In 2021, Qatar experienced considerable incidence of SARS-CoV-2 infection that was dominated sequentially by the Alpha, Beta, and Delta variants. Using the cycle threshold (Ct) value of an RT-qPCR-positive test to proxy the inverse of infectiousness, we investigated infectiousness of SARS-CoV-2 infections by variant, age, sex, vaccination status, prior infection status, and reason for testing in a random sample of 18,355 RT-qPCR-genotyped infections. Regression analyses were conducted to estimate associations with the Ct value of RT-qPCR-positive tests. Compared to Beta infections, Alpha and Delta infections demonstrated 2.56 higher Ct cycles (95% CI: 2.35-2.78), and 4.92 fewer cycles (95% CI: 4.67-5.16), respectively. The Ct value declined gradually with age and was especially high for children <10 years of age, signifying lower infectiousness in small children. Children <10 years of age had 2.18 higher Ct values than adults.
cycles (95% CI: 1.88-2.48) than those 10-19 years of age. Compared to unvaccinated individuals, the Ct value was higher among individuals who had received one or two vaccine doses, but the Ct value decreased gradually with time since the second-dose vaccination. Ct value was 2.07 cycles higher (95% CI: 1.42-2.72) for those with a prior infection than those without prior infection. The Ct value was lowest among individuals tested because of symptoms and was highest among individuals tested as a travel requirement. Delta was substantially more infectious than Beta. Prior immunity, whether due to vaccination or prior infection, is associated with lower infectiousness of breakthrough infections, but infectiousness increases gradually with time since the second-dose vaccination.

KEYWORDS
COVID-19, SARS-CoV-2 variant, vaccine, reinfection, breakthrough infection, immunity, epidemiology, PCR

Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic continues with progressive viral evolution more than two years after it first emerged (1). Between January 18, 2021 and May 31, 2021, Qatar experienced a SARS-CoV-2 Alpha (2) (B.1.1.7) variant wave (3) that was immediately followed by a Beta (2) (B.1.351) variant wave (4). Starting in June 2021, the Delta (2) (B.1.617.2) variant dominated a prolonged low-incidence phase that persisted until November of 2021 (5–7). We investigated the effects of SARS-CoV-2 variant, age, vaccination, and prior infection on infectiousness of SARS-CoV-2 infections utilizing the threshold cycle (Ct) values from SARS-CoV-2 reverse transcription quantitative polymerase chain reaction (RT-qPCR) as the proxy for infectiousness.

In real-time PCR, the RT-qPCR Ct value refers to the number of amplification cycles at which fluorescent signals generated in a reaction crosses a pre-set, detection threshold. The higher the concentration of PCR targets in the reaction, the earlier the cycle it is detected and the lower the Ct value it generates (8). In RT-qPCR assays for detection of viruses such as SARS-CoV-2, Ct values are inversely proportional to the viral load, and are strongly correlated to the culturability of the virus (9, 10). Therefore, RT-qPCR Ct values have been widely used to proxy SARS-CoV-2 infectiousness with lower Ct values indicating higher infectiousness and higher Ct values indicating lower infectiousness (10–15). Earlier studies found that lower Ct values (or higher viral loads) in samples of SARS-CoV-2 cases were associated with higher transmission rate and transmission risk, such as in studies of household transmission and among contacts of cases (11, 13). We assessed differences in Ct values in a random sample of 18,355 RT-qPCR-genotyped SARS-CoV-2 infections in relation to variant status, age, sex, vaccination status, prior infection status, and reason for testing.

Methods

Study population, data sources, and study design

This cross sectional study was conducted in the resident population of Qatar, applying a methodology used recently to investigate effects of the BA.1/BA.2 subvariant, vaccination, and prior infection on infectiousness of SARS-CoV-2 Omicron (2) (B.1.1.529) infections (16). Similarly, several effects on the infectiousness of SARS-CoV-2 infections were investigated including pre-Omicron variants (Alpha, Beta, and Delta), mRNA COVID-19 vaccination status [BNT162b2 (Pfizer-BioNTech) (17) and mRNA-1273 (Moderna) (18)], prior infection status, reason for RT-qPCR testing, study-period month of the RT-qPCR test (to account for the evolving phase of SARS-CoV-2 incidence), and demographic factors, including sex, age, and nationality.

The present study was conducted on a sample of 18,355 SARS-CoV-2 RT-qPCR-positive swabs that were collected randomly on a weekly basis from among all RT-qPCR-confirmed infections in Qatar between March 23, 2021 and November 6, 2021. These documented infections were RT-qPCR genotyped as part of a national project for surveillance of SARS-CoV-2 variants in Qatar (7, 19–21). Details of laboratory methods for RT-qPCR testing and variant ascertainment are provided in Section 1 of the Supplementary Material.
Coronavirus disease 2019 (COVID-19) laboratory testing, vaccination, clinical infection, and demographic data for this population were extracted from the national, federated SARS-CoV-2 databases, which include all RT-qPCR testing, reason for RT-qPCR testing, COVID-19 vaccinations, and related demographic details since the start of the pandemic. Further description of Qatar’s national COVID-19 databases has been reported previously (4, 6, 7, 15, 22).

Every SARS-CoV-2 RT-qPCR test conducted in Qatar is classified based on the reason for testing (clinical symptoms, contact tracing, surveys or random testing campaigns, individual requests, routine healthcare testing, pre-travel, at port of entry, or other). RT-qPCR testing is performed at a mass scale and most infections are diagnosed not for appearance of symptoms, but because of routine testing (6). Qatar has unusually young, diverse demographics, in that only 9% of its residents are ≥50 years of age, and 89% are expatriates from over 150 countries (22, 23). Nearly all individuals were vaccinated in Qatar; however, vaccinations performed elsewhere were recorded in the health system at the port of entry upon arrival to Qatar, per national requirements.

For standardization of RT-qPCR Ct values, we analyzed only RT-qPCR-confirmed infections diagnosed with the TaqPath COVID-19 Combo Kit [Thermo Fisher Scientific, USA (24)]. For each individual, all RT-qPCR-positive swabs during the study period were included, provided that at least 90 days had elapsed between two consecutive positive swabs to avoid inclusion of positive results from the same infectious episode (25, 26). A summary measure was derived for the primary outcome, the RT-qPCR Ct value (9), by averaging Ct values of the N, ORF1ab, and S gene targets. This average Ct value was used as the dependent variable in all analyses.

Both vaccination status and prior infection status were ascertained at the time of the RT-qPCR test. Vaccination status was defined by the number of administered vaccine doses and months elapsed since the last vaccine dose, with one month defined as 30 days. Only individuals vaccinated with BNT162b2 (17) or mRNA-1273 (18) vaccines were included in the analyses, as these constituted only 0.5% of all RT-qPCR-genotyped infections. Otherwise, data for the remaining study variables were complete.

**Oversight**

Hamad Medical Corporation and Weill Cornell Medicine-Qatar Institutional Review Boards approved this retrospective study with a waiver of informed consent. The study was reported following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. The STROBE checklist is found in Supplementary Table 1.

**Statistical analysis**

Frequency distributions and measures of central tendency were used to describe the study population with respect to a priori determined factors. These included SARS-CoV-2 variant, vaccination status (factoring dose number and months since vaccination), prior infection status, reason for RT-qPCR testing, study-period month of the RT-qPCR test, and demographic factors, age, sex, and nationality.

Association of each of these factors with Ct value was assessed using univariable linear regression analyses. Unadjusted β coefficients, 95% confidence intervals (CIs), and the F-test of overall covariate significance were reported. Adjusted β coefficients and associated 95% CIs and p-values were estimated using multivariable linear regression analyses that included all covariates in the model.

