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Follow up and comparative assessment of IgG, IgA, and neutralizing antibody responses to SARS-CoV-2 between mRNA-vaccinated naïve and unvaccinated naturally infected individuals over 10 months

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ABSTRACT

Background: Evidence on the effectiveness of vaccination-induced immunity compared to SARS-CoV-2 natural immunity is warranted to inform vaccination recommendations.
Aim: In this study, we aimed to conduct a comparative assessment of antibody responses between vaccinated naïve (VN) and unvaccinated naturally infected individuals (NI) over 10 Months.
Method: The study comprised fully-vaccinated naïve individuals (VN; n = 596) who had no history of SARS-CoV-2 infection, and received two doses of either BNT162b2 or mRNA-1273, and naturally infected individuals who had a documented history of SARS-CoV-2 infection and no vaccination record (NI cohort; n = 218). We measured the levels of neutralizing total antibodies (NtAbs), anti-S-RBD IgG, and anti-S1 IgA titers among VN and NI up to ~10 months from administration of the first dose, and up to ~7 months from SARS-CoV-2 infection, respectively. To explore the relationship between the antibody responses and time, Spearman's correlation coefficient was computed. Furthermore, correlations between the levels of NtAbs/anti-S-RBD IgG and NtAbs/anti-S1 IgA were examined through pairwise correlation analysis.
Results: Up to six months, VN individuals had a significantly higher NtAb and anti-S-RBD IgG antibody responses compared to NI individuals. At the 7th month, there was a significant decline in antibody responses among VN individuals, but not NI individuals, with a minimum decrease of 3.7-fold ($p < 0.001$). Among VN individuals, anti-S1 IgA levels began to decrease significantly (1.4-fold; $p = 0.007$) after two months, and both NtAb and S-RBD IgG levels began to decline significantly (NtAb: 2.0-fold; $p = 0.042$, S-RBD IgG: 2.4-fold; $p = 0.035$) after three months. After 10 months, the most significant decline among VN individuals was observed for S-RBD-IgG (30.0-fold; $P < 0.001$), followed by NtAb (15.7-fold; $P < 0.001$) and S-

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IgA (3.7-fold; $P < 0.001$) (most stable). Moreover, after 5 months, there was no significant difference in the IgA response between the two groups.
Conclusion: These findings have important implications for policymakers in the development of vaccination strategies, particularly in the consideration of booster doses to sustain long-lasting protection against COVID-19.

Introduction

The recent Coronavirus disease 19 (COVID-19) outbreak has declared a global emergency. On March 11, 2020, the World Health Organization (WHO) declared the disease as a pandemic [1]. The Food and Drug Administration (FDA) and the European Medicines Agency (EMA) authorized the first mRNA-based vaccines: BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna). The efficacy of BNT162b2 and mRNA-1273 was reported to be 90.3–97.6% [2], and 89.3–96.8% [3], respectively.

While COVID-19 vaccinations are typically advised for all people 12 years of age or above [4], and the overall probability of serious adverse effects is thought to be very low, the risk/benefit ratio may differ for those who do not expect the same benefit or who are at a greater risk of side effects. Individuals previously infected with SARS-COV-2 and recovered constitute a significant subpopulation in this category, which today accounts for ~532 million people globally [5].

On December 21, 2020, Qatar launched a mass coronavirus disease 2019 (COVID-19) immunization campaign, first using BNT162b2 and, five months later, the mRNA-1273 vaccine [6,7]. As of February 26, 2022, ~ 88% of persons aged 12 and above have been fully vaccinated with a minimum of two doses [8]. When vaccination was ramped up, the country experienced two back-to-back waves dominated by the B.1.1.7 (or alpha) and B.1.351 (or beta) variants from January to June 2021 [9]. The B.1.617.2 (or delta) variant was first detected in the community at the end of March 2021, and by the summer of 2021, it had become the dominant variant [10]. Despite widespread vaccination, the number of people infected with SARS-CoV-2 increased gradually in Qatar beginning in November 2021, with a significant ten-fold increase in the number of new COVID-19 cases in just two weeks, beginning December 29, 2021, and ending January 12, 2022, when Qatar reached an all-time high number of new daily cases [11]. As a result, protecting against novel variants using pre-existing antibodies derived from natural infection or vaccination has become a major problem.

Vaccinations are now presently recommended by the Centers for Disease Control (CDC) for all eligible individuals, including those who have been previously infected [12]. Nevertheless, a heated public discussion is still raging over whether recovered COVID-19 patients have adequate natural immunity and if COVID-19 vaccination provides any significant additional benefit. According to recent data, people who have been fully-vaccinated and previously infected with SARS-CoV-2 have a low risk of infection for at least 6 months before antibody levels begin to decline [12]. Furthermore, a new study suggests that spontaneous infections give protection against reinfection for at least 8–12 months and that vaccination provides significant protection against the Delta variant [13].

