Introduction

Recently, the new strain of the Coronavirus (COVID-19) emerged as a serious infectious respiratory disease that is life threatening, especially for elderly patients who have chronic illnesses. The virus is currently known as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and it was identified in Wuhan city, China for the first time in December 2019.1,2

On January 7, 2020, the whole genome sequencing of the novel SARS-CoV-2 virus was conducted in China.3 The World Health Organization (WHO) declared the pandemic as a Public Health Emergency of International Concern (PHEIC).4 Due to the worldwide high impact of the SARS-CoV-2 pandemic, scientists are urged to focus their research on the discovery of a vaccine that could save humanity.5

As per the Saudi Ministry of Health, Saudi Arabia is ranked as one of the most affected countries, with over a quarter of a million confirmed cases and 3000 SARS-CoV-2 related deaths.

Abstract

Aim: To find out if there is any correlation between COVID-19 antibody serological testing and symptom severity. Methods: This study is a case series of 44 consecutive patients confirmed with COVID-19 who are divided into a group of 23 patients with mild disease and a group of 21 patients with severe disease. All 44 samples were confirmed positive SARS-CoV-2. Subsequent recombinant SARS-CoV-2 S1/S2 IgG test was performed for all patients and all patients developed neutralizing antibodies with altered range.

Main outcomes: IgG level and its correlation with disease severity, demographic data, underlying comorbidities, clinical presentation, and treatment comparison between mild and severe disease groups. Results: Quantitative SARS COV-2 IgG was significantly higher in moderate and severe disease groups compared with those in the mild disease group. COVID-19 infection was more prevalent in male, Saudi nationals and smokers with comorbidities and higher inflammatory markers are more in the severe group than in the mild group which necessitates more management options to be taken for severe group patients. Conclusion: IgG antibody level was higher in the severe disease group. Also, the study showed significant differences between the mild and severe disease groups in terms of demographic, clinical, and management variables.

Keywords: Antibody serology, COVID-19, Saudi Arabia, Security Forces Hospital

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The current diagnosis of SARS-CoV-2 mainly relies on the detection of viral RNA in the respiratory tract samples. Therefore, many companies have established molecular diagnostic kits for the detection of SARS-CoV-2. Molecular analyses are currently dependent on reverse transcription followed by real-time PCR which targets different genes.[5]

Studies on severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) showed that virus-specific antibodies were detectable in 80–100% of patients at 2 weeks duration after the onset of symptoms. Currently, the antibody response against SARS-CoV-2 remains poorly understood and the clinical use of serological testing is unclear.[6]

Due to limited testing in many geographical regions, it is clear that the total number of actual COVID-19 cases is much higher than the number of confirmed ones. In most of the confirmed COVID-19 cases, the patients are symptomatic showing fever, dry cough, and pneumonia, but also more atypical symptoms such as gastrointestinal manifestations as well as anosmia.[7] Primary care and emergency physicians are the gatekeepers of the health system. So, they should be aware of the disease variability and presentations which enable them to identify the infected patients early and stop the spread of the virus by following isolation precautions and management as needed.

Most patients with SARS-CoV-2 infections had mild to severe respiratory illness with symptoms such as fever, cough, and shortness of breath, which might appear 2–14 d after exposure.[8] Serological tests can be useful in identifying persons who possibly might be protected from a subsequent infection and this can help more persons recovering from infection to return to work or school.[9] Compared to RT-PCR assays, detection by antibody assays are often faster, less expensive, and easy-to-use.[9]

Seroconversion for IgG and IgM occurred simultaneously or sequentially. During the first three weeks after symptom onset, there were increases in virus-specific IgG and IgM antibody titers. However, IgM showed a slight decrease in the >3-week. Both IgG and IgM titers plateaued within six days after seroconversion.[9] Serological testing may be helpful for the diagnosis of suspected patients with negative RT-PCR results and for the identification of asymptomatic infections.[6]

Materials and Methods

The convenient sample technique was used as all patients confirmed positive for SARS CoV-2 were included in the study and data were collected through the medical record (MR-V) computerized program, which is used to monitor and follow up the patients including all their laboratory, radiological investigations, and any medication that the patients received either as outpatients or during hospital admissions.

Data collected included patient demographic information, comorbidities, triage vital signs, initial laboratory tests, inpatient medications, and treatments (including invasive mechanical ventilation). Initial laboratory testing was defined as the first test results available, typically within 24 hours of admission.

The study protocol was approved by the research and ethic committee of the hospital.

PCR testing was performed for a total of 44 patients; 23 patients had mild respiratory symptoms while the rest 21 patients had severe symptoms and required ICU care. All 44 samples were confirmed positive for SARS-CoV-2. Subsequent, recombinant SARS-CoV-2 S1/S2 IgG assay was performed for all patients and all developed neutralizing antibodies with altered range.

