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The Predictors of COVID-19 Immunogenicity Elicited by Vaccines Against SARS-CoV-2 in Stem Cell Transplant Recipients

Kemik İliği Nakli Alıcılarında COVID-19'a Karşı Aşılar Tarafından Oluşturulan İmmünojenitenin Belirleyicileri

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ABSTRACT

Introduction: *The literature falls short in providing thorough investigations into the influence of COVID-19 vaccination among those undergoing hematopoietic stem cell transplantation (HSCT).*

Materials and Methods: *This prospective study evaluates COVID-19 antibody levels in HSCT recipients. The HSCT patients, having undergone transplantation at least three months prior, received BNT162b2 mRNA, Gam-COVID-Vac adenoviral, or BBIBP-CorV inactivated vaccines. Blood samples were taken 2-24 weeks post second dose.*

Results: *The study involved 28 participants, comprising nine allogeneic-HSCT and 19 autologous-HSCT recipients. Among them, 18 (64.2%) exhibited positive results in SARS-CoV-2 neutralizing antibody tests, occurring at a median of 10.5 weeks (ranging from 2 to 24 weeks). In multivariate logistic regression analysis, age and a higher Charlson Comorbidity Index emerged as statistically significant variables linked with suboptimal antibody responses. Interestingly, no significant disparities surfaced in terms of anti-SARS-CoV-2 spike, SARS-CoV-2 (IgG + neutralizing) antibodies, and SARS-CoV-2 (neutralizing) antibodies titers across various vaccine types and transplantation modes. However, the anti-SARS-CoV-2 nucleocapsid titers demonstrated a significant increase in patients*

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who received the BBIBP-CorV inactivated vaccine (Sinopharm, China). Moreover, within the non-vaccinated BMT subgroup, a slightly higher yet insignificant incidence of COVID-19 was observed in comparison to the vaccinated subgroup (2/28-7.1% vs. 3/11-27.2%, p= 0.125). During the six-month post-vaccination follow-up, COVID-19 incidence was 144.9 per 1000 patient-years in the vaccinated group, contrasting with 545.4 per 1000 patient-years in the unvaccinated group. Hence, a substantial vaccination efficacy of 73.4% was noted. No fatalities were reported among either vaccinated or unvaccinated HSCT patients who contracted COVID-19 during the 30-day follow-up period.

Conclusion: *The inactivated vaccine demonstrated antibody responses comparable to the Pfizer-BioNTech vaccine.*

Key Words: *Antibody; Stem cell transplantation; COVID-19; Hematology; Vaccine*

ÖZ

Kemik İliği Nakli Alıcılarında COVID-19'a Karşı Aşılar Tarafından Oluşturulan İmmünojenitenin Belirleyicileri

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Giriş: *Literatürdeki veriler, hematopoietik kök hücre nakli (HKHN) alıcılarında COVID-19 aşısının etkisine ilişkin kapsamlı araştırmalar sağlama konusunda kısıtlıdır.*

Materyal ve Metod: *Bu prospektif çalışma, HKHN alıcılarında COVID-19 antikor düzeylerini değerlendirmektedir. Hematopoietik kök hücre nakli alıcılarına nakilden en az üç ay sonra BNT162b2 mRNA, Gam-COVID-Vac adenoviral veya BBIBP-CorV inaktif aşılarından biri uygulandı. Kan örnekleri ikinci dozdan 2-24 hafta sonra alındı.*