Two-sided p-value <0.05 indicated statistical significance. Interactions were not considered. Statistical analyses were conducted in STATA/SE version 16 (32).

**Results**

Figure 1 shows the process of selecting the study population and Table 1 describes study population characteristics. This was a national study involving a random sample of 18,355 RT-qPCR-confirmed SARS-CoV-2 infections. Therefore, the study population is broadly representative of the population of Qatar. The sample included 3,347 (18.2%) Alpha infections, 5,576 (30.4%) Beta infections, and 9,432 (51.4%) Delta infections (Table 1).

Compared to Beta infections, Alpha and Delta infections were associated with 2.56 higher Ct cycles (95% CI: 2.35-2.78), and 4.92 fewer cycles (95% CI: 4.67-5.16) (Table 2), respectively, indicating the highest infectiousness for the Delta variant.
Ct value declined gradually with age and was especially high for children <10 years of age, signifying lower infectiousness of small children. Children <10 years of age had 2.18 higher Ct cycles (95% CI: 1.88-2.48) than those 10-19 years of age (Table 2). The 10-19 age group was chosen as a reference, and not the <10 age group, because of the different manifestations of this infection in small children. Males had higher Ct values than females and there were some differences in Ct value by nationality.

Compared to unvaccinated individuals, Ct value was higher among individuals who received one or two vaccine doses (Table 2). However, Ct value decreased gradually with time since second-dose vaccination. Very few individuals received a booster dose during the study period (Table 1) to allow for estimation of effect of booster vaccination on Ct value. Ct value was 2.07 cycles higher (95% CI: 1.42-2.72) for those with a prior infection compared to those without prior infection.

The Ct value was lowest when testing was performed due to suspicion of infection exposure (Table 2), such as appearance of symptoms or recent exposure to an infected person (contact tracing). The Ct value was highest for infections diagnosed because of routine testing for reasons unrelated to infection exposure, such as in a random survey or because of travel requirements. Stratified analyses for Alpha (Table 3), Beta (Table 4), and Delta (Table 5) infections suggested similar findings.

**Discussion**

Delta infections were associated with considerably lower Ct values than Beta infections, indicating higher infectiousness of this variant, perhaps because of higher viral load and/or longer duration of infection. This appears to be the first direct comparison of the infectiousness of Delta versus Beta infections, and supports the high infectiousness of the Delta variant compared to pre-Omicron variants such as Alpha, as reported previously (33, 34). This difference in viral load between Delta and Beta appears also to extend to severity of infection, as Delta infections were found associated with higher severity than Beta infections (35). Of note, Beta infections were also found earlier to be associated with higher severity than Alpha infections (36). Worth mentioning is that factors other than viral load, such as the variations in the spike proteins or any other differences in the biological properties of the viruses, may also affect the infectiousness of different SARS-CoV-2 variants (37).
TABLE 1 Characteristics of the 18,355 RT-qPCR-genotyped SARS-CoV-2 infections between March 23 and November 6, 2021.

| Characteristics | Total sample N (%) | Alpha infections N (%) | Beta infections N (%) | Delta infections N (%) |
|----------------|-------------------|------------------------|-----------------------|-----------------------|
| **Total N**    | 18,355            | 3,347 (18.2)           | 5,576 (30.4)          | 9,432 (51.4)          |
| **Demographic characteristics** |                   |                        |                       |                       |
| Median age (IQR) — years | 32 (22-41)         | 33 (25-41)             | 33 (25-42)            | 31 (18-40)            |
| Age group in years — no. (%) |                   |                        |                       |                       |
| <10            | 1,956 (10.7)      | 286 (8.5)              | 424 (7.6)             | 1,246 (13.2)          |
| 10-19          | 2,042 (11.1)      | 277 (8.3)              | 499 (8.9)             | 1,266 (13.4)          |
| 20-29          | 3,670 (20.0)      | 749 (22.4)             | 1,104 (19.8)          | 1,817 (19.3)          |
| 30-39          | 5,624 (30.6)      | 1,104 (33.0)           | 1,866 (33.5)          | 2,654 (28.1)          |
| 40-49          | 3,263 (17.8)      | 627 (18.7)             | 1,074 (19.3)          | 1,562 (16.6)          |
| 50-59          | 1,240 (6.8)       | 210 (6.3)              | 431 (7.7)             | 599 (6.4)             |
| 60-69          | 462 (2.3)         | 73 (2.2)               | 134 (2.4)             | 219 (2.3)             |
| 70-79          | 95 (0.5)          | 14 (0.4)               | 31 (0.6)              | 50 (0.5)              |
| 80+            | 39 (0.2)          | 7 (0.2)                | 13 (0.2)              | 19 (0.2)              |
| **Sex**        |                   |                        |                       |                       |
| Female         | 6,805 (37.1)      | 1,114 (33.3)           | 1,813 (32.5)          | 3,878 (41.1)          |
| Male           | 11,550 (62.9)     | 2,233 (66.7)           | 3,763 (67.5)          | 5,554 (58.9)          |
| **Nationality** |                   |                        |                       |                       |
| Bangladeshi    | 1,077 (5.9)       | 240 (7.2)              | 470 (8.4)             | 367 (3.9)             |
| Egyptian       | 1,098 (6.0)       | 115 (3.4)              | 311 (5.6)             | 672 (7.4)             |
| Filipino       | 1,555 (8.5)       | 340 (10.2)             | 582 (10.4)            | 633 (6.7)             |
| Indian         | 3,873 (21.1)      | 855 (25.5)             | 1,355 (24.3)          | 1,663 (17.6)          |
| Nepalese       | 1,084 (5.9)       | 225 (6.7)              | 459 (8.2)             | 400 (4.2)             |
| Pakistani      | 1,017 (5.5)       | 223 (6.7)              | 279 (5.0)             | 515 (5.5)             |
| Qatari         | 3,903 (21.3)      | 555 (16.6)             | 850 (15.2)            | 2,498 (26.5)          |
| Sri Lankan     | 488 (2.7)         | 106 (3.2)              | 216 (3.9)             | 166 (1.8)             |
| Sudanese       | 394 (2.1)         | 92 (2.7)               | 108 (1.9)             | 194 (2.1)             |
| Other nationalities | 3,866 (21.1)  | 596 (17.8)             | 946 (17.0)            | 2,324 (24.6)          |
| **Reason for RT-qPCR testing** |                   |                        |                       |                       |
| Clinical suspicion | 6,499 (35.4)     | 1,067 (31.9)           | 2,477 (44.4)          | 2,955 (51.3)          |
| Contact tracing | 2,261 (12.3)      | 404 (12.1)             | 775 (13.9)            | 1,082 (11.5)          |
| Healthcare routine testing | 532 (2.9)    | 115 (3.4)              | 218 (3.9)             | 199 (2.1)             |
| Survey         | 2,770 (15.1)      | 552 (16.5)             | 938 (16.8)            | 1,280 (13.6)          |
| Port of entry  | 3,245 (17.7)      | 522 (15.6)             | 291 (5.2)             | 2,432 (25.8)          |
| Pre-travel     | 1,243 (6.8)       | 201 (6.0)              | 225 (4.0)             | 817 (8.7)             |
| Individual request | 1,620 (8.8)  | 435 (13.0)             | 603 (10.8)            | 582 (6.2)             |
| Other          | 185 (1.0)         | 51 (1.5)               | 49 (0.9)              | 85 (0.9)              |
| **RT-qPCR test study-period month** |                   |                        |                       |                       |
| 23 March-21 April, 2021 | 5,185 (28.2) | 1,415 (42.3)          | 3,564 (63.9)          | 206 (2.2)             |
| 22 April-21 May, 2021 | 2,502 (13.6) | 736 (22.0)             | 1,262 (22.6)          | 504 (5.3)             |
| 22 May-20 June, 2021 | 1,287 (7.0)   | 597 (17.8)             | 226 (4.1)             | 464 (4.9)             |
| 21 June-20 July, 2021 | 1,263 (6.9)  | 258 (7.7)              | 111 (2.0)             | 894 (9.5)             |
| 21 July-19 August, 2021 | 3,647 (19.9) | 253 (7.6)              | 326 (5.8)             | 3,086 (32.5)          |
| 20 August-18 September, 2021 | 2,807 (15.3) | 88 (2.6)                | 87 (1.6)              | 2,632 (27.9)          |
| 19 September-18 October, 2021 | 976 (5.3)  | 0 (0.0)                | 0 (0.0)              | 976 (10.3)            |
| 19 October-06 November, 2021 | 688 (3.7)  | 0 (0.0)                | 0 (0.0)              | 688 (7.3)             |
| **Vaccine and natural immunity** |                   |                        |                       |                       |
| **Vaccination status** |                   |                        |                       |                       |