The relative degree of antibody response provided by vaccine-induced immunity compared to the immune responses induced by natural infection remain unclear, particularly in terms of neutralizing capacity and IgA response, with most studies focusing on investigating IgG and IgM levels only [12]. Furthermore, there is presently no FDA-approved serology test that clinicians or the general public may use to determine if a person is immune to SARS-CoV-2 infection [12]. Therefore, this study aimed to comprehensively assess the dynamics of neutralizing total antibodies (NtAbs), anti-S-RBD-IgG, and anti-S1 IgA antibody responses among vaccinated naïve (VN) and unvaccinated naturally infected (NI) individuals in Qatar.

Methods

Ethical approval

Qatar University Institutional Review Board (QU-IRB 1537-FBA/21) reviewed and approved the study. Before collecting the samples, the participants were required to provide their informed consent by answering questions related to their demographic information and medical history, including any past occurrence of COVID-19 infection. The sample collection process was conducted in an anonymous manner, with no identifying information being used.

Study design and sample collection

The study included 814 samples collected between February and December 2021 from staff and students of Qatar University, the largest national university in Qatar. A self-administered questionnaire was used to gather information on participants' demographic characteristics, vaccination schedules, and previous SARS-CoV-2 infection status. Based on their vaccination and infection history, the study participants were stratified into two main groups: unvaccinated individuals with a prior history of SARS-CoV-2 infection (NI; n = 218) and vaccinated, previously uninfected individuals who tested negative for anti-N antibodies and received two doses of either BNT162b2 or mRNA-1273 (VN; n = 596). Samples with unknown vaccination date were excluded. Venous blood samples were collected at various time points up to 7 months post-SARS-CoV-2 infection (median: 2.27 months) for the NI group (n = 218) and up to 10 months post-receiving the first dose (median: 4.30 months) for the VN group (n = 596).

Serology testing

All samples were centrifuged, and plasma was isolated from whole blood in order to test for: (1) neutralizing total antibodies (NtAbs), (2) antibodies against the RBD of the viral spike protein's S1 subunit (anti-S-RBD IgG), (3) IgA against the recombinant S1 domain of the viral spike protein (anti-S1 IgA), and (4) anti-nucleocapsid IgG (anti-N).

Neutralizing total antibodies (NtAbs)

Neutralizing Antibodies (NtAbs) were measured using the automated analyzer Mindray CL-900i® (Catalog No. SARS-CoV-2 Neutralizing Antibody 121, Mindray, China) with a WHO conversion factor of 1 AU= 3.31 IU/mL and a reference range of 10 AU/mL to 400 AU/mL. Phosphate-buffered saline (PBS) was used to dilute samples with values over the specified range. The test is based on a chemiluminescent immunoassay that employs competitive binding. It works by disrupting the interaction between the enzyme-

conjugated ACE2 surface receptor and the receptor binding domain (RBD) of the viral spike protein, which is bound to magnetic beads. We recently evaluated this new assay and reported that it has great specificity and sensitivity in comparison to two reference techniques [14,15].

Antibodies against the RBD of the viral spike protein's S1 subunit (anti-S-RBD IgG)

Antibodies against the RBD of the viral spike protein's S1 subunit (anti-S-RBD IgG) were measured using the automated analyzer Mindray CL-900i® (Catalog No. SARS-CoV-2 Anti-S-RBD IgG122, Mindray, China), with a cut-off index of 10–1000 AU/mL and a WHO standardization factor of 1.15 BAU/mL.

IgA against the recombinant S1 domain of the viral spike protein (anti-S1 IgA)

Euroimmun Anti-SARS-CoV-2-ELISA (IgA) (catalog number: EI 2606–9601 A) was used to detect IgA against a recombinant S1 domain of the SARS-CoV-2. The IgA ratio was estimated by dividing the sample's extinction by the calibrator. Ratios were classified as follows: less than 0.8; negative, 0.8 or more; positive.

Anti-nucleocapsid IgG (anti-N)

SARS-CoV-2 anti-nucleoprotein IgG antibody levels (anti-N) was measured using the Architect automated chemiluminescent assay (Abbott Laboratories, USA). The purpose of this test was to screen the samples for prior infection, owing to the fact that IgG antibodies produced against the receptor binding domain (RBD) on the spike protein are different from those produced against the nucleoprotein of the virus. Hence, the presence of positive anti-N results indicates previous exposure to the complete virus [16]. Samples collected from individuals with previous SARS-CoV-2 exposure were eliminated from the VN group.

