two tail and 0.05 level of significance, we calculated the power 89% and 88%, respectively, for Sinovac/CoronaVac and Pfizer/BioNTech groups, respectively.

Antibody titers for treatment subgroups in patients with BS were compared with the Kruskal–Wallis test. Because of the skewness of antibody levels, log transformation was applied on this variable. After the distribution of antibody levels was normalized, linear regression analysis was used to determine the factors affecting the antibody titers on log scale. Multivariable regression analysis was performed to determine the effects of time to the second vaccine dose, vaccine type, smoking, body mass index and current medical treatment on the antibody titers on a log scale after adjusting age and sex. In addition, we used dummy variable in order to assess each treatment effect on antibody titers in a linear-regression model.

All statistical tests were two-tailed, and values of $p<0.05$ were considered statistically significant. All statistical analyses were performed by SPSS software version 21 (Chicago, IL) and R software (version 4.0.2).

Results

We studied 166 (92M/74F; mean age: 42.9 ± 9.6 years) patients with BS and 165 (75M/90F; mean age: 42.4 ± 10.4 years) HCs. A total of 80 (42M/38F) patients with BS and 89 (36M/53F) HCs received two doses of CoronaVac, while 86 (50M/36F) patients with BS and 76 (39M/37F) HCs were vaccinated with two doses of BioNTech.

Demographic and clinical characteristics of the patients with BS are shown in Table 1. A total of 31 (18.8%) patients had only skin-mucosa lesions, whereas the remaining had one or more major organ involvement such as eye (52.4%), vascular (34.3%), neurological (9.6%) and joint (16.3%). Fifty-eight (34.9%) had at least one comorbid disease such as chronic obstructive pulmonary disease, cardiovascular diseases, hypertension, diabetes mellitus and kidney failure. A total of 159 (95.8%) patients were prescribed one or more of the following drugs such as colchicine ($n=83$, 50%), low-dose prednisolone ($n=31$, 18.7%), non-biological DMARDs ($n=99$, 59.6%) and anti-TNF agents ($n=66$, 39.8%). Treatment regimens were defined as no treatment ($n=7$, 4.2%), solo colchicine ($n=36$, 21.7%), non-biological DMARD-based treatment ($n=57$, 34.3%) and anti-TNF-based treatment ($n=66$, 39.8%). Those who were labeled as having non-biological DMARD-based regimen were receiving DMARDs ($n=57$) combined with colchicine ($n=25$) and low-dose prednisolone ($n=12$). Anti-TNF-based regimen included anti-TNF agents ($n=66$) combined with non-biological DMARDs ($n=53$), colchicine ($n=22$) and low-dose prednisolone ($n=19$). There was no statistical difference between the two vaccine groups with regard to mean age, gender ratio, median disease duration, major organ involvement (except joint involvement) and medical treatment regimens.

Antibody results

Patients with BS and their respective healthy controls in either vaccine group were similar with regard to mean age and gender (Table 2). The median time between the second dose of vaccination and blood drawal was also similar between patients and HCs in both groups. Except three patients in the CoronaVac and one in the BioNTech group, all patients and HCs had detectable antibody. Among those vaccinated with CoronaVac, patients with BS had significantly lower antibody titers compared to HCs (Table 2). In the BioNTech group, however, antibody titers were similar between patients and HCs (Table 2). Figure 1 depicts box plots of log-transformed antibody levels between the study groups. Figure 2 shows scatter plot distribution of antibody levels between the study groups. BioNTech induced significantly higher antibody titers compared to CoronaVac among BS patients as well as HCs ($p<0.001$ for each comparison).