(Continued)
Prior immunity against SARS-CoV-2 infection, whether due to vaccination or prior infection, was associated with higher Ct value at infection, and thus lower infectiousness of breakthrough infections. This confirms earlier findings (15, 16), and suggests that strength of immunity is manifest not only in protection against infection, but also against the infectiousness, if a breakthrough infection occurs (15). However, this effect appeared to depend on the time since the prior immunological event (Table 2). Ct values decreased gradually with time since second-dose vaccination, paralleling the established pattern of waning of vaccine effectiveness after the second dose (6, 38, 39).

Ct values decreased with age, perhaps reflecting slower virus clearance with aging (40) and confirming our earlier findings (16). Ct values were particularly high for infections among small children <10 years of age. This finding supports a lesser role for small children than adults in the transmission of infection, as suggested in studies of secondary transmission within households (41–43). There were differences in Ct value by sex and nationality, but these may be a consequence of different test-seeking behaviors for different socio-economic groups in Qatar’s diverse population. Ct values also varied by reason for testing, with lower Ct values of infections diagnosed because of suspicion of infection, and higher Ct values of infections diagnosed through routine testing unrelated to infection exposure. This finding also confirms our earlier finding for Omicron infections (16).

The study has limitations. RT-qPCR genotyping in Qatar started only after the Alpha wave peaked in the first week of March 2021 and thus many Alpha infections may have been older infections explaining the relatively higher Ct values of these infections compared to Delta or Beta infections. The study included only documented RT-qPCR-conﬁrmed infections. It is possible that infections in those with a prior infection or those vaccinated are less likely to be diagnosed, perhaps because of minimal or no symptoms (15). Nevertheless, RT-qPCR testing in Qatar is done at a mass scale, where a signiﬁcant proportion of the population is being tested weekly (6). The majority of infections are identiﬁed via routine testing and not because of appearance of symptoms (Table 1) (6).

Other limitations include the small number of individuals who received the booster dose by the end of the study precluding the estimation of effect of booster vaccination on Ct value and the inability to factor in the duration between symptom onset and RT-qPCR test (for symptomatic cases) as the date of symptom onset was not available. The study population consisted mostly of working-age adults; thus, the results may not be generalizable to the elderly.

Prior immunity against SARS-CoV-2 infection, whether due to vaccination or prior infection, was associated with higher Ct value at infection, and thus lower infectiousness of breakthrough infections. This conﬁrms earlier ﬁndings (15, 16), and suggests that strength of immunity is manifest not only in protection against infection, but also against the infectiousness, if a breakthrough infection occurs (15). However, this effect appeared to depend on the time since the prior immunological event (Table 2). Ct values decreased gradually with time since second-dose vaccination, paralleling the established pattern of waning of vaccine effectiveness after the second dose (6, 38, 39).

Ct values decreased with age, perhaps reﬂecting slower virus clearance with aging (40) and conﬁrming our earlier ﬁndings (16). Ct values were particularly high for infections among small children <10 years of age. This ﬁnding supports a lesser role for small children than adults in the transmission of infection, as suggested in studies of secondary transmission within households (41–43). There were differences in Ct value by sex and nationality, but these may be a consequence of different test-seeking behaviors for different socio-economic groups in Qatar’s diverse population. Ct values also varied by reason for testing, with lower Ct values of infections diagnosed because of suspicion of infection, and higher Ct values of infections diagnosed through routine testing unrelated to infection exposure. This finding also conﬁrms our earlier ﬁnding for Omicron infections (16).
### TABLE 2  Associations with RT-qPCR Ct value among the 18,355 RT-qPCR-genotyped SARS-CoV-2 infections between March 23 and November 6, 2021.