Bulgular: *Çalışmaya, dokuzu allojenik ve 19'u otolog olmak üzere toplam 28 HKHN alıcısı dahil edildi. Bunların 18'inde (%64.2) ortalama 10.5 haftada (2 ile 24 hafta arasında değişen) SARS-CoV-2 nötralizan antikor testleri pozitif saptandı. Çok değişkenli lojistik regresyon analizinde, ileri yaş ve yüksek Charlson Komorbidite indeksi, optimalin altında antikor yanıtıyla istatistiksel olarak anlamlı düzeyde ilişkili bulundu. İlginç bir şekilde, farklı aşı türleri ve nakil türleri arasında, SARS-CoV-2 spike antikor, SARS-CoV-2 (IgG + nötralizan) antikor ve SARS-CoV-2 nötralizan antikor titreleri açısından anlamlı bir farklılık saptanmadı. Ancak anti-SARS-CoV-2 nükleokapsid antikor titresi, BBIBP-CorV inaktif aşısı (Sinopharm, Çin) yapılan hastalarda önemli bir artış gösterdi. Ayrıca aşılanmamış HKHN alıcıları alt grubunda, aşılanmış alt gruba kıyasla biraz daha yüksek ancak istatistiksel olarak anlamsız COVID-19 insidansı gözlendi (%2/28-7.1'e karşı %3/11-27.2, p= 0.125). Aşılamadan sonraki altı aylık takip sırasında, aşılanan grupta COVID-19 insidansı 1000 hasta yılı başına 144.9 iken, aşılanmamış grupta 1000 hasta yılı başına 545.4 idi. Dolayısıyla %73.4'lük önemli bir aşılama etkinliği kaydedildi. COVID-19 ile infekte olan hem aşılanmış hem de aşılanmamış HKHN alıcılarında 30 günlük takip süresi içinde mortalite görülmedi.*

Sonuç: *Hematopoietik kök hücre nakli alıcılarında inaktif COVID-19 aşısı, Pfizer-BioNTech aşısıyla benzer antikor yanıtları gösterdi.*

Anahtar Kelimeler: *Antikor; Kemik iliği nakli; COVID-19, Hematoloji; Aşı*

INTRODUCTION

Patients with hematologic malignancies and hematopoietic stem cell transplantation (HSCT) are excessively vulnerable groups for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection. Infection-related hospitalization, intensive care unit admission, and mortality rates are significantly higher in these patients[1,2]. Thus, protecting this population from the infection with effective vaccination is of utmost importance.

As per the European Society for Blood and Marrow Transplantation and the American Society of Transplantation and Cellular Therapy, patients with HSCT are recommended to receive SARS-CoV-2 vaccination after three months of transplantation[3,4]. However, immunological response to vaccines might be reduced due to the immunosuppressive nature of the disease and treatments. The efficacy of the vaccines in patients with HSCT is not well known since they were excluded from the vaccine phase three studies[5,6].

Although there are some clinical studies, the data on serological responses after SARS-CoV-2 vaccination in HSCT patients are scarce[7-10]. Therefore, we conducted this prospective study to evaluate antibody levels (Abs) predictive factors of poor response, COVID-19 contraction rates and vaccine efficacy in HSCT recipients at our facility.

MATERIALS and METHODS

Study Design and Participants

In this prospective single-center study, patients with allogenic (allo-HSCT) or autologous HSCT (auto-HSCT) history were vaccinated with one of the following vaccines according to standard protocols: BNT162b2 mRNA vaccine (Pfizer-BioNTech, Germany), Gam-COVID-Vac adenoviral-based vaccine (Sputnik V, Russia) or BBIBP-CorV inactivated vaccine (Sinopharm, China). The choice of vaccine type was based on patient preferences.

All participants received two doses of vaccines between January-July 2021. Clinical status of the underlying malignancy, details of treatment, conditioning regimens, immunosuppressive drug use, and graft versus host disease (GvHD) status at the time of vaccination were also recorded. No control group was used in the study.

a) Inclusion criteria: i) allogeneic-HSCT or autologous-HSCT history of ≥3 months prior to vaccination[3,4], ii) age ≥18 years at inclusion.

b) Exclusion criteria: patients i) receiving ≥2 mg/kg/day of steroid[11] or equivalent, ii) with an interval between the second dose of vaccination and blood collection for SARS-CoV-2 antibody control exceeding 24 weeks.

Blood collection

Blood samples were collected between two and 24 weeks after the second dose of the vaccine. Vaccine-related adverse events including local and systemic reactions were inquired at the time of blood collection.