As shown in Table 3, Figs. 3 and 4, among different treatment regimen subgroups in both vaccine groups, those who were using anti-TNF based treatment had the lowest median (IQR) antibody titers. However, the difference was statistically significant only among those vaccinated with CoronaVac (Table 3). Among patients vaccinated with BioNTech,

Table 1 Demographic and clinical characteristics of the patients with Behçet's syndrome

	Total, $n=166$	Vaccine type		
		CoronaVac, $n=80$	BioNTech, $n=86$	p
M/F, n (%)	92.0 (55.4)	42.0 (52.5)	50.0 (58.1)	0.465
Age, mean ± SD, years	42.9 ± 9.6	43.9 ± 9.8	42.1 ± 9.4	0.224
Disease duration, median (IQR), years	10.0 (6.75–16.25)	10.0 (6.0–18.25)	10.0 (7.0–16.25)	0.427
Comorbid disease, n (%)	58 (34.9)	24 (30.0)	34 (39.5)	0.198
Organ Involvement, n (%)				
Eye involvement	87 (52.4)	45 (56.3)	42 (48.8)	0.339
Vascular involvement	57 (34.3)	30 (37.5)	27 (31.4)	0.408
Neurological involvement	16 (9.6)	9 (11.3)	7(8.1)	0.602
Joint involvement	27 (16.3)	20 (25.0)	7 (8.1)	0.005
Currently under medical treatment, n (%)	159 (95.8)	77 (96.3)	82 (95.3)	0.773
Colchicine, n (%)	83 (50)	39 (48.8)	44 (51.2)	0.756
Prednisolone, n (%)	31 (18.7)	14 (17.5)	17 (19.8)	0.708
Non-biological DMARDs, n (%)	99 (59.6)	49 (61.3)	50 (58.1)	0.683
Azathioprine, n (%)	86 (51.8)	44 (55.0)	42 (48.8)	0.427
Other DMARDs[ab], n (%)	16 (9.6)	7 (8.8)	9 (10.5)	0.708
Anti-TNF agents[cd]	66 (39.8)	33 (41.3)	33 (38.4)	0.705
Treatment regimens, n (%)				
No treatment	7 (4.2)	3 (3.8)	4 (4.7)	0.601
Colchicine alone	36 (21.7)	14 (17.5)	22 (25.6)	
Non-biological DMARD-based	57 (34.3)	30 (38.8)	27 (31.4)	
Anti-TNF agents based	66 (39.8)	33 (41.3)	33 (38.4)	

DMARDs disease-modifying anti-rheumatic drugs, *TNF* tumor necrosis factor

[a]CoronaVac: Mycophonalate mofetil: $n=5$, cyclosporine: 2

[b]BioNTech: Mycophonalate mofetil: $n=4$, cyclosporine: 3, leflunomide: $n=1$, methotrexate: $n=1$

[c]CoronaVac: Etanercept: $n=2$, Infliximab: $n=18$, adalimumab: $n=11$, certolizumab pegol: $n=2$

[d]BioNTech: Etanercept: $n=2$, Infliximab: $n=19$, adalimumab: $n=12$

Table 2 Demographic characteristics and antibody titers in patient and control groups

	Sinovac/CoronaVac			Pfizer/BioNTech		
	Patients with BS ($n=80$)	Healthy controls ($n=89$)	p	Patients with BS ($n=86$)	Healthy controls ($n=76$)	p
Age, mean ± SD, year	43.9 ± 9.8	44.8 ± 10.0	0.542	42.1 ± 9.4	39.5 ± 10.2	0.154
Gender, male, n (%)	42 (52.5)	36 (40.4)	0.117	50 (58.1)	39 (51.3)	0.384
Time interval between blood drawal and second dose of vaccine, median (IQR) days	49 (40–70) Min–max: 23–116	54 (36–65) Min–max: 25–100	0.659	53 (34–82) Min–max: 26–115	57 (35–78) Min–max: 21–119	0.275
Detectable antibody, n (%)	77 (96.3)	89 (100)	0.104	85 (98.8)	76 (100.0)	1.000
Antibody titers, median (IQR)	36.5 (12.5–128.5)	102.0 (59.0–180.0)	< 0.001	1648.5 (527.0–3693.8)	1516.0 (836.3–2599.5)	0.512

there was no statistically significant difference between different treatment regimen groups.

Table 4 shows multivariable regression analysis that evaluates factors associated with antibody levels in the BS cohort. CoronaVac (compared to BioNTech) ($p<0.001$) and treatment regimen type (anti-TNF-based regimen) ($p=0.014$) were found to be significantly associated with decreased antibody titers among BS patients. Increasing age also tended to be associated with lower antibody titers ($p=0.056$).