| Characteristics                     | RT-qPCR Ct value | Univariable analysis | F-test | Multivariable analysis |
|-------------------------------------|-------------------|----------------------|--------|------------------------|
|                                     | Mean (SD)         | \( \beta \) coefficient [95% CI] p-value |         | \( \beta \) coefficient [95% CI] p-value |
| **Age group in years**              |                   |                      |        |                        |
| <10                                 | 25.51 (5.06)      | 2.28 [1.93, 2.63]    | <0.001 | 2.18 [1.88, 2.48]      |
| 20-29                               | 23.74 (5.80)      | 0.52 [0.21, 0.82]    | 0.001  | -0.24 [-0.51, 0.04]    |
| 30-39                               | 23.63 (5.73)      | 0.41 [0.12, 0.69]    | 0.005  | -0.39 [-0.65, 0.12]    |
| 40-49                               | 23.43 (5.78)      | 0.20 [-0.11, 0.51]   | 0.204  | -0.52 [-0.81, 0.23]    |
| 50-59                               | 23.55 (5.50)      | 0.33 [-0.07, 0.72]   | 0.106  | -0.44 [-0.80, 0.09]    |
| 60-69                               | 23.35 (5.31)      | 0.12 [-0.46, 0.71]   | 0.677  | -0.55 [-1.06, -0.04]   |
| 70-79                               | 22.70 (5.23)      | -0.52 [-1.68, 0.63]  | 0.375  | -1.01 [-1.99, -0.03]   |
| 80+                                 | 22.86 (5.27)      | -0.37 [-2.15, 1.42]  | 0.688  | -0.83 [-2.33, 0.68]    |
| **Sex**                             |                   |                      |        |                        |
| Female                              | 23.05 (5.48)      | Ref.                 | Ref.   | Ref.                   |
| Male                                | 24.17 (5.72)      | 1.13 [0.96, 1.29]    | <0.001 | 0.60 [0.45, 0.76]      |
| **Nationality**                     |                   |                      |        |                        |
| Qatari                              | 23.13 (5.31)      | Ref.                 | Ref.   | Ref.                   |
| Bangladeshi                         | 24.34 (5.94)      | 1.20 [0.82, 1.58]    | <0.001 | 0.55 [0.20, 0.90]      |
| Egyptian                            | 23.53 (5.38)      | 0.40 [0.02, 0.77]    | 0.039  | 0.23 [0.09, 0.56]      |
| Filipino                            | 23.25 (5.72)      | 0.11 [-0.22, 0.45]   | 0.496  | 0.19 [-0.12, 0.49]     |
| Indian                              | 24.40 (5.96)      | 1.27 [1.02, 1.52]    | <0.001 | 0.65 [0.41, 0.90]      |
| Nepalese                            | 24.31 (5.80)      | 1.18 [0.80, 1.56]    | <0.001 | 0.85 [0.49, 1.20]      |
| Pakistani                           | 24.23 (5.69)      | 1.09 [0.71, 1.48]    | <0.001 | 0.24 [-0.10, 0.59]     |
| Sri Lankan                          | 24.18 (5.70)      | 1.05 [0.52, 1.58]    | <0.001 | 0.29 [0.17, 0.47]      |
| Sudanese                            | 23.79 (5.06)      | 0.66 [0.07, 1.24]    | 0.027  | 0.64 [0.14, 1.14]      |
| Other nationalities§                | 23.51 (5.55)      | 0.38 [0.13, 0.63]    | 0.003  | 0.29 [0.07, 0.50]      |
| **SARS-CoV-2 variant**              |                   |                      |        |                        |
| Beta**                              | 23.72 (5.14)      | Ref.                 | Ref.   | Ref.                   |
| Alpha                               | 27.89 (5.65)      | 4.17 [3.94, 4.39]    | <0.001 | 2.56 [2.35, 2.78]      |
| Delta                               | 22.31 (5.21)      | -1.41 [-1.59, -1.24] | <0.001 | -4.92 [-5.16, -4.67]   |
| **Reason for RT-qPCR testing**      |                   |                      |        |                        |
| Survey                              | 24.23 (5.52)      | Ref.                 | Ref.   | Ref.                   |
| Clinical suspicion                  | 22.64 (5.42)      | -1.59 [-1.84, -1.34] | <0.001 | -1.48 [-1.69, -1.26]   |
| Contact tracing                     | 23.52 (5.52)      | -0.71 [-1.02, -0.40] | <0.001 | -0.53 [-0.80, -0.26]   |
| Healthcare routine testing          | 24.20 (5.65)      | -0.03 [-0.55, 0.49]  | 0.913  | -0.72 [-1.17, -0.28]   |
| Port of entry                       | 24.24 (5.66)      | 0.01 [-0.27, 0.29]   | 0.934  | 0.84 [0.59, 1.09]      |
| Pre-travel                          | 25.66 (5.66)      | 1.43 [1.06, 1.81]    | <0.001 | 1.29 [0.97, 1.62]      |
| Individual request                  | 24.89 (6.03)      | 0.66 [0.32, 1.00]    | <0.001 | 0.24 [0.07, 0.54]      |
| Other                               | 26.11 (5.62)      | 1.88 [1.05, 2.71]    | <0.001 | -1.01 [-1.73, -0.29]   |
| **RT-qPCR test study period month** |                   |                      |        |                        |
| 23 March-21 April, 2021             | 23.39 (5.15)      | Ref.                 | Ref.   | Ref.                   |
| 22 April-21 May, 2021               | 24.20 (5.45)      | 0.82 [0.55, 1.08]    | <0.001 | 1.00 [0.77, 1.23]      |
| 22 May-20 June, 2021                | 27.50 (6.46)      | 4.12 [3.78, 4.46]    | <0.001 | 4.08 [3.76, 4.39]      |
| 21 June-20 July, 2021               | 23.07 (5.97)      | -0.32 [-0.66, 0.02]  | 0.068  | 2.57 [2.23, 2.91]      |
| 21 July-19 August, 2021             | 23.29 (5.77)      | -0.09 [-0.33, 0.14]  | 0.442  | 3.80 [3.52, 4.09]      |
| 20 August-18 September, 2021        | 23.96 (5.62)      | 0.58 [0.32, 0.83]    | <0.001 | 4.97 [4.66, 5.29]      |
| 19 September-18 October, 2021       | 23.04 (5.20)      | -0.35 [-0.72, 0.03]  | 0.074  | 4.46 [4.05, 4.87]      |
| 19 October-06 November, 2021        | 21.76 (4.85)      | -1.62 [-2.06, -1.18] | <0.001 | 3.66 [3.20, 4.12]      |
| **Vaccination status**              |                   |                      |        |                        |

(Continued)
| Characteristics | RT-qPCR Ct value | Univariable analysis | F-test<sup>†</sup> | Multivariable analysis<sup>†</sup> |
|-----------------|------------------|----------------------|-------------------|-----------------------------|
|                 | Mean (SD)        | β coefficient [95% CI] | p-value | β coefficient [95% CI] | p-value |
|                 |                  | Ref.                 | 0.790    | 0.57 [0.26, 0.87] | <0.001 |
| Unvaccinated    | 23.98 (5.65)     | -0.05 [-0.40, 0.31] | 0.790    | 0.57 [0.26, 0.87] | <0.001 |
| One dose        | 23.93 (5.71)     | -0.05 [-0.40, 0.31] | 0.790    | 0.57 [0.26, 0.87] | <0.001 |
| Two doses       |                  |                      |          |                      |        |
| <3 months before the RT-qPCR test | 24.43 (5.86) | 0.45 [0.14, 0.77] | 0.004    | 0.86 [0.59, 1.13] | <0.001 |
| 3-<6 months before the RT-qPCR test | 22.59 (5.40) | -1.39 [-1.63, -1.15] | <0.001 | 0.08 [0.17, 0.32] | 0.547 |
| 6-<9 months before the RT-qPCR test | 21.79 (5.12) | -2.19 [-2.66, -1.71] | <0.001 | -0.26 [-0.72, 0.19] | 0.262 |
| ≥9 months before the RT-qPCR test | 18.81 (2.22) | -5.17 [-10.68, 0.34] | 0.066    | -3.23 [-7.89, 1.42] | 0.173 |
| Three doses     |                  |                      |          |                      |        |
| ≤1 month before the RT-qPCR test | 22.99 (5.40) | -0.99 [-5.92, 3.94] | 0.693    | -1.16 [-5.52, 2.79] | 0.520 |
| >1 month before the RT-qPCR test | 19.80 (2.97) | -4.18 [-9.69, 1.33] | 0.137    | -1.83 [-6.47, 2.81] | 0.439 |
| Prior SARS-CoV-2 infection |                  |                      |          |                      |        |
| Never           | 23.14 (5.51)     | Ref.                 | <0.001   | 3.95 [3.73, 4.17] | <0.001 |
| <90 days before the study RT-qPCR test‡‡ | 27.65 (4.93) | 4.51 [4.27, 4.74] | <0.001 | 2.07 [1.42, 2.72] | <0.001 |
| Prior infection‡‡ | 25.88 (5.93) | 2.74 [1.99, 3.48] | <0.001 | 2.07 [1.42, 2.72] | <0.001 |

CI, confidence interval; Ct, cycle threshold; RT-qPCR, real-time reverse-transcription polymerase chain reaction; Ref., reference; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation.

<sup>†</sup>The two-tailed F-test of the univariable analysis.

<sup>‡</sup>RT-qPCR Ct value was adjusted for age-group, sex, nationality, SARS-CoV-2 variant, reason for RT-qPCR test, RT-qPCR test study-period month, vaccination status, and prior SARS-CoV-2 infection.

<sup>‡‡</sup>The 10-19 age group was chosen as a reference, and not the <10 age group, because of the different manifestations of this infection in small children.

<sup>§</sup>Nationalities were chosen to represent the most populous groups on Qatar.

<sup>¶</sup>These comprise 99 other nationalities in Qatar.

<sup>**</sup>Beta was chosen as a reference because of interest in directly comparing Delta to Beta infections.

<sup>††</sup>An RT-qPCR-positive test that occurred <90 days before the study RT-qPCR-positive test was included as a separate category in the analysis and was not considered a prior infection. This RT-qPCR-positive test and the study RT-qPCR-positive test may both reflect the same prolonged infection.