The study protocol was approved by the local institutional review board committee (reference code: 21- 428). Informed consent was obtained from all participants.

Serological testing procedures

SARS-CoV-2 neutralizing Abs were quantified by using FDA-approved enzyme immunoassay (ELISA)-based surrogate neutralization assay (cPass, Genscript), as instructed by the manufacturer[12]. Anti-SARS-CoV-2 spike (S) and anti-SARS-CoV-2 nucleocapsid (N) were detected by using electrochemiluminescence immunoassay (ECLIA) from Roche, as instructed by the manufacturer[13]. The cut-off index (COI) was considered 1 for anti-SARS-CoV-2 (N) and 0.8 U/mL for anti-SARS-CoV-2 (S) antibodies. For SARS-CoV-2 (IgG + Neutralizing) Abs Quant assay chemiluminescent microparticle immunoassay (CMIA), on the Alinity I system was used for the qualitative and quantitative determination of IgG antibodies, including neutralizing antibodies, to the receptor binding domain (RBD) of the S1 subunit of the spike protein of SARS-CoV-2 in serum and plasma.

COVID-19 Contraction Analysis

We compared the incidence of COVID-19 between two time points: T1, which corresponds to day 15 after the second dose of the COVID-19 vaccine in the first vaccinated case during

the study period (i.e., February 15, 2021), and T2, which is 180 days after T1 (i.e., day 195). This comparison was conducted both in our study sample and in the non-vaccinated bone marrow transplant (BMT) population in our setting. COVID-19 infection data was collected from the electronic medical record system of the hospital. This system is integrated with the public health system of the country to disclose the results of the samples collected at other health centers.

Statistical Analysis

Descriptive statistics were calculated as mean, standard deviation, count, and percent, depending on the type of variables. The relationships between vaccine response and categorical variables were assessed with the Pearson Chi-square test or Fisher-Freeman-Halton test. Numerical variables of those with and without vaccine response, the time interval between the second vaccine dose (Sinopharm and Pfizer-BioNTech vaccines) to antibody control, and the antibody response of the previously COVID-19 infected cohort vs. others were compared with Mann-Whitney U test. A $p \leq 0.05$ was considered the threshold for statistical significance.

The following variables were entered into the multivariate binary logistic regression model, and their adjusted effects were identified: gender, type of bone marrow transplant (BMT), Charlson Comorbidity Index (CCI) value, the interval between the second dose of the vaccine and blood collection (in weeks), age, and anti-SARS-CoV-2 (S). The final model was determined by removing variables with no significant effect using the Backward LR variable elimination method. The sensitivity of this model in predicting those with a vaccine response was 83.3% (=15/18), and the specificity in predicting those without a vaccine response was 60% (=6/10). The overall accuracy of the model was calculated as 75%. All analyses were performed by using the statistical software SPSS (ver. 25).

RESULTS

Patient Characteristics

A total of 28 HSCT recipients (n= 9 allo-HSCT and n= 19 auto-HSCT) were included in the study. The characteristics of the patients included in the univariate analysis are summarized in Table 1. The median age was 45 years (range 19-69, mean 43.6 ± 14.1). Overall, the most common hematological disease was diffuse large B-cell lymphoma (n= 7, 25%) and multiple myeloma (n= 7, 25%) followed by Hodgkin lymphoma (n= 6, 21.4%).

The median interval between stem cell transplantation and the first dose of vaccine was 17 interquartile range (IQR) 13-31, mean 23.4 ± 15.4) months and the median interval between two vaccine doses was 21 (IQR 21-21, mean 21.0 ± 1.1) days. The median time interval between the second vaccine dose to antibody control was 10.5 (IQR 8.7-12, mean 11 ± 5.1) weeks; IQR 8-15.7, mean 10.9 ± 5.4 for Sinopharm and IQR. 9.7-11.2, mean 9.8 ± 2.5 for Pfizer-BioNTech. There was no significant difference between the Sinopharm and Pfizer-BioNTech cohort (p= 0.977).