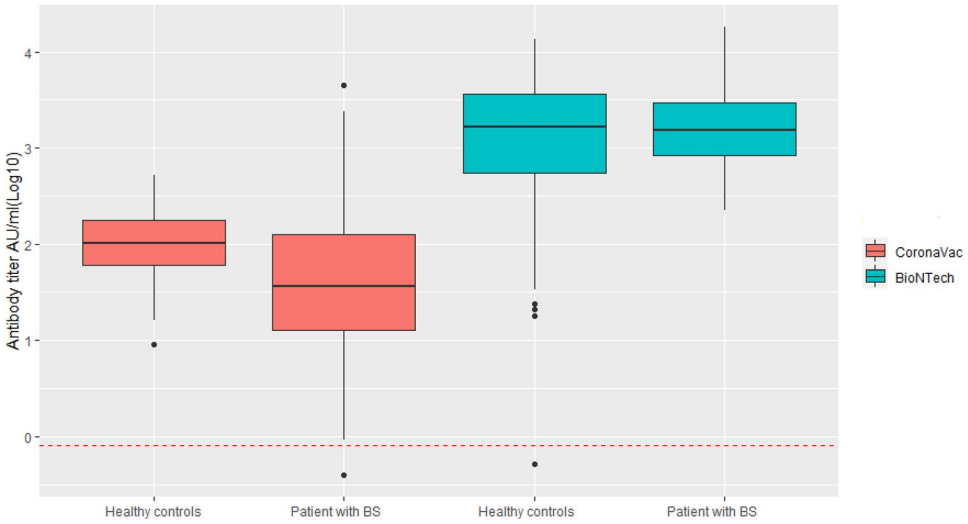

Fig. 1 Box plots showing log-transformed antibody levels according to vaccine type across the study groups. *BS* Behçet's syndrome. Dotted line shows cutoff line for seropositivity

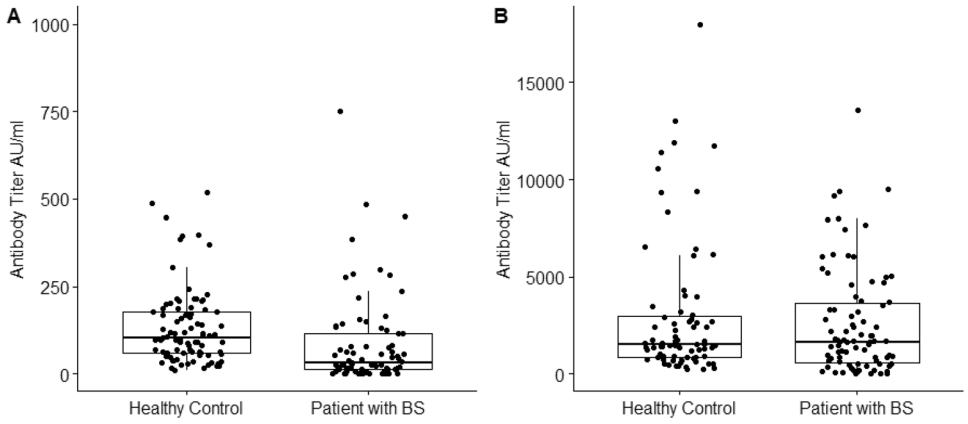

Fig. 2 Scatter plot showing the distribution of antibody titers among patients and healthy controls according to vaccine type: CoronaVac (**A**) and BioNTech (**B**)

Discussion

In this study, we compared antibody response to two different types of SARS CoV-2 vaccines (mRNA -Pfizer/BioNTech and inactivated-Sinovac/CoronaVac) in patients with BS and HCs. To our knowledge, this is the first study evaluating humoral response to SARS CoV-2 vaccines in a BS cohort. We showed that the great majority among both BS patients and HCs had detectable antibody responses after either BioNTech or CoronaVac. BioNTech induced significantly higher titers compared to CoronaVac. Among those vaccinated with CoronaVac, BS patients were found to have significantly lower antibody titers than HCs. Again, in the CoronaVac group, patients who were using anti-TNF-based regimens were found to have significantly lower antibody levels compared to those who were using solo colchicine- or DMARD-based regimens. Among BS patients vaccinated with BioNTech, however, no difference was observed between treatment subgroups as well as between overall patients and their respective HCs.