<sup>‡‡</sup>Prior infection was defined as an RT-qPCR-positive test that occurred ≥90 days before the RT-qPCR-positive test that is included in the study.

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TABLE 3 Associations with RT-qPCR Ct value among 3,347 Alpha RT-qPCR-genotyped SARS-CoV-2 infections between March 23 and November 6, 2021.

| Characteristics | RT-qPCR Ct value | Univariable analysis | F-test<sup>†</sup> | Multivariable analysis<sup>†</sup> |
|-----------------|------------------|----------------------|-------------------|-----------------------------|
|                 | Mean (SD)        | β coefficient [95% CI] | p-value | β coefficient [95% CI] | p-value |
| Age group in years |                  |                      |          |                      |        |
| 10-19<sup>‡</sup> | 26.24 (5.93)     | Ref.                 | <0.001   | Ref.                 |        |
| <10             | 27.60 (5.17)     | 1.36 [0.43, 2.29] | 0.004    | 1.28 [0.50, 2.06] | 0.001 |
| 20-29           | 28.48 (5.50)     | 2.24 [1.46, 3.01] | <0.001   | 0.20 [0.49, 0.88] | 0.577 |
| 30-39           | 28.12 (5.72)     | 1.88 [1.14, 2.62] | <0.001   | 0.04 [0.63, 0.71] | 0.910 |
| 40-49           | 27.81 (5.78)     | 1.57 [0.78, 2.37] | <0.001   | -0.16 [0.87, 0.55] | 0.661 |
| 50-59           | 27.94 (5.32)     | 1.70 [0.69, 2.71] | 0.001    | -0.18 [-1.07, 0.71] | 0.694 |
| 60-69           | 27.07 (5.33)     | 0.83 [0.62, 2.28] | 0.263    | -1.14 [-2.38, 0.10] | 0.072 |
| 70-79           | 24.88 (6.01)     | -1.36 [-4.38, 1.66] | 0.377    | -2.70 [-5.23, -0.17] | 0.037 |
| 80+             | 25.93 (3.81)     | -0.30 [-4.52, 3.91] | 0.887    | -0.13 [-3.65, 3.40] | 0.943 |
| Sex             |                  |                      |          |                      |        |
| Female          | 26.24 (5.81)     | Ref.                 | <0.001   | Ref.                 |        |
| Male            | 28.71 (5.38)     | 2.47 [2.07, 2.86] | <0.001   | 0.74 [0.35, 1.13] | <0.001 |
| Nationality<sup>§</sup> |                  |                      |          |                      |        |
| Qatari          | 26.21 (5.58)     | Ref.                 | <0.001   | Ref.                 |        |
| Bangladeshi     | 29.34 (5.07)     | 3.13 [2.30, 3.96] | <0.001   | 1.77 [0.98, 2.56] | <0.001 |
| Egyptian        | 26.45 (6.07)     | 0.24 [0.87, 1.34] | 0.674    | 0.39 [0.57, 1.35] | 0.429 |
| Filipino        | 26.57 (5.76)     | 0.36 [0.38, 1.10] | 0.339    | 0.84 [0.14, 1.53] | 0.019 |

(Continued)
| Characteristics                  | RT-qPCR Ct value | Univariable analysis | F-test | Multivariable analysis |
|---------------------------------|------------------|----------------------|--------|------------------------|
|                                 | Mean (SD)        | β coefficient [95% CI] | p-value | β coefficient [95% CI] | p-value |
| **Indian**                      |                  |                      |        |                        |        |
|                                 | 29.57 (5.23)     | 3.36 [2.78, 3.95]    | <0.001 | 1.95 [1.36, 2.55]      | <0.001 |
| **Nepalese**                    |                  |                      |        |                        |        |
|                                 | 29.44 (5.15)     | 3.23 [2.38, 4.08]    | <0.001 | 2.32 [1.51, 3.12]      | <0.001 |
| **Pakistani**                   |                  |                      |        |                        |        |
|                                 | 28.08 (5.24)     | 1.87 [1.02, 2.72]    | <0.001 | 0.70 [0.09, 1.50]      | 0.083  |
| **Sri Lankan**                  |                  |                      |        |                        |        |
|                                 | 27.74 (6.08)     | 1.53 [0.39, 2.67]    | 0.009  | 0.72 [0.31, 1.74]      | 0.170  |
| **Sudanese**                    |                  |                      |        |                        |        |
|                                 | 26.50 (5.11)     | 0.29 [-0.92, 1.50]   | 0.635  | 0.90 [0.16, 1.96]      | 0.097  |
| **Other nationalities**         |                  |                      |        |                        |        |
|                                 | 27.06 (5.77)     | 0.85 [0.22, 1.48]    | 0.009  | 0.66 [0.09, 1.23]      | 0.223  |
| **Reason for RT-qPCR testing**  |                  |                      |        |                        |        |
| Survey                          | 28.26 (5.43)     | Ref.                 | Ref.   |                        |        |
| Clinical suspicion              | 26.39 (5.87)     | -1.87 [-2.43, -1.30] | <0.001 | -1.54 [-2.04, -1.04]   | <0.001 |
| Contact tracing                 | 27.05 (5.87)     | -1.21 [-1.92, -0.50] | 0.001  | -0.54 [-1.15, 0.08]    | 0.088  |
| Healthcare routine testing      | 28.20 (5.77)     | -0.06 [-1.17, 1.05]  | 0.915  | -0.42 [-1.38, 0.53]    | 0.387  |
| Port of entry                   | 28.61 (5.07)     | 0.35 [-0.30, 1.01]   | 0.291  | -0.17 [-0.76, 0.42]    | 0.568  |
| Pre-travel                      | 30.58 (4.45)     | 2.32 [1.43, 3.21]    | <0.001 | 0.01 [-0.77, 0.80]     | 0.976  |
| Individual request              | 29.58 (5.18)     | 1.33 [0.64, 2.02]    | <0.001 | 0.38 [0.23, 0.99]      | 0.221  |
| Other                           | 28.81 (5.13)     | 0.56 [-1.02, 2.13]   | 0.490  | -1.42 [-2.80, -0.05]   | 0.042  |
| **RT-qPCR test study-period month** |                |                      |        |                        |        |
| 23 March-21 April, 2021         | 25.15 (5.76)     | Ref.                 | Ref.   |                        |        |
| 22 April-21 May, 2021           | 27.82 (5.20)     | 2.67 [2.23, 3.11]    | <0.001 | 1.95 [1.53, 2.38]      | <0.001 |
| 22 May-20 June, 2021            | 31.55 (4.25)     | 6.40 [5.92, 6.87]    | <0.001 | 4.92 [4.43, 5.41]      | <0.001 |
| 21 June-20 July, 2021           | 30.10 (5.24)     | 4.95 [4.29, 5.61]    | <0.001 | 3.75 [3.09, 4.40]      | <0.001 |
| 21 July-19 August, 2021         | 30.94 (2.92)     | 5.79 [5.12, 6.46]    | <0.001 | 4.52 [3.84, 5.21]      | <0.001 |
| 20 August-18 September, 2021    | 32.41 (2.03)     | 7.26 [6.19, 8.33]    | <0.001 | 6.06 [5.00, 7.12]      | <0.001 |
| 19 September-18 October, 2021   | **                | **                   | **     | **                     | **     |
| 19 October-06 November, 2021   | **                | **                   | **     | **                     | **     |
| **Vaccination status**          |                  |                      |        |                        |        |
| Unvaccinated                    | 27.52 (5.71)     | Ref.                 | Ref.   |                        |        |
| One dose                        | 28.32 (5.56)     | 0.80 [0.06, 1.54]    | 0.034  | 1.37 [0.73, 2.00]      | <0.001 |
| Two doses                       |                  |                      |        |                        |        |
| <3 months before the RT-qPCR test| 30.47 (4.63)     | 2.95 [2.24, 3.67]    | <0.001 | 1.54 [0.91, 2.18]      | <0.001 |
| 3–<6 months before the RT-qPCR test| 30.61 (3.40)     | 3.10 [1.90, 4.29]    | <0.001 | 1.14 [0.04, 2.25]      | 0.042  |
| 6–<9 months before the RT-qPCR test| 33.89 (2.36)     | 6.38 [0.06, 12.69]   | 0.048  | 5.10 [0.32, 10.52]     | 0.065  |
| ≥9 months before the RT-qPCR test| **                | **                   | **     | **                     | **     |
| Three doses                     |                  |                      |        |                        |        |
| ≤1 month before the RT-qPCR test| 29.24 (-)        | 1.73 [-9.21, 12.66]  | 0.757  | -4.05 [-13.26, 5.15]   | 0.388  |
| >1 month before the RT-qPCR test| **                | **                   | **     | **                     | **     |
| Prior SARS-CoV-2 infection      |                  |                      |        |                        |        |
| Never                           | 27.04 (5.88)     | Ref.                 | Ref.   |                        |        |
| <90 days before the study RT-qPCR test† | 30.50 (3.79)     | 3.46 [2.02, 3.90]    | <0.001 | 3.07 [2.66, 3.49]      | <0.001 |
| Prior infection‡                 | 32.05 (3.14)     | 5.01 [3.19, 6.83]    | <0.001 | 1.83 [0.24, 3.42]      | 0.024  |