Serological response to COVID-19 vaccination

Overall, SARS-CoV-2 neutralizing antibody tests were positive in 18 (64.2%) recipients at a median of 10.5 weeks (range, 2-24 weeks) after the full vaccination schedule.

None of the analyzed antibody levels differed significantly between the cohort who had previous COVID-19 infection before vaccination (n= 4) vs. others (p> 0.05) (Table 2).

In univariate analysis, the vaccine response in allo-HSCT recipients was significantly higher than in auto-HSCT recipients (p= 0.047). There was no statistically significant difference in other parameters including the type of vaccine between the two groups.

However, in multivariate logistic regression analysis, age and higher CCI were the statistically significant variables that were associated with poor antibody response. Univariate and multivariate analysis results are summarized in Table 3.

Comparison of serological response in Sinopharm and Pfizer-BioNTech subgroups

When we compared the serological response to Pfizer-BioNTech and Sinopharm vaccines in

Table 1. Univariate analysis of predictive factors of vaccine response

	SARS-CoV-2 (Neutralizing) Abs Response			
	Negative	Positive	Total	
	n (%)	n (%)	n	p*
Gender				
• Male	7 (41.2%)	10 (58.8%)	17	p> 0.05
• Female	3 (27.3%)	8 (72.7%)	11	
Age				
	48 ± 11.85	41.28 ± 15.235		p> 0.05
Charlson Comorbidity Index				
	1.5 ± 0.972	2.33 ± 1.372		p> 0.05
Type of BMT				
• Allogenic	1 (11.1%)	8 (88.9%)	9	p< 0.05
• Autologous	9 (47.4%)	10 (52.6%)	19	
Comorbidities				
• G6PD deficiency	2 (28.6%)	13 (61.9%)	21	p> 0.05
• Diabetes mellitus	2 (33.3%)	4 (66.7%)	6	p> 0.05
• BPH	0	1 (100%)	1	p> 0.05
• Hyperlipidemia	0	1 (100%)	1	p> 0.05
• Hypothyroidism/ • Hyperthyroidism	2 (66.7%)	1 (33.3%)	3	p> 0.05
• Hypertension	3 (60%)	2 (40%)	5	p> 0.05
• COPD	0	1 (100%)	1	p> 0.05
Interval Between Second Dose of Vaccine and Blood Collection				
• 1-4 weeks	2 (50%)	2 (50%)	4	p> 0.05
• 5-8 weeks	1 (33.3%)	2 (66.7%)	3	
• 9-12 weeks	4 (26.7%)	11 (73.3%)	15	
• 17-20 weeks	3 (60%)	2 (40%)	5	
• 24 weeks	0 (35.7%)	1 (100%)	1	
Radiotherapy History				
• Yes	3 (42.9%)	4 (57.1%)	7	p> 0.05
• No	7 (33.3%)	14 (66.7%)	21	
Conditioning Regimen				
• BEAM	3 (27.3%)	8 (72.7%)	11	p> 0.05
• Melphalan	5 (71.4%)	2 (28.6%)	7	
• Myeloablative	1 (12.5%)	7 (87.5%)	8	
• Others	1 (50%)	1 (50%)	2	
Status of the Disease Pre-Transplantation				
• Complete response	7 (33.3%)	14 (66.7%)	21	p> 0.05
• VGPR/PR	2 (50%)	2 (50%)	4	
• Active disease	1 (33.3%)	2 (66.7%)	3	
Status of the Disease Post-Transplantation				
• Complete response during the vaccination and antibody control period	7 (29.2%)	17 (70.8%)	24	p> 0.05
• VGPR/PR	3 (75%)	1 (25%)	4	

BEAM: Carmustine etoposide cytarabine melphalan, BMT: Bone marrow transplantation, BPH: Benign prostatic hyperplasia, COPD: Chronic obstructive pulmonary disease, G6PD: Glucose-6-phosphate dehydrogenase, SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, VGPR/PR: Very good partial response/partially response.