A few studies compared immune responses to mRNA and inactivated vaccine among immune-competent adults [20], general population [21], healthcare workers [22] and individuals aged 60 years and older [23]. Similar to that observed in our study, vaccination with BNT162b2 induced significantly higher levels of SARS-CoV-2-specific and neutralizing antibody responses compared to CoronaVac [20–23]. Both vaccines induced SARS-CoV-2-specific CD4+ and CD8+ T cell responses but CoronaVac elicited significantly higher CD4+ and CD8+ T cell responses to the structural protein than BNT162b2 [20]. One large population study in Chile ($n = 56.261$) showed that 3 weeks after the second dose, the IgG seropositivity was lower for CoronaVac recipients compared to BNT162b2 (77.4% vs 96.5%) [21]. Moreover, overtime, a decline in IgG seropositivity was observed in CoronaVac recipients, while seropositivity continued to be high

Table 3 Detectable antibody test and antibody titers among patients with Behcet's syndrome according to different treatment regimens

	Sinovac/CoronaVac					Pfizer/BioNTech				
	No treatment $n=3$	Colchicine $n=14$	DMARD-based regimen $n=30$	Anti-TNF-based regimen $n=33$	p	No treatment $n=4$	Colchicine $n=22$	DMARD-based regimen $n=27$	Anti-TNF-based regimen $n=33$	p
Detectable antibody, n (%)	3 (100.0)	14 (100.0)	29 (96.7)	31 (93.9)	0.769	4 (100.0)	22 (100.0)	27 (100.0)	32 (97.0)	0.654
Antibody titers, median (IQR)	115.0 (17.0–166.0)	49.5 (25.5–324.5)	77.0 (27.3–165.8)	12.0 (1.5–39.5)	< 0.001	3923.0 (1234.0–5878.8)	1671.0 (1011.3–3019.8)	1745.0 (908.0–4688.0)	856.0 (188.5–3896.0)	0.197

DMARD disease-modifying anti-rheumatic drug, *TNF* tumor necrosis factor

and stable in those who had received the BNT162b2 vaccine [21]. Another study found that among those who received two doses of CoronaVac, the antibody level increased 105-fold and ninefold with booster BNT162b2 and CoronaVac, respectively [22].

Head-to-head evaluations of humoral responses to SARS-CoV-2 vaccines in immune-compromised populations are also rare [24–28]. In line with our results, antibody titers were reduced with inactivated vaccine compared to mRNA vaccine among both patients and HCs [24–28]. In lupus, an impaired antibody response compared to matched healthy population was reported in both vaccine groups [24]. Among patients with multiple sclerosis (MS), except those who were treated with anti-CD 20 treatment, no significant difference was observed between patients receiving different treatment regimens as well as those who were off treatment in either vaccine group [25]. MS patients treated with anti-CD 20 agents had reduced seropositivity with either vaccine [25, 26]. Among solid organ transplant recipients, while one study observed reduced seropositivity only after CoronaVac (67.5% vs 100%) [27], another reported significantly lower seroconversion rates after either vaccine (29%) in contrast to 100% of healthy controls [28].

While we observed significantly diminished antibody titers in BS patients, especially in those treated with anti-TNF agents compared to healthy individuals among CoronaVac recipients, no such difference was detected in the BioNTech group. We and others have previously shown that immunocompromised patients often fail to show an adequate response to SARS-CoV-2 vaccines, as indicated by lower protective immune response rates compared with healthy individuals [5–8, 24–36]. Almost all DMARDs including mycophenolate mofetil, methotrexate, rituximab, abatacept and glucocorticoids have been shown to blunt humoral responses [7, 24–26, 31–33]. On the other hand, except a few [32, 36], most studies based on the immunogenicity of mRNA vaccines indicated that anti-TNF agents are not associated with a reduced humoral response [34, 35]. Contrasting with these, one large study reported a negative effect of anti-TNF agents on anti-SARS-CoV-2 IgG response among patients with autoimmune diseases vaccinated with two doses of CoronaVac [37].