CI, confidence interval; Ct, cycle threshold; RT-qPCR, real-time reverse-transcription polymerase chain reaction; Ref., reference; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation.

*The two-tailed F-test of the univariable analysis.
†RT-qPCR Ct value was adjusted for age-group, sex, nationality, reason for RT-qPCR test, RT-qPCR test study-period month, vaccination status, and prior SARS-CoV-2 infection.
‡Nationalities were chosen to represent the most populous groups on Qatar.
¶These comprise 63 other nationalities in Qatar.
**Inestimable quantity due to very small number of observations.
††An RT-qPCR-positive test that occurred <90 days before the study RT-qPCR-positive test was included as a separate category in the analysis and was not considered a prior infection. This RT-qPCR-positive test and the study RT-qPCR-positive test may both reflect the same prolonged infection.
‡‡Prior infection was defined as an RT-qPCR-positive test that occurred ≥90 days before the RT-qPCR-positive test that is included in the study.
### TABLE 4  Associations with RT-qPCR Ct value among 5,576 Beta RT-qPCR-genotyped SARS-CoV-2 infections between March 23 and November 6, 2021.

| Characteristics                  | RT-qPCR Ct value Mean (SD) | Univariable analysis | F-test* p-value | Multivariable analysis† p-value |
|----------------------------------|----------------------------|----------------------|----------------|-------------------------------|
|                                  |                           | β coefficient [95% CI] | p-value        | β coefficient [95% CI]        |
| Age group in years               |                           |                      |                |                               |
| <0.001                           |                           |                      |                |                               |
| 10-19†                           | 23.53 (5.25)              | Ref.                 | <0.001         | 1.80 [1.22, 2.38]             |
| <10                              | 25.91 (5.02)              | 2.38 [1.72, 3.04]    | <0.001         |                               |
| 20-29                            | 23.56 (5.24)              | 0.04 [0.50, 0.58]    | 0.892          |                               |
| 30-39                            | 23.40 (5.09)              | -0.13 [-0.63, 0.38]  | 0.623          |                               |
| 40-49                            | 23.63 (5.05)              | 0.10 [-0.44, 0.65]   | 0.705          |                               |
| 50-59                            | 23.93 (5.01)              | 0.40 [-0.26, 1.06]   | 0.235          |                               |
| 60-69                            | 23.52 (4.29)              | -0.01 [-0.98, 0.97]  | 0.988          |                               |
| 70-79                            | 22.59 (5.51)              | -0.93 [-2.78, 0.92]  | 0.323          |                               |
| 80+                              | 23.36 (5.43)              | -0.17 [-2.98, 2.64]  | 0.904          |                               |
| Sex                              |                            |                      |                |                               |
| Female                           | 23.49 (5.15)              | Ref.                 | 0.020          |                               |
| Male                             | 23.83 (5.13)              | 0.34 [0.05, 0.63]    | 0.020          |                               |
| Nationality§                     |                            |                      |                |                               |
| Qatari                           | 23.88 (5.28)              | Ref.                 | 0.132          |                               |
| Bangladeshi                      | 23.80 (4.98)              | -0.08 [-0.66, 0.50]  | 0.790          |                               |
| Egyptian                         | 23.86 (5.08)              | -0.02 [-0.69, 0.65]  | 0.950          |                               |
| Filipino                         | 23.42 (5.02)              | -0.46 [-1.00, 0.08]  | 0.098          |                               |
| Indian                           | 23.81 (5.20)              | -0.07 [-0.51, 0.38]  | 0.771          |                               |
| Nepalese                         | 23.37 (5.15)              | -0.50 [-1.09, 0.08]  | 0.090          |                               |
| Pakistani                        | 24.34 (5.21)              | 0.46 [0.24, 1.15]    | 0.197          |                               |
| Sri Lankan                       | 23.17 (4.90)              | -0.71 [-1.47, 0.06]  | 0.071          |                               |
| Sudanese                         | 23.09 (4.61)              | -0.79 [-1.82, 0.24]  | 0.133          |                               |
| Other nationalities¶             | 23.72 (5.16)              | -0.16 [-0.64, 0.31]  | 0.506          |                               |
| Reason for RT-qPCR testing       |                            |                      | <0.001         |                               |
| Survey                           | 24.30 (4.85)              | Ref.                 |                |                               |
| Clinical suspicion               | 22.78 (4.89)              | -1.52 [-1.89, -1.14] | <0.001         |                               |
| Contact tracing                  | 23.46 (5.03)              | -0.84 [-1.31, -0.36] | 0.001          |                               |
| Healthcare routine testing       | 23.45 (4.93)              | -0.85 [-1.59, -0.12] | 0.023          |                               |
| Port of entry                    | 27.24 (5.46)              | 2.94 [2.29, 3.60]    | <0.001         |                               |
| Pre-travel                       | 26.82 (5.25)              | 2.52 [1.79, 3.24]    | <0.001         |                               |
| Individual request               | 24.14 (5.15)              | -0.16 [-0.67, 0.35]  | 0.549          |                               |
| Other                            | 24.86 (6.00)              | 0.56 [-0.87, 2.00]   | 0.442          |                               |
| RT-qPCR test study period month  |                            |                      | <0.001         |                               |
| 23 March-21 April, 2021          | 22.79 (4.73)              | Ref.                 |                |                               |
| 22 April-21 May, 2021            | 23.16 (4.70)              | 0.37 [0.07, 0.67]    | 0.016          |                               |
| 22 May-20 June, 2021             | 26.81 (5.64)              | 4.02 [3.40, 4.65]    | <0.001         |                               |
| 21 June-20 July, 2021            | 28.73 (3.86)              | 5.94 [5.06, 6.81]    | <0.001         |                               |
| 21 July-19 August, 2021          | 30.48 (2.85)              | 7.69 [7.16, 8.21]    | <0.001         |                               |
| 20 August-18 September, 2021     | 30.13 (3.66)              | 7.34 [6.36, 8.33]    | <0.001         |                               |
| 19 September-18 October, 2021    | -**                       | -**                  |                |                               |
| 19 October-06 November, 2021    | -**                       | -**                  |                |                               |
| Vaccination status               |                            |                      | <0.001         |                               |
| Unvaccinated                     | 23.59 (5.08)              | Ref.                 |                |                               |
| One dose                         | 23.21 (4.91)              | -0.38 [-0.82, 0.06]  | 0.091          |                               |