Statistical analysis

GraphPad Prism (version 9.3.1, GraphPad Software, Inc., San Diego, CA, USA) and IBM SPSS 28.0.1.0 (SPSS Chicago IL, USA) were used to perform the statistical analysis. Continuous variables were summarized by median and interquartile range (IQR). The collected dataset was subjected to the Shapiro–Wilk normality test to evaluate the normality of the data. Due to the absence of normal distribution, nonparametric tests were performed using Kruskal-Wallis to test for the differences between independent samples. In the different scatter plots, the central horizontal bar line shows the median titre, and the error bars show the 95% confidence interval. The confidence intervals (CI) were set at 95%. Spearman rank correlation (r) test was used to investigate the correlation of each antibody response with time (months). In addition, the correlation of S-RBD IgG and anti S1 IgA levels against NtAb levels were analyzed. r, 0–0.19 was regarded as very weak, 0.2–0.39 as weak, 0.40–0.59 as moderate, 0.6–0.79 as strong and 0.8–1 as very strong correlation [17]. To assess the dynamics and distribution of antibody levels we utilized a simple nonlinear regression model. All p-values were set at a significance level of 0.05. Using logistic regression models, we estimated odds ratios (ORs) and 95% CIs for NtAb, S-RBD IgG and anti-S1 IgA seropositivity according to age and gender. We fit multivariable logistic regression models to estimate gender-adjusted and age-adjusted ORs.

Results

Participant characteristics

A total of 814 subjects were included in this study. VN subjects (n = 596) had no previous history of infection (also anti-N negative) and received two doses of either BNT16b2 or mRNA-1273. In the VN group, samples were collected at median: 4.3 months after receiving the first dose of either BNT16b2 or mRNA-1273 vaccines. The VN group consisted of 48.8% females, 46.6% males, and 4.5% of unspecified gender. NI subjects (n = 218) were unvaccinated COVID-19-recovered individuals. In the NI group, samples were collected at median: 2.3 months after SARS-COV-2 infection. The NI group consisted of 13.8% females and 86.2% males (Table 1). Among the 218 NI subjects, 23.4% were symptomatic (51/218), 9.2% were pauci-symptomatic (20/218), 61.9% were asymptomatic (135/218), and 5.5% had unspecified COVID-19 severity (12/218) (Table 1). Univariate logistic regression analysis revealed that age (OR: 0.362, 95% CI: 0.146–0.898, p = 0.028) and time after receiving first dose (OR: 0.268; 95% CI: 0.091–0.788, p = 0.017) were significantly associated with anti-S1 IgA positivity among the VN group. After adjustment for the significant covariates, both age (OR: 0.345; 95% CI: 0.137–0.867, p = 0.024) and time after receiving first dose (OR: 0.198; 95% CI: 0.058–0.673, p = 0.009) remained significantly associated with anti-S1 IgA positivity among VN group. Nevertheless, among the NI group, only time post-SARS-CoV-2 infection (OR: 0.417; 95% CI: 0.212–0.820, p = 0.011) was significantly associated with S1 IgA positivity (Table S1).

Table 1
Participant demographics.

Characteristics	VN (n = 596)	NI (n = 218)	p value
Gender, n (%)			**< 0.001**
Female, n (%)	291 (48.8%)	30 (13.8%)	
Male, n (%)	278 (46.6%)	188 (86.2%)	
Unspecified gender, n (%)	39 (4.5%)	0 (0%)	
Age in years, median (IQR)	32 (21 – 43)	36 (29 – 43)	**< 0.001**
COVID-19 severity			**< 0.001**
Symptomatic, n (%)	0 (0%)	51 (23.4%)	
Pauci-symptomatic, n (%)	0 (0%)	20 (9.2%)	
Asymptomatic, n (%)	0 (0%)	135 (61.9%)	
Unspecified, n (%)	0 (0%)	12 (5.5%)	
Immune response			
NtAb			**< 0.001**
Positive, n (%)	593 (99.7%)	204 (93.6%)	
Negative, n (%)	2 (0.3%)	14 (6.4%)	
Anti S-RBD IgG			**< 0.001**
Positive, n (%)	590 (99.7%)	203 (93.1)	
Negative, n (%)	2 (0.3%)	15 (6.9%)	
Anti-S1 IgA			**< 0.001**
Positive, n (%)	569 (95.6%)	172 (79.3%)	
Negative, n (%)	26 (4.4%)	45 (20.7%)	
Time in months after receiving first dose, median (IQR)	4.3 (2.2–6.2)	NA	
Time in months after SARS-CoV-2 infection, median (IQR)	NA	2.3 (1.5 – 3.3)	

VN: vaccinated naïve, NI: naturally infected, IQR: interquartile range (25th and 75th percentiles).