There is limited information in the literature regarding humoral responses to vaccine among patients with BS. We came across to only one study which investigated antibody response to hepatitis B vaccination (hepatitis B surface antigen prepared by using the recombinant DNA technology) in 13 patients with BS and 15 HCs [38]. After the third dose of vaccination, protective seroconversion rates were 12/13 (92.8%) and 14/15 (93.8%) among BS patients and HCs, respectively [38]. The mean anti-HBs titers in BS and HC groups were 641.885 ± 422.5971 mIU/mL and 428.600 ± 395.8020 mIU/mL, respectively ($p = 0.182$) [38].

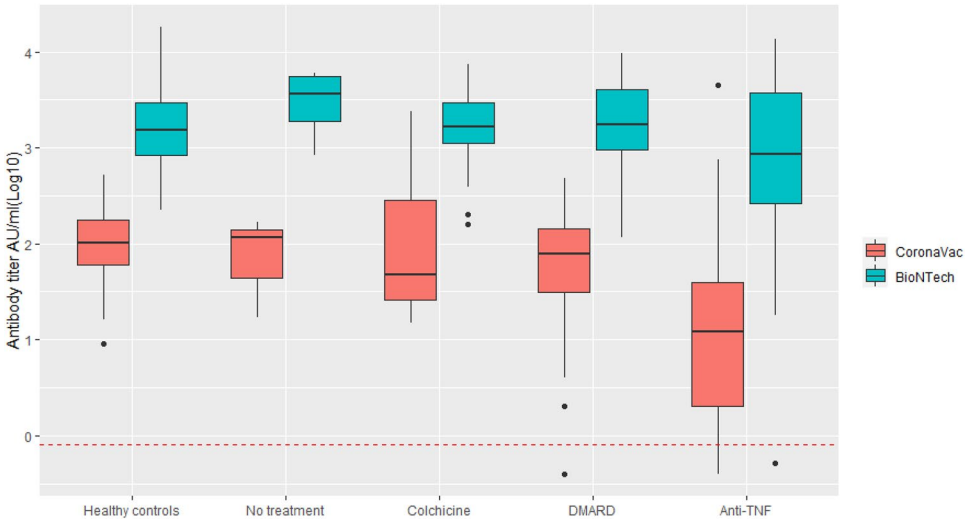

Fig. 3 Box plots showing log-transformed antibody levels regarding vaccine type across different treatment regimens groups and healthy controls. Dotted line shows cutoff line for seropositivity. *DMARD* disease-modifying anti-rheumatic drug, *TNF* tumor necrosis factor

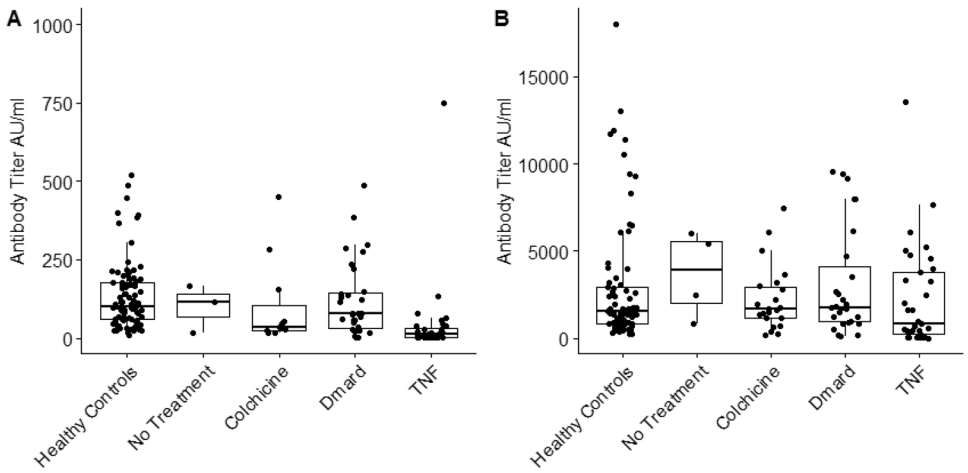

Fig. 4 Scatter plot distribution of antibody titers according to different treatment regimens among BS patients and HCs vaccinated either with CoronaVac (**A**) or BioNTech (**B**). *DMARD* disease-modifying anti-rheumatic drug, *TNF* tumor necrosis factor