Table 1. Univariate analysis of predictive factors of vaccine response (continue)

	SARS-CoV-2 (Neutralizing) Abs Response			
	Negative	Positive	Total	
	n (%)	n (%)	n	p*
Vaccine Type				
• BNT162b2 mRNA	2 (25%)	6 (75%)	8	
• BBIBP-CorV inactivated	7 (38.9%)	11 (61.1%)	18	p> 0.05
• Gam-COVID-Vac adenoviral-based	1 (50%)	1 (50%)	2	

* Fisher-Freeman-Halton exact test.
Blood sample was not collected 13-16 weeks after the second dose of vaccine.

Table 2. Antibody levels based on COVID-19 infection history

	Previous COVID-19 infection, mean ± SD (n= 4)	No previous COVID-19 infection, mean ± SD (n= 24)
Anti-SARS-CoV-2 (S)	7282 ± 11304	1428 ± 5176
Anti-SARS-CoV-2 (N)	9.5 ± 13	5 ± 11.7
SARS-CoV-2 (IgG + Neutralizing) Abs	15719 ± 21028	2790 ± 3620
SARS-CoV-2 (Neutralizing) Abs, titer	63.8 ± 38.6	45.5 ± 33.5

Table 3. Multivariate analysis results

			95% CI for OR	
	p	OR	Lower	Upper
Charlson Comorbidity Index (CCI) value	**0.022**	2.943	1.171	7.398
Age	**0.034**	0.917	0.846	0.994
Constant	0.147	10.743		

Variable(s) entered on step 1: Gender, type of BMT, Charlson comorbidity index (CCI) value, interval between the second dose of vaccine and blood collection (weeks), age, anti-SARS-CoV-2 (S).

the overall study group, the anti-SARS-CoV-2 (N) antibody response was significantly higher (p< 0.001) in the patients vaccinated with Sinopharm. However, there was no difference in the anti-SARS-CoV-2 (S), SARS-CoV-2 (IgG + Neutralizing) antibodies, and SARS-CoV-2 (Neutralizing) antibodies (Table 4).

COVID-19 contraction analysis

The non-vaccinated BMT subgroup contracted COVID-19 at a non-significantly higher rate than the vaccinated subgroup at the six-month follow-up (2/28-7.1% vs. 3/11-27.2% p= 0.125) (Table 5). In the vaccinated group, COVID-19 incidence did not differ significantly between the

Table 4. Comparison of the serological responses to the BioNTech-Pfizer and Sinopharm vaccines

	BioNTech - Pfizer	Sinopharm	p*	p**
Anti-SARS-CoV-2 (S)	3623 ± 8675 (n= 8)	1927 ± 5792 (n= 17)	0.566	0.628
Anti-SARS-CoV-2 (N)	0.17 ± 0.28 (n= 8)	8.8 ± 13.9 (n= 17)	0.021	<0.001
SARS-CoV-2 (IgG + Neutralizing) Abs	2062 ± 2905 (n= 6)	6663 ± 11656 (n= 11)	0.363	0.366
SARS-CoV-2 (Neutralizing) Abs	56.7 ± 38 (n= 8)	47.2 ± 33.6 (n= 17)	0.535	0.382

Abs: Antibodies.
*: Independent samples t-test; **: Mann-Whitney U test.

Table 5. COVID-19 contraction data of the study cohort during six month follow-up

	Incidence (x/y) after six months (day 195) of the second dose	Incidence/total patient years after six months of the second dose
Study sample	2/28 (7%)	2/13.8 (14.5%)
Neutralizing antibody positive	0/17 (0%)	0/8.3 (0%)
Neutralizing antibody negative	2/10* (20%)	2/4.9 (40.8%)
Non vaccinated BMT cases	3/11 (27.3%)	3/5.5 (84.7%)
Sinopharm subgroup	2/18 (11.1%)	2/8.8 (22.7%)
BioNTech/Pfizer subgroup	0/8 (0%)	0/3.9 (0%)