Dynamics of antibody responses over time among vaccinated naïve and naturally infected individuals

Among the VN participants, the positivity rates for NtAb and anti-S-RBD IgG was 99.7%. For anti-S1-IgA, the positivity rate was 95.8% (Table 1). Among the NI participants, the positivity rate for NtAb antibodies was 93.6%. For anti-S-RBD-IgG and anti S1 IgA, the positivity rates were 93.1% and 79.3%, respectively (Table 1).

After seven months from receiving the first dose of either mRNA vaccine, a significant decline was observed for VN subjects in NtAb, IgG, and IgA (Fig. 1 A-C), with at least 3.7-fold (< .001) (Fig. 1 C). On the other hand, no significant difference was observed among NI subjects, seven months post-SARS-CoV-2 infection compared to one-month post-SARS-CoV-2 infection. Two months after vaccination with the first dose of either mRNA vaccine, IgA showed a significant 1.4-fold decline (p = 0.007) (Fig. 1 C). For NtAb and S-RBD IgG, both started to decline significantly (NtAb: 2.0-fold; p = 0.042, IgG: 2.4-

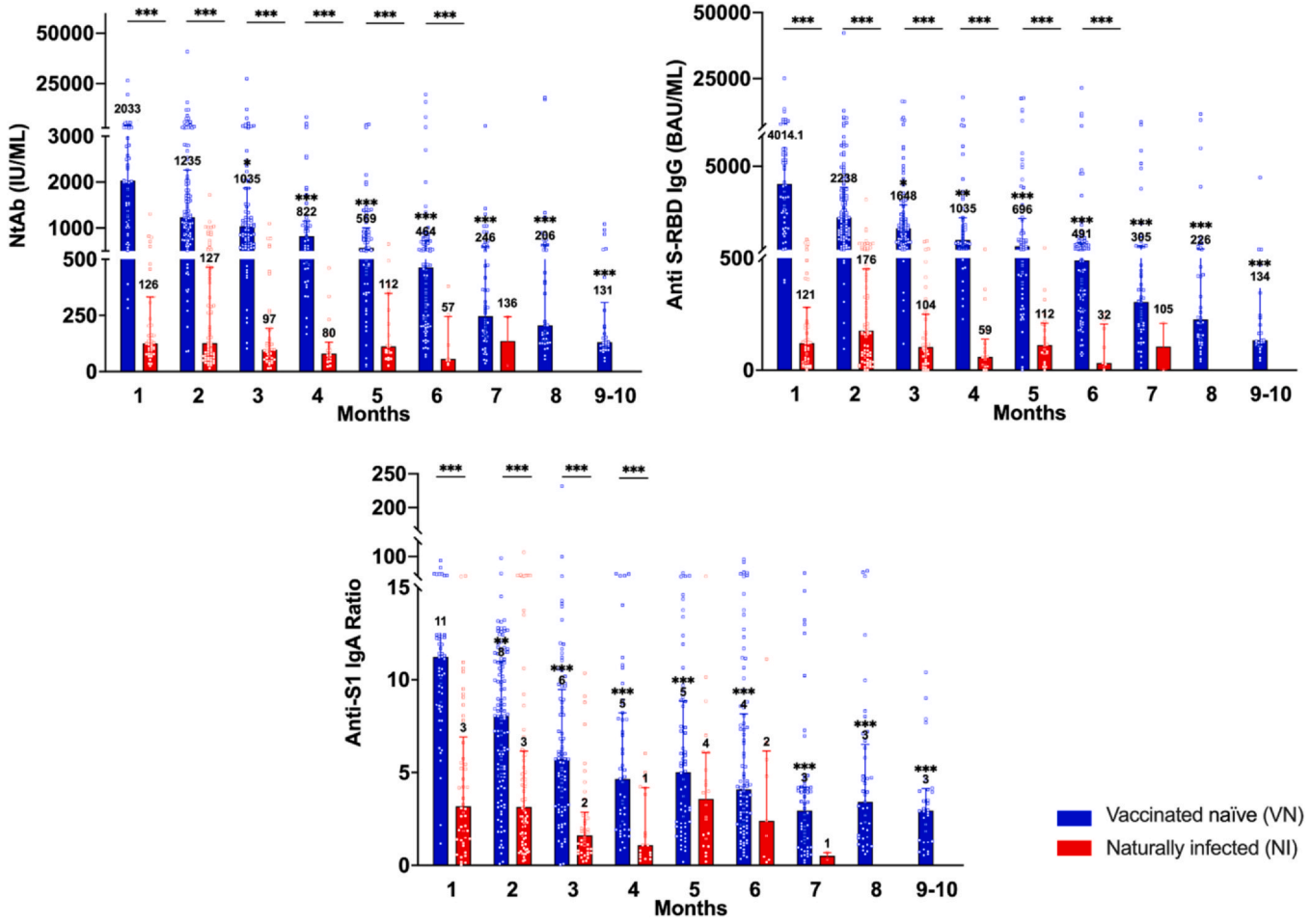

Fig. 1. Antibody response among vaccinated naïve (VN) and naturally infected (NI) individuals. (A) NtAb (IU/mL). (B) Anti-S-RBD IgG antibody levels (BAU/mL). (C) Anti-S1 IgA ratios measure by Euroimmune ELISA. Plotted values and horizontal bars indicate the median and interquartile range (IQR). Statistical significance was determined using Kruskal-Wallis test via GraphPad Prism. Statistical significance with horizontal bars indicates significance between the two groups. Statistical significance with asterisk only (no horizontal bars) indicates statistical significance between antibody response at each month in comparison to the 1st month. P value asterisk indicates * $p \leq 0.05$, * * $p \leq 0.01$, * ** $p \leq 0.001$. Only significant correlations are shown.

fold; $p = 0.035$) (Fig. 1A,B) after three months. The level of antibodies among VN individuals reached almost the same level as that observed for NI participants, with no significant difference in NtAb, IgG, or IgA observed between VN and NI groups at 7 months. By the end of the 10-months period among the VN group, the most significant decline observed for IgG (30.0-fold, <.001) (Fig. 1B), followed by NtAb at 15.7-fold ($P < .001$) (Fig. 1A), and IgA at 3.7-fold ($P < .001$) (Fig. 1 C).