Table 4 Multivariable regression analysis assessing factors associated with antibody levels (AU/mL Log)

Variable	Beta (95% CI)	SE	*p*
Age	− 0.013 (− 0.027 to 0.000)	0.007	0.056
Sex (reference category: female)	− 0.173 (− 0.423 to 0.078)	0.127	0.175
Time elapsed between second vaccine dose and blood draw	− 0.004 (− 0.009 to 0.001)	0.003	0.144
Smoking (reference category: non-smoking)	− 0.192 (− 0.424 to 0.040)	0.117	0.104
Vaccine type (reference category: BioNTech)	− 1.537 (− 1.769 to − 1.304)	0.118	< 0.001
Treatment regimens			
Colchicine alone	− 0.121 (− 0.727 to 0.484)	0.306	0.692
Conventional DMARDs	− 0.120 (− 0.710 to 0.471)	0.299	0.689
Anti-TNF agents	− 0.756 (− 1.354 to − 0.158)	0.303	0.014

DMARD disease-modifying anti-rheumatic drug, *TNF* tumor necrosis factor, *SE* standard error

It has to be noted that all BS patients in the study were using only colchicine without any immunosuppressives [38].

In this study, we did not aim to evaluate side effects due to vaccine, which could be a limitation. On the other hand, in our previous study, we specifically studied adverse events and disease flares induced after vaccines against COVID-19 among BS patients ($n = 256$) compared with familial Mediterranean fever (FMF) ($n = 247$) and AIIRD ($n = 601$)

[14]. We observed that BioNTech induced significantly more side effects (mostly mild and transient) when compared to CoronaVac in all study groups. Patients with BS (16.0%) and FMF (17.4%) were found to flare significantly more frequently when compared to those with AIIRD (6.0%) ($p < 0.001$). Disease exacerbations among BS patients were characterized mostly by skin-mucosa lesions and developed regardless of vaccine type. On the other hand, 4.3% patients with BS developed major organ attack such as uveitis, venous thrombosis, or CNS lesions.

This study has several limitations. We did not measure the neutralizing activity of the serum against SARS-CoV-2 or T cell responses. All patients were followed in a single university hospital; our results could not be generalized. Selection bias could not be ruled out. Serum sampling time was not standardized. Also, we evaluated antibody levels at only single time point. Antibody titers could change over time. Although we only included those who had tested PCR negative for COVID-19, there might be some patients who were unaware of their infection and this might have caused increased antibody titers. We were not able to evaluate the disease activity at the time of blood sampling. The number of BS patients who do not use any immunosuppressive or immunomodulating agents including colchicine was low.

Conclusions

We found a robust antibody response to both inactivated vaccine and mRNA-based vaccines among patients with BS as well as healthy controls. BioNTech induced significantly higher titers compared to CoronaVac among both patients and healthy controls. In the CoronaVac group, antibody titers were decreased among BS patients when compared to healthy controls. This was especially true for those who were using anti-TNF agents. Among those vaccinated with BioNTech, however, antibody titers did not differ significantly between BS patients and healthy controls as well as between those receiving different treatment regimens. Further studies should assess whether reduced antibody titers are associated with lower protection against COVID-19.

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Author contributions AO, OKN, ZA, ES and VH contributed to the study conception and design, including material preparation and review the articles. AO, OKN, YT, ZA, YTT, SG, EY, DU, UU and ES collected and analyzed the data. The first draft of the manuscript was written by AO and ES, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript and also agreed to accept full responsibility for the entire work.

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Data availability statement The data that support the findings of this study are available on request from the corresponding author (ES). The data are not publicly available due to (restrictions, their containing information that could compromise the privacy of research participants).

Declarations

Conflict of ınterest Ayse Ozdede, Okan Kadir Nohut, Zeynep Atli, Yeşim Tuyji Tok, Sabriye Guner, Erkan Yilmaz, Didar Ucar, Ugur Uygunoglu and Vedat Hamuryudan declare that they have no conflict of interest. Emire Seyahi has received honoraria, consulting or speaker fees from Novartis, Pfizer, AbbVie and Gilead.

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