Abbott molecular systems were used to perform the SARS-CoV-2 PCR assay. The assay is engineered with Dual target assay for RdRp and N-gene for nucleic acid qualitative detection in nasopharyngeal swaps. Abbott Molecular m2000sp analyzers were used to perform nucleic acid extraction using a magnetic microparticle-based protocol.

Serological processing was performed by using a LIAISON®XL Analyzer and the indirect (CLIA) method was used for the quantitative determination of IgG anti-S1 and IgG anti-S2 specific antibodies to SARS-CoV-2. In the first incubation, the SARS-CoV-2 IgG antibodies present in the samples bind to the magnetic particles through the specific S1 and S2 antigens. In the next incubation, the antibody conjugate reacts with IgG SARS-CoV-2 previously bound to the magnetic particles after which the boundless material is detached with a wash cycle. Consequently, the starter reagent is added and a flash chemiluminescence reaction is induced. The light signal, and therefore the quantity of antibody conjugate, is measured by a photomultiplier as per relative light units (RLU) and which reveals the IgG–SARS-CoV2 concentration of the examined samples.

The study protocol was approved on 01/03/2020 by the Research and Ethics Committee of the hospital. The convenient sampling technique was used as all patients confirmed positive for SARS CoV-2 were included in the study.

Statistical analysis

We summarized the categorical data with absolute numbers and percentages. For continuous data, we used means and standard deviations (SDs) or medians and interquartile ranges (IQRs). Normality was tested using Shapiro–Wilks, Anderson–Darling, and Kolmogorov–Smirnov test. A comparison between the groups for categorical variables was made using a Chi-square test or Fisher’s exact test. For continuous data, a student’s t-test or Mann–Whitney U test was used. An association with P value ≤0.05 was considered statistically significant. All the analyses were performed using the SAS version 9.4 (SAS Institute, Inc, Cary, NC) and R software (R foundation for statistical computing, Vienna, Austria).
**Result**

A total of 44 patients were confirmed with COVID-19 through PCR tests. The mean quantitative SARS COV-2 IgG of the mild disease group was 81.16 while that of the moderate and severe disease group was 148.1 with a significant P value of 0.002. Post PCR confirmation, the antibody level test mean duration was 22.3 days in the mild disease group and 35.43 days in the moderate and severe disease groups with a significant P value of 0.006 [Table 1] [Figure 1].

Demographic characteristics between the two groups showed that a majority of the moderate and severe disease group patients were male with a P value of 0.011, while the majority of the mild disease group were female. Moreover, the majority of the affected patients in the moderate and severe disease groups were Saudi nationals, while non-Saudi nationals were found in majority in the mild disease group (P value <.001). Most of the patients in the moderate and severe disease group were smokers (P value <.001) when compared to the mild disease group. The mean age of the moderate and severe disease group was 59.05 while that of the mild disease group was 34.7 (P value <.001; Table 2) [Figure 2].

In the moderate and severe disease group, 61.9% patients had diabetes while none had diabetes in the mild disease group (P value <.001). Similarly, 76.19% had hypertension in the moderate and severe disease group while only 13.04% had hypertension in the mild disease group (P value <.001). Most of the patients in the moderate and severe disease group were smokers (P value <.001) when compared to the mild disease group. The majority of the affected patients in the moderate and severe disease group were smokers (P value <.001) when compared to the mild disease group [Table 3].

At presentation, all patients in the moderate and severe disease group complained of cough while only 39.13% had cough in the mild disease group (P value <.001). Similarly, 76.19% had hypertension in the moderate and severe disease group while only 13.04% had hypertension in the mild disease group (P value <.001). Chronic kidney disease and other illnesses were higher in the moderate and severe disease group but not significant compared to the mild disease group [Table 3].

Upon comparison of the vital signs between the two groups, the median temperatures of the severe and mild disease group were 38.3°C and 37.35°C, respectively (P value 0.031). Significant differences between both the groups were found with regard to oxygen saturation (SpO2). The median oxygen saturation of the severe disease group was 94.00% while it was 100% in the mild disease group (P value < 0.001). The median respiratory rate (RR) of the severe disease group was 59.00 and that of the mild disease group was 20.00 (P value 0.003; Table 5).

With regard to laboratory investigations, lymphocytes were significantly lower in the severe disease group (mean = 9.90) compared to the mild disease group (mean = 27.95) (P value = 0.014). Other significant values between the two