In the VN group, The antibody titers tended to decline significantly over the 10-month period with strong Spearman correlation coefficients of - 0.627, - 0.628, and - 0.430, for NtAb, S-RBD IgG, and IgA, respectively (Fig. 2 A,B,C). On the other hand, in the NI group, significant, but very weak correlations were observed for NtAb and anti-S1 IgA with Spearman correlation coefficients of − 0.143 and − 0.154, respectively (Fig. 2 A,C), and no significant correlation was observed for anti-S-RBD IgG (Fig. 2 B).

Pairwise correlational analysis of Anti-SRBD IgG and Anti-S1 IgA, each against NtAb were performed. As depicted in the correlation plots in Fig. 3, Anti-S-RBD IgG and anti-S1 IgA showed strong to very strong significant correlation with NtAb levels among VN individuals (anti-S1-IgA/NtAb; r = 0.688 and S-RBD IgG/NtAb; r = 0.932) and moderate to very strong significant correlation among NI individuals (anti-S1-IgA/NtAb; r = 0.520 and S-RBD IgG/NtAb; r = 0.809) (Fig. 3 A,B).

Discussion

Vaccination efforts have been critical in mitigating the spread of COVID-19, however, there is limited data on the durability of vaccine-induced immune responses in individuals with no prior exposure to the virus, particularly in comparison to unvaccinated individuals who were previously exposed to the virus. In this study, we conducted the first comprehensive evaluation of the levels of SARS-CoV-2 NtAb, anti-S-RBD-IgG, and anti-S1-IgA antibodies in fully-vaccinated individuals who received two doses of either BNT162b2 or mRNA-1273 vaccines and had no prior exposure to the virus, and compared the antibody responses to those of unvaccinated naturally infected individuals.

Our study demonstrated that mRNA vaccines elicited significantly higher levels of NtAb, anti-S-RBD-IgG, and anti-S1-IgA than natural immunity (Fig. 1). These findings align with previous research suggesting that mRNA vaccines trigger higher antibody levels and greater antibody breadth than natural exposure to SARS-CoV-2 [17]. Nevertheless, despite the substantial increase in vaccine-induced antibody levels, the response appeared to be relatively short-lived, particularly for NtAbs and anti-SRBD IgG levels, with a 30.0- and 15.7-fold decline in antibody levels, respectively, over time (Fig. 1). Further evaluation of the dynamics and distribution of antibody levels over time revealed strong and steady decline in antibody responses among VN individuals compared to NI subjects