BMT: Bone marrow transplantation, BOC: Bahrain oncology center.
*One case did not have neutralizing antibody data
[1]COVID-19 contraction analysis was performed for the dates 15 February 2021 to 15 August 2021.

neutralizing antibody-positive cohort and others at the six-month follow-up (p= 0.128), as well as between the Pfizer-BioNTech receiving cohort and the Sinopharm receiving cohort (p= 1). COVID-19 incidence during the six-month post-vaccination follow-up after vaccination was 144.9 per 1000 patient-years in the overall vaccinated group (227.27 per 1000 patient-years in the Sinopharm group and 0 per 1000 patient-years in the Pfizer-BioNTech group), compared to 545.4 per 1000 patient-years in the unvaccinated group, suggesting an overall vaccination efficacy of 73.4% (95% CI= 72%-74.7%). The vaccine efficacy for Sinopharm was 58.3% (95% CI= 57.4%-59.2%), and 99.99% (95% CI= 99.9%-100%) in the Pfizer-BioNTech group. None of the vaccinated or unvaccinated HSCT patients who contracted COVID-19 died during the 30-day follow-up.

Of note, four recipients had prior PCR-confirmed COVID-19 infection before vaccination, and one of them was hospitalized due to severe infection. Of the four previously infected cases, two patients had another COVID-19 infection episode within six months after the second dose of vaccine: one of them 2-4 weeks and the other one 5-12 weeks after the second dose of vaccine.

DISCUSSION

This study focused on the assessment of post-vaccination COVID-19 antibody titers among BMT patients and subsequently compared their incidence of COVID-19 contraction with that of the non-vaccinated cohort. Accordingly, age and higher CCI were significantly associated with poor antibody response in the multivariate analysis. There was no significant difference in anti-SARS-CoV-2 (S), SARS-CoV-2 (IgG + Neutralizing) and SARS-CoV-2 (Neutralizing) antibody titers among the patients vaccinated with mRNA (Pfizer-BioNTech) and inactive (Sinopharm) COVID-19 vaccine. COVID-19 incidence was not significantly higher in the unvaccinated BMT patients compared to the vaccinated BMT patients. In addition, there was no significant difference in COVID-19 incidence between neutralizing antibody-positive and -negative patients. Although not statistically significant, Sinopharm recipients were more likely to be infected with COVID-19 compared to individuals vaccinated with Pfizer-BioNTech.

There are various parameters that may affect the response to vaccination in BMT patients including underlying comorbid conditions, age, the types of conditioning regimens used, radiation therapy, status of underlying hematological malignancy in pre- and post-transplant period, the types of vaccines administered, and the timing of serological test after vaccination[14]. In this study, we have shown that advanced age and a higher Charlson Comorbidity Index (CCI) are major factors affecting the response to COVID-19 vaccination, consistent with previous studies[15-17]. Importantly, there was no significant difference between the efficacy of inactivated and mRNA vaccines in both allo-HSCT and auto-HSCT groups. Although a significant relationship

was found between underlying comorbidity and vaccine response, this can be interpreted as the comorbidities of the patients not having a significant effect on the vaccine response. The other parameters appeared to have no significant effects on the response to COVID-19 immunization.

While previous research has demonstrated elevated COVID-19 IgG titers following mRNA vaccination compared to inactivated vaccine within the general population[18], our study, in contrast, did not reveal any notable distinction in antibody titers for anti-SARS-CoV-2 (S), SARS-CoV-2 (IgG + Neutralizing) Antibodies, and SARS-CoV-2 (Neutralizing) Antibodies. Furthermore, there was a significant elevation in the anti-SARS-CoV-2 (N) titers, while the SARS-CoV-2 (IgG + Neutralizing) antibody titers exhibited a non-significant increase following the administration of the Sinopharm vaccine.