(Continued)
### TABLE 4 Continued

| Characteristics | RT-qPCR Ct value | Univariable analysis | F-test* | Multivariable analysis† |
|-----------------|------------------|----------------------|---------|------------------------|
|                 | Mean (SD)        | β coefficient [95% CI] | p-value | β coefficient [95% CI] | p-value |
| Two doses       |                  |                      |         |                        |         |
| <3 months before the RT-qPCR test | 24.26 (5.31) | 0.67 [0.18, 1.16] | 0.008 | 0.68 [0.23, 1.13] | 0.003 |
| 3-<6 months before the RT-qPCR test | 29.16 (4.58) | 5.57 [4.60, 6.54] | <0.001 | 0.48 [-0.47, 1.43] | 0.325 |
| 6-<9 months before the RT-qPCR test | 30.28 (4.50) | 6.69 [2.93, 10.45] | <0.001 | 0.06 [-3.28, 3.40] | 0.973 |
| ≥9 months before the RT-qPCR test | -** | -** | -** | -** | -** |
| Three doses     |                  |                      |         |                        |         |
| ≤1 month before the RT-qPCR test | 25.13 (2.72) | 1.54 [-5.49, 8.57] | 0.668 | 2.39 [-3.76, 8.53] | 0.446 |
| >1 month before the RT-qPCR test | -** | -** | -** | -** | -** |
| Prior SARS-CoV-2 infection |                  |                      |         |                        |         |
| Never | 23.19 (5.01) | Ref. | Ref. | Ref. | Ref. |
| ≤90 days before the study RT-qPCR test†† | 27.82 (4.17) | 4.63 [4.21, 5.04] | <0.001 | 4.14 [3.75, 4.53] | <0.001 |
| Prior infection‡‡ | 25.83 (5.31) | 2.64 [1.38, 3.89] | <0.001 | 2.04 [0.91, 3.17] | <0.001 |

CI, confidence interval; Ct, cycle threshold; RT-qPCR, real-time reverse-transcription polymerase chain reaction; Ref., reference; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation.

*The two-tailed F-test of the univariable analysis.
†RT-qPCR Ct value was adjusted for age-group, sex, nationality, reason for RT-qPCR test, RT-qPCR test study-period month, vaccination status, and prior SARS-CoV-2 infection.
‡The 10-19 age group was chosen as a reference, and not the <10 age group, because of the different manifestations of this infection in small children.
§Nationalities were chosen to represent the most populous groups on Qatar.
¶These comprise 60 other nationalities in Qatar.
**Inestimable quantity due to very small number of observations.
††An RT-qPCR-positive test that occurred <90 days before the study RT-qPCR-positive test was included separately in the analysis, but was not considered a prior infection. This RT-qPCR-positive test and the study RT-qPCR-positive test may both reflect the same prolonged infection.
‡‡Prior infection was defined as an RT-qPCR-positive test that occurred ≥90 days before the RT-qPCR-positive test that is included in the study.

### TABLE 5 Associations with RT-qPCR Ct value among 9,432 Delta RT-qPCR-genotyped SARS-CoV-2 infections between March 23 and November 6, 2021.

| Characteristics | RT-qPCR Ct value | Univariable analysis | F-test* | Multivariable analysis† |
|-----------------|------------------|----------------------|---------|------------------------|
|                 | Mean (SD)        | β coefficient [95% CI] | p-value | β coefficient [95% CI] | p-value |
| Age group in years |                  |                      |         |                        |         |
| 10-19‡         | 22.45 (5.07) | Ref. | Ref. | Ref. | Ref. |
| <10             | 24.89 (4.91) | 2.44 [2.04, 2.84] | <0.001 | 2.45 [2.07, 2.83] | <0.001 |
| 20-29           | 21.90 (5.12) | -0.55 [-0.91, -0.18] | 0.003 | -0.54 [-0.91, -0.16] | 0.005 |
| 30-39           | 21.93 (5.15) | -0.52 [-0.86, -0.18] | 0.003 | -0.64 [-1.00, -0.28] | <0.001 |
| 40-49           | 21.53 (5.24) | -0.92 [-1.30, -0.54] | <0.001 | -1.00 [-1.39, -0.61] | <0.001 |
| 50-59           | 21.75 (4.95) | -0.70 [-1.20, -0.20] | 0.006 | -0.84 [-1.34, -0.34] | 0.001 |
| 60-69           | 22.01 (5.28) | -0.44 [-1.17, 0.29] | 0.239 | -0.61 [-1.33, 0.10] | 0.093 |
| 70-79           | 22.16 (4.76) | -0.29 [-1.73, 1.16] | 0.696 | -0.04 [-1.42, 1.33] | 0.952 |
| 80+             | 21.39 (5.29) | 1.06 [-3.37, 1.26] | 0.371 | -0.76 [-2.94, 1.42] | 0.493 |
| Sex             |                  |                      | <0.001 |                        |         |
| Female          | 21.92 (5.12) | Ref. | Ref. | Ref. | Ref. |
| Male            | 22.58 (5.26) | 0.66 [0.44, 0.87] | <0.001 | 0.48 [0.27, 0.70] | <0.001 |
| Nationality§     |                  |                      | <0.001 |                        |         |
| Qatari          | 22.19 (4.95) | Ref. | Ref. | Ref. | Ref. |
| Bangladeshi     | 21.75 (5.63) | -0.44 [-1.01, 0.13] | 0.129 | -0.14 [-0.71, 0.42] | 0.617 |
| Egyptian        | 22.88 (5.22) | 0.68 [0.24, 1.13] | 0.002 | -0.08 [-0.50, 0.35] | 0.717 |