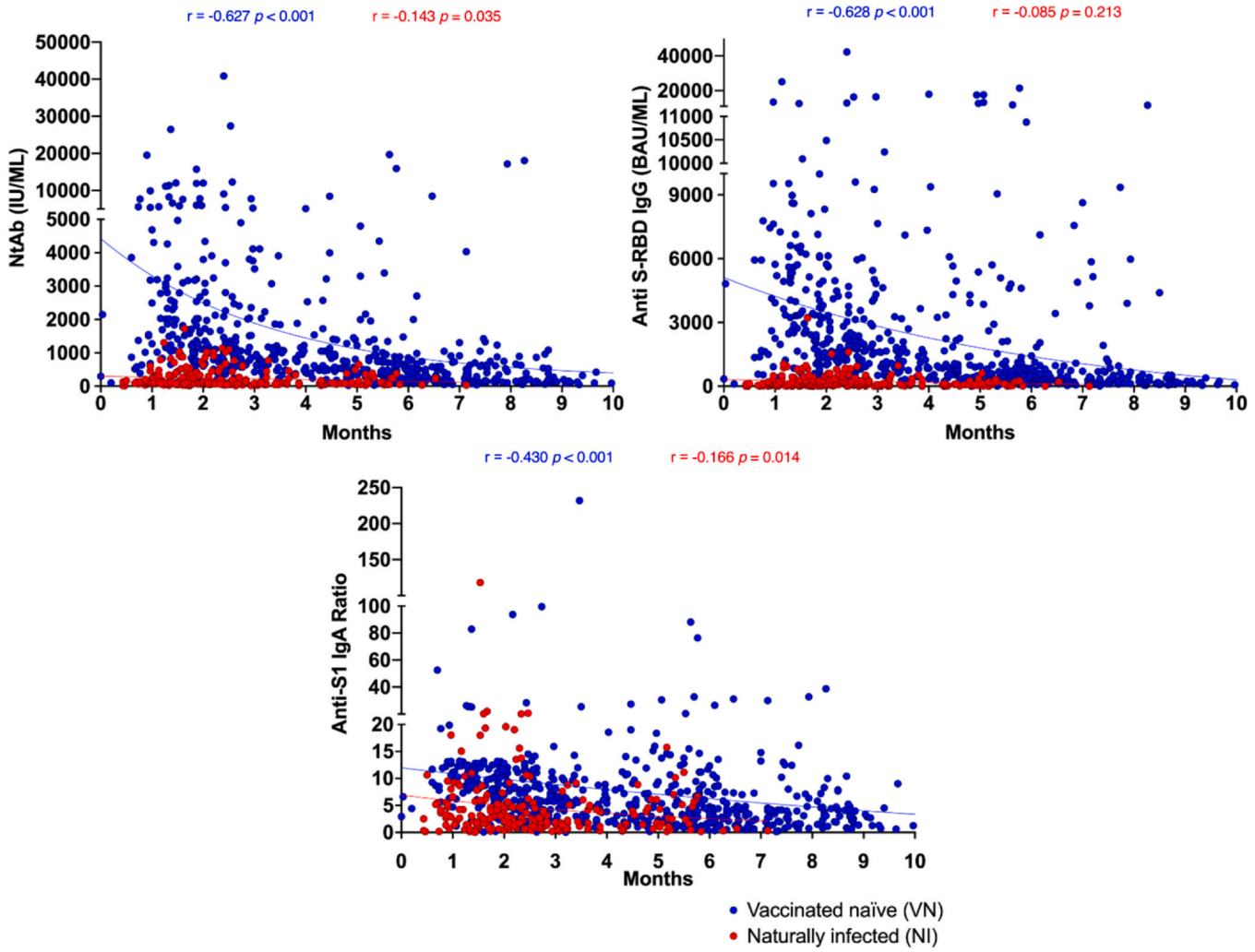

Fig. 2. Dynamics and distribution of antibody levels over time (months) among vaccinated naïve (VN) and naturally infected (NI) individuals. (A) NtAb levels (IU/mL). (B) Anti-S-RBD IgG antibody levels (BAU/mL). (C) Anti-S1 IgA ratios measure by Euroimmune ELISA. The x-axis indicates the time in months after receiving first dose for VN individuals, and time post-SARS-CoV-2 infection for NI individuals. Circles represent the observed levels of circulating antibodies. Spearman's correlation coefficient (r) and *p* values are indicated. r, 0–0.19 was regarded as very weak, 0.2–0.39 as weak, 0.40–0.59 as moderate, 0.6–0.79 as strong and 0.8–1 as very strong correlation. All p-values were set at a significance level of 0.05.

(Fig. 2). It has been reported that the humoral immune response tend to decline between 3 and 6 months after complete vaccination [18]. For instance, IgG and neutralizing titres were reported to significantly decline 3 months post-vaccination by 7- and 4-folds, respectively [19,20]. While another study reported that neutralizing titers and binding anti-RBD antibodies following mRNA-1273 vaccine declined with half-lives of 68–202 days (~2.267–6.733 months) and 52–109 days (~1.733–3.633 months), respectively [21]. Taken together, these findings add to the growing body of evidence suggesting that regular boosters may be necessary to maintain protection against SARS-CoV-2, particularly in individuals who have not been previously exposed to the virus.