The mRNA vaccine induces T cell responses that narrowly target the spike protein which is also the most prone antigen to mutations. However, inactivated whole-virus vaccine also leads to broader responses against epitopes of spike, nucleocapsid, and membrane proteins[19]. Hence, BBIBP-CorV could further mitigate the possibility of immune escape by new mutations compared with the BNT162b2 vaccine. This immune mechanism may explain the similarity of anti-SARS-CoV-2 (S), SARS-CoV-2 (IgG + Neutralizing) antibody, and SARS-CoV-2 (Neutralizing) antibody titers, as well as the higher anti-SARS-CoV-2 (N) antibody titers in BBIBP-CorV whole-virus vaccine compared to BNT162b2 vaccine. In addition, the variabilities of the antibody responses may be a result of the genetic variability among individuals, including ABO Groups, HLA, or other immune response genes[20]. It has been observed that the antibody response after the COVID-19 vaccine wanes over time and mostly within six months[21-25]. It is important to note that, definitive levels for protective antibodies have yet to be defined. Hence, preventive measures such as using masks and practicing social distancing should be maintained by the patients regardless of antibody results.

The detection of anti-spike antibodies was linked to a relatively diminished likelihood of PCR-confirmed SARS-CoV-2 infection during the six-month follow-up period (0/17 vs. 2/10 p= 0.128). The presence of anti-spike antibodies was found to be associated with a substantially reduced risk of PCR-confirmed SARS-CoV-2 infection over six months of follow-up[26]. However, in our study, no significant difference was found in the incidence of PCR-positive COVID-19 infection among neutralizing antibody-positive and -negative patients. This might be explained by the difference between spike protein antibody and neutralizing antibody protection or the host's immune status. In addition, individuals vaccinated with Sinopharm have been found more likely to contract COVID-19 compared to those vaccinated with Pfizer-BioNTech in the normal population (adjusted incidence rate ratio, 1.62; 95% CI, 1.43-1.85)[27]. In our study, individuals vaccinated with Sinopharm were also observed to have lower protection against COVID-19 infection compared to those vaccinated with Pfizer-BioNTech, although this difference was not statistically significant.

Our study has several limitations. One of the main limitations is the small sample size, which may have impacted the robustness of our analysis. The interval between the second dose of vaccine and blood collection for antibody response was relatively wide although the samples were collected within six months of hospitalization. While acknowledging that PCR-negative cases may also develop COVID-19, the contraction data in our study primarily relied on PCR analysis[28]. Baseline COVID-19 antibody levels were not known in any case; however, since the study was conducted during the early stages of the pandemic, it was less likely to observe baseline positivity. Gam COVID-19 vaccine was administered to only two patients, Hence, no analysis could be performed regarding the Gam vaccine results. The unvaccinated BMT patient cohort was used to evaluate the overall vaccine efficacy; however, we did not have their COVID-19 antibody levels during the study period. Nevertheless, to our knowledge, this is the first study comparing the Sinopharm vaccine

and Pfizer-BioNTech vaccine in HSCT patients. Remarkably, the antibody response elicited by the Sinopharm vaccine was not lower than that elicited by the Pfizer-BioNTech vaccine in our study sample. Moreover, the fact that, as expected, the Sinopharm vaccine significantly increased the anti-SARS-CoV-2 nucleocapsid (N) antibody titer more than Pfizer-BioNTech, may be an advantage in that the elicited immunogenicity can also be effective against the spike antigen of the mutant viruses. COVID-19 contraction rate was non-significantly lower in vaccinated versus non-vaccinated cohort.

ETHICS COMMITTEE APPROVAL

This study was approved by the King Hamad University Hospital Institutional Review Board (Decision no: 21-428, Date: 03.05.2021).

CONFLICT of INTEREST

No conflicts of interest are disclosed by the authors.

AUTHORSHIP CONTRIBUTIONS

Concept and Design: UE, HE, LK, CPO, HAb, NB, OS, EF, ORS

Analysis/Interpretation: HA, HE, ORS

Data Collection or Processing: CSDR, JP, CV, SH

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Review and Correction: UE, HE, HA, CSDR, JP, CV, SH, LK, CPO, HAb, NB, OS, EF, ORS

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