(Continued)
| Characteristics | RT-qPCR Ct value Mean (SD) | Univariable analysis | F-test | Multivariable analysis |
|-----------------|---------------------------|---------------------|--------|------------------------|
|                 | β coefficient [95% CI]     | p-value             |        | β coefficient [95% CI]  | p-value |
| Filipino        | 21.30 (5.46)              | -0.89 [-1.35, -0.44] | <0.001 | -0.37 [-0.83, 0.08]    | 0.106   |
| Indian          | 22.21 (5.27)              | 0.02 [-0.30, 0.34]   | 0.900  | -0.29 [-0.64, 0.06]    | 0.110   |
| Nepalese        | 22.50 (5.17)              | 0.31 [0.24, 0.86]    | 0.265  | -0.12 [0.68, 0.44]     | 0.677   |
| Pakistani       | 22.50 (5.29)              | 0.30 [0.19, 0.80]    | 0.227  | 0.07 [-0.41, 0.56]     | 0.766   |
| Sri Lankan      | 23.21 (5.54)              | 1.02 [0.20, 1.83]    | 0.015  | 0.33 [-0.44, 0.10]     | 0.399   |
| Sudanese        | 22.89 (4.85)              | 0.70 [0.36, 1.46]    | 0.073  | 0.87 [0.16, 1.58]      | 0.017   |
| Other nationalities§ | 22.51 (5.25)             | 0.32 [0.02, 0.61]    | 0.034  | 0.13 [-0.15, 0.42]     | 0.357   |
| Reason for RT-qPCR testing |                |                    |        |                        |        |
| Survey          | 22.44 (5.08)              | Ref.                | Ref.   |                        |        |
| Clinical suspicion | 21.16 (4.99)            | -1.28 [-1.61, -0.94] | <0.001 | -1.36 [-1.69, -1.04]   | <0.001 |
| Contact tracing | 22.25 (5.15)              | -0.19 [-0.60, 0.23]  | 0.371  | -0.37 [-0.76, 0.03]    | 0.073   |
| Healthcare routine testing | 22.71 (5.26)          | 0.27 [-0.49, 1.04]   | 0.483  | -0.17 [-0.90, 0.56]    | 0.650   |
| Port of entry   | 22.94 (5.18)              | 0.50 [0.16, 0.85]    | 0.004  | 0.93 [0.59, 1.27]      | <0.001 |
| Pre-travel      | 24.14 (5.27)              | 1.70 [1.25, 2.15]    | <0.001 | 1.80 [1.37, 2.22]      | <0.001 |
| Individual request | 22.15 (5.41)            | -0.29 [-0.79, 0.21]  | 0.262  | 0.36 [-0.14, 0.86]     | 0.158   |
| Other           | 25.20 (5.18)              | 2.76 [1.63, 3.89]    | <0.001 | -0.01 [-1.11, 1.09]    | 0.989   |
| RT-qPCR test study-period month |                |                    |        |                        |        |
| 23 March-21 April, 2021 | 21.55 (4.55)            | Ref.                | Ref.   |                        |        |
| 22 April-21 May, 2021 | 21.54 (4.89)            | -0.02 [-0.85, 0.81]  | 0.968  | -0.17 [-0.96, 0.61]    | 0.666   |
| 22 May-20 June, 2021 | 22.64 (5.69)            | 1.09 [0.25, 1.93]    | 0.011  | 1.05 [0.24, 1.86]      | 0.011   |
| 21 June-20 July, 2021 | 20.34 (4.44)            | -1.22 [-1.99, -0.44] | 0.002  | -1.14 [-1.90, -0.38]   | 0.003   |
| 21 July-19 August, 2021 | 21.90 (5.07)            | 0.35 [-0.38, 1.07]   | 0.348  | 0.13 [-0.58, 0.84]     | 0.722   |
| 20 August-18 September, 2021 | 23.47 (5.41)         | 1.92 [1.19, 2.65]    | <0.001 | 1.55 [0.84, 2.27]      | <0.001 |
| 19 September-18 October, 2021 | 23.04 (5.20)          | 1.49 [0.72, 2.26]    | <0.001 | 1.23 [0.47, 1.98]      | 0.001   |
| 19 October-06 November, 2021 | 21.76 (4.85)           | 0.21 [-0.59, 1.01]   | 0.606  | 0.26 [-0.53, 1.05]     | 0.524   |
| Vaccination status |                | <0.001              |        |                        |        |
| Unvaccinated    | 22.56 (5.31)              | Ref.                | Ref.   |                        |        |
| One dose        | 21.22 (5.24)              | -1.34 [-2.02, -0.66] | <0.001 | 0.35 [-0.29, 0.99]     | 0.281   |
| Two doses       | <3 months before the RT-qPCR test | 22.26 (4.98)        | -0.30 [-0.72, 0.11] | 0.151  | 0.87 [0.47, 1.27]      | <0.001 |
|                 | 3–6 months before the RT-qPCR test | 21.98 (5.04)        | -0.59 [-0.84, -0.33] | <0.001 | 0.22 [-0.06, 0.50]     | 0.120   |
|                 | 6–<9 months before the RT-qPCR test | 21.62 (4.97)        | -0.94 [-1.40, -0.49] | <0.001 | -0.23 [-0.72, 0.25]    | 0.347   |
|                 | ≥9 months before the RT-qPCR test | 18.81 (2.22)        | -3.75 [-5.85, -1.65] | 0.149  | -3.15 [-7.17, 1.57]    | 0.191   |
| Three doses     | ≤1 month before the RT-qPCR test | 17.72 (2.35)        | -4.84 [-12.05, 2.36] | 0.188  | -3.46 [-10.16, 3.23]   | 0.311   |
|                 | >1 month before the RT-qPCR test | 19.80 (2.97)        | -2.77 [-7.87, 2.33]  | 0.287  | -1.18 [-5.89, 3.53]    | 0.623   |
| Prior SARS-CoV-2 infection |                | <0.001              |        |                        |        |
| Never           | 21.93 (5.11)              | Ref.                | Ref.   |                        |        |
| <90 days before the study RT-qPCR test†† | 25.32 (4.95)          | 3.39 [3.05, 3.72]    | <0.001 | 4.03 [3.69, 4.38]      | <0.001 |
| Prior infection‡‡ | 24.00 (5.64)             | 2.07 [1.13, 3.02]    | <0.001 | 2.15 [1.26, 3.04]      | <0.001 |

CI, confidence interval; Ct, cycle threshold; RT-qPCR, real-time reverse-transcription polymerase chain reaction; Ref., reference; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation.

*The two-tailed F-test of the univariable analysis.

†RT-qPCR Ct value was adjusted for age-group, sex, nationality, reason for RT-qPCR test, RT-qPCR test study-period month, vaccination status, and prior SARS-CoV-2 infection.

‡The confidence interval of the univariable analysis. The univariable analysis included a variable for vaccination status that was adjusted for the presence of prior SARS-CoV-2 infection.

§Nationalities were chosen to represent the most populous groups on Qatar.

¶These comprise 87 other nationalities in Qatar.

††An RT-qPCR-positive test that occurred <90 days before the study RT-qPCR-positive test was included as a separate category in the analysis and was not considered a prior infection. This RT-qPCR-positive test and the study RT-qPCR-positive test may both reflect the same prolonged infection.

‡‡Prior infection was defined as an RT-qPCR-positive test that occurred ≥90 days before the RT-qPCR-positive test that is included in the study.
whether due to vaccination or prior infection, is associated with lower infectiousness of breakthrough infections. However, infectiousness of breakthrough infections increases gradually with time since second-dose vaccination, paralleling the waning of vaccine effectiveness after the second dose. These scientific insights enhance our understanding of the evolving epidemiology of the virus with implications for appropriate public health response against its different variants.

Data availability statement

The datasets presented in this article are not readily available because these are properties of the Qatar Ministry of Public Health that were provided to the researchers through a restricted-access agreement that prevents sharing the datasets with a third party or publicly. The data are available under restricted access for confidentiality. The raw data are protected and are not available due to data privacy laws. Aggregate data are available within the manuscript. Requests to access the datasets should be directed to Her Excellency the Minister of Public Health, https://www.moph.gov.qa/english/OurServices/eservices/Pages/Governmental-Health-Communication-Center.aspx.

Ethics statement

The studies involving human participants were reviewed and approved by Hamad Medical Corporation and Weill Cornell Medicine-Qatar Institutional Review Boards. Written informed consent from the participants’ legal guardian/next of kin was not required to participate in this study in accordance with the national legislation and the institutional requirements.

Author contributions

SQ co-designed the study, performed the statistical analyses, and co-wrote the first draft of the article. PT and MH conducted the multiplex, RT-qPCR variant screening and viral genome sequencing. HC co-designed the study and supported the statistical analyses. LA-R conceived and co-designed the study, led the statistical analyses, and co-wrote the first draft of the article. All authors contributed to data collection and acquisition, database development, discussion and interpretation of the results, and to the writing of the manuscript. All authors have read and approved the final manuscript.

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Conflict of interest

AB has received institutional grant funding from Gilead Sciences unrelated to the work presented in this paper.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fimmu.2022.984784/full#supplementary-material
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