Despite a similar overall decline observed in vaccine-induced IgA response, it appeared to be relatively more stable compared to NtAbs and anti-SRBD IgG levels, with only a minor 3.7-fold decline in anti-S1 IgA levels observed after around 10 months from the initial vaccination (Fig. 1). Furthermore, despite the initial boost in anti-S1 IgA levels among individuals who received the vaccine, at 5 months onwards, anti-S1 IgA levels were comparable to those observed in naturally infected participants, with no significant difference observed between the two groups (Fig. 1). Aligning with our findings, IgA antibodies IgA antibodies were reported to remain relatively stable for at least 6 months after symptom onset, while neutralizing antibody titers declined rapidly during the first few months after symptom onset [22]. Furthermore, a robust and long-lasting IgA response for up to six months after the second dose has been previously reported among individuals who received mRNA vaccines and were not previously infected with the virus [23,24]. The stable IgA response may provide additional protection against SARS-CoV-2 infection, and thus, monitoring of IgA response after vaccination, is as important as testing IgG and neutralizing responses for developing effective vaccination strategies against SARS-CoV-2.

Further assessment of the contribution of anti-S-RBD IgG and anti-S1 IgA isotypes to virus neutralization among VN and NI individuals revelead that both IgG and IgA significantly contributed to serum neutralization potential among both VN and NI groups ($p \leq 0.001$), but anti-S-RBD IgG appeared to contribute more than IgA, especially among VN individuals, as evidenced by Spearman correlation coefficients = 0.945 in VN and 0.809 in NI individuals for anti-S-RBD IgG/NtAb compared to anti-S1-IgA/NtAb (Spearman correlation coefficients = 0.682 in VN, and 0.501 in NI individuals) (Fig. 3). These findings align with previous research demonstrating that neutralizing activity of serum antibodies was primarily mediated by IgG antibodies [25]. Several studies revealed that high anti-RBD and neutralizing antibody levels were induced in vaccinated individuals, with a high correlation between RBD binding and

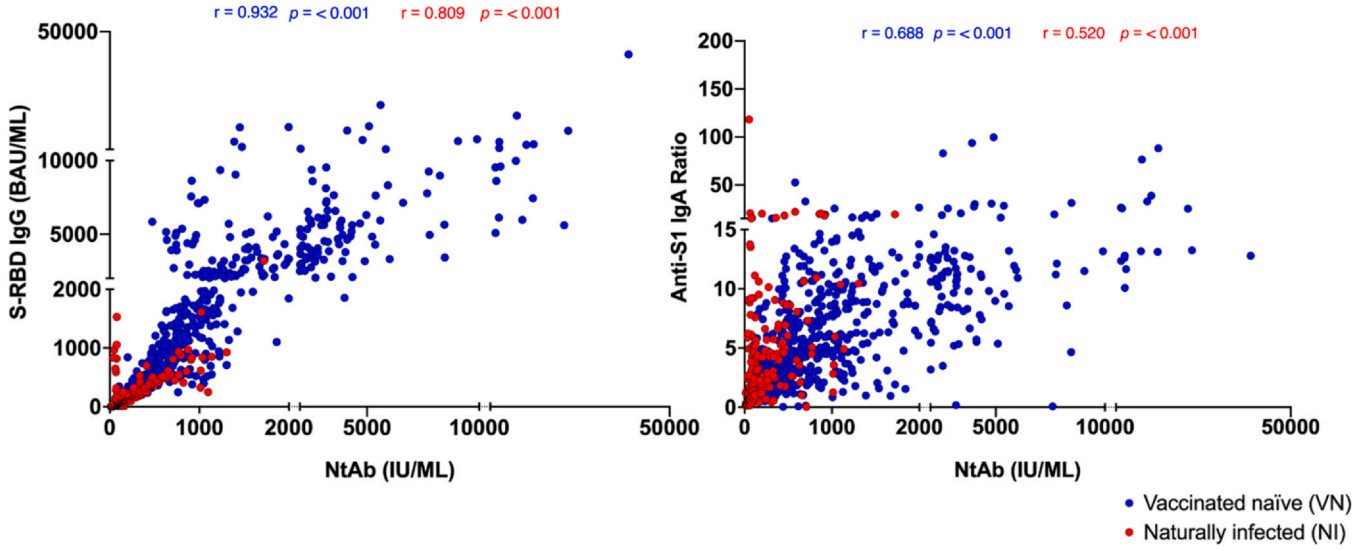

Fig. 3. Pairwise correlation analysis for the measured antibody parameters in vaccinated naïve (VN) and naturally infected (NI) individuals. (A) Anti-S-RBD IgG antibody levels (BAU/mL) against NtAb levels (IU/mL). (B) Anti-S1 IgA ratios measure by Euroimmune ELISA against NtAb levels (IU/mL). Spearman's correlation coefficient (r) and p-value are indicated. r, 0–0.19 was regarded as very weak, 0.2–0.39 as weak, 0.40–0.59 as moderate, 0.6–0.79 as strong and 0.8–1 as very strong correlation. All p-values were set at a significance level of 0.05.

neutralizing antibodies [26]. Additionally, studies suggest that higher levels of IgG antibodies induced by mRNA vaccines may explain their higher efficacy compared to other COVID-19 vaccines [27]. Therefore, some healthcare settings use anti-RBD IgG levels to predict vaccine effectiveness in vaccinated individuals. Nevertheless, with the emerging new variants, it remains unclear whether the levels of anti-RBD IgG, as determined by commercially available assays, can indicate the presence of neutralizing antibodies against the currently circulating SARS-CoV-2 variants.

Overall, our finding suggests that vaccine-induced immunity may not be as durable as expected. However, it is important to note that the vaccine still provides significant protection against severe disease and hospitalization, even with waning antibody levels [12,13]. Therefore, efforts are being made to evaluate the need for booster shots to sustain vaccine-induced immunity against the circulating variants of the SARS-CoV-2 virus. It is critical to continue monitoring the antibody response in both vaccinated and naturally infected individuals to better understand the duration of immunity and inform public health strategies for managing the ongoing COVID-19 pandemic.

The current study has several limitations to be addressed. First of all, it is noteworthy to mention that various variables could influence the level of immune response elicited after infection. It should be noted that our NI group included only 23.4% symptomatic subjects, while the remaining were paucisymptomatic (9.2%), asymptomatic (61.9%), or with unspecified severity (5.5%), which could have affected our results. In those with more severe COVID-19, binding and NtAb antibody titers have risen faster and reached a greater peak [28]. Individuals with symptomatic SARS-CoV-2 infection have greater antibody titers than asymptomatic and hospitalized people have higher antibody titers than those who are managed as outpatients [29]. Furthermore, several studies have shown a link between cycle threshold (Ct) and antibody titer, with lower Ct values linked with greater antibody titers at the population level [29]. These factors could have impacted the elicited immune response. Furthermore, we have not measured antibody levels prior to vaccine administration. Additionally, our analyses was limited by missing data on demographics and potential risk factors.

Despite these limitations, this study has several strengths that merit attention. First, most of the published studies have mainly focused on IgG, whereas studies on NtAb antibodies, and IgA response are very limited, particularly among naturally infected unvaccinated subjects. Second, in this study, we assessed anti-N antibodies, which is crucial to identify those who had been exposed to a virus but were asymptomatic prior to vaccination, especially among those vaccinated with vaccines containing only S protein. In addition, despite the relatively small sample size across the analyzed groups, we utilized strict inclusion criteria and included participants from a wide age range to achieve valid comparisons.

Conclusion

Our study provides important insights into the durability of vaccine- and natural infection-induced immunity. In the current study, we evaluated the antibody responses of NtAb, anti-S1-IgA, and anti-SRBD IgG antibodies over 10 months. While mRNA vaccination elicited higher antibody titers compared to natural infection, this "boost" in vaccinated individuals was relatively short-lived. Thus, the consideration of booster doses may be necessary to provide long-lasting immunity. Most importantly, our study sheds light on the understudied IgA antibody response, which was found to be persistent and more stable over time compared to NtAb and anti-SRBD IgG, suggesting a potential protective role of IgA antibodies against SARS-CoV-2. However, further research is needed to fully understand the role of IgA antibodies in COVID-19 immunity and the potential benefits of harnessing their protective effects to sustain protection against COVID-19.

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Ethical statement

The study was conducted according to the guidelines of the Declaration of Helsinki and was reviewed and reviewed by Qatar University Institutional Review Board (QU-IRB 1537-FBA/21) reviewed and approved the study. Informed consent was obtained from all subjects involved in the study before collecting samples.

CRediT authorship contribution statement

Conceptulization: GKN. Participant recruitment and demographic data collection: HID. Laboratory testing: BYA-H, PBN, DWA, SY, NY. Supervision: GKN, HA-S, HMY. Data analysis: SY, GKN. First draft writing: SY, GKN. Review and editing: SY, EN, DWA, NY, NA-D, HA-S, BYA-H, AHE, MP, NL, HID, HMY, PBN, LJA-R, and GKN.

Data Availability

All data produced in the present study are available upon reasonable request to the authors.

Declaration of Competing Interest

There are no known conflicts of interest associated with this publication.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jiph.2023.08.009.

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