| Variable | Mild | Moderate and Severe | Total | P |
|----------|------|---------------------|-------|---|
| Age, mean±SD | 34.70±10.53 | 59.05±14.67 | 46.32±17.56 | <.001 |
| Gender | | | | 0.011 |
| Male | 10 (43.48%) | 17 (80.95%) | 27 (61.36%) |
| Female | 13 (56.52%) | 4 (19.05%) | 17 (38.64%) |
| Nationality | | | | <.001 |
| Saudi | 6 (26.09%) | 16 (76.19%) | 22 (50.00%) |
| Non-Saudi | 17 (73.91%) | 5 (23.81%) | 22 (50.00%) |
| Smoking | | | | <.001 |
| Yes | 0 (0.00%) | 19 (90.48%) | 19 (43.18%) |
| No | 23 (100.00%) | 2 (9.52%) | 25 (56.82%) |
| Diabetes* | Mild | Moderate and Severe | Total | P |
| Yes | 0 (0.00%) | 13 (61.90%) | 13 (29.55%) | <.001 |
| No | 23 (100.00%) | 8 (38.10%) | 31 (70.45%) |
| Hypertension | | | | <.001 |
| Yes | 3 (13.04%) | 16 (76.19%) | 19 (43.18%) |
| No | 20 (86.96%) | 5 (23.81%) | 25 (56.82%) |
| CKD | | | | <.001 |
| Yes | 0 (0.00%) | 2 (9.52%) | 2 (4.55%) | 0.222 |
| No | 23 (100.00%) | 19 (90.48%) | 42 (95.45%) |
| Other illness | | | | 0.095 |
| Yes | 1 (4.55%) | 5 (23.81%) | 6 (13.95%) |
| No | 21 (95.45%) | 16 (76.19%) | 37 (86.05%) |
| Cough# | Mild | Moderate and Severe | Total | P |
| Yes | 9 (39.13%) | 21 (100.00%) | 30 (68.18%) | <.001 |
| No | 14 (60.87%) | 0 (0.00%) | 14 (31.82%) |
| Fever | | | | 0.004 |
| Yes | 13 (56.52%) | 20 (95.24%) | 33 (75.00%) |
| No | 10 (43.48%) | 1 (4.76%) | 11 (25.00%) |
| Sore Throat | | | | 0.022 |
| Yes | 6 (26.09%) | 0 (0.00%) | 6 (13.64%) |
| No | 17 (73.91%) | 21 (100.00%) | 38 (86.36%) |
| Diarrhea | | | | 0.222 |
| Yes | 0 (0.00%) | 2 (9.52%) | 2 (4.55%) |
| No | 23 (100.00%) | 19 (90.48%) | 42 (95.45%) |
| SOB | | | | 0.002 |
| Yes | 2 (8.70%) | 11 (52.38%) | 13 (29.55%) |
| No | 21 (91.30%) | 10 (47.62%) | 31 (70.45%) |
In terms of both ward or intensive care admission and management options, more patients of the severe disease group were admitted to ICU and kept on ventilators compared to those of the mild disease group patients. Different pharmacological regimens were given to the severe disease group patients than those of the mild disease group patients. A significant P value was found [Table 7].

**Discussion**

This study was conducted on 44 consecutive patients confirmed with COVID-19 in the Security Forces Hospital, Riyadh. The serological assay detects the presence of IgG or IgM or both. A positive interpretation has been defined as a positive IgM or convalescent sera with 4 times more IgG titer than that of the acute phase.\(^1\) We came up with a highly significant correlation of quantitative SARS COV-2 IgG between patients in the moderate or severe disease group compared to patients in the mild disease group with a P value of 0.002 which is consistent with a study done in China.\(^2\) Antibodies increase during the later course of illness, and the median duration of COVID-19 IgG detection was around 14 days after the onset of symptoms.\(^3\)

Unfortunately, we tested SARS COV-2 IgG only once for the two groups with a mean duration of 22.30 days for the mild disease group while the mean duration for the moderate and severe disease group was 35.43 days; the significant duration difference with a P value of 0.006 could explain the significant difference in the SARS COV-2 IgG. The strength and duration of immunity after infection are key issues for “shield immunity.” While IgG

![Figure 1: Baseline characteristics of patients infected with 2019-nCoV](image)

\(\text{Table 5: Vital sign characteristics of patients infected with 2019-nCoV}\)

| Variable* | Mild and Severe | Total | P     |
|-----------|-----------------|-------|-------|
| Temp, median (IQR) | 37.35 (0.60) | 37.60 (1.40) | 0.031 |
| Systolic BP, mean±SD | 124.7±15.03 | 134.8±20.23 | 0.158 |
| Diastolic BP, mean±SD | 73.60±9.44 | 77.05±14.34 | 0.498 |
| SpO\(_2\), median (IQR) | 100.0 (2.00) | 96.00 (5.50) | <.001 |
| RR, median (IQR) | 20.00 (1.00) | 21.50 (6.40) | 0.003 |
| HR, median (IQR) | 96.00 (16.00) | 90.00 (74.00) | 0.060 |

\(\text{Table 6: Laboratory characteristics of patients infected with 2019-nCoV}\)

| Variable* | Mild | Moderate and Severe | Total | P     |
|-----------|------|---------------------|-------|-------|
| Hbg, median (IQR) | 13.20 (3.50) | 13.70 (2.50) | 13.20 (2.50) | 0.970 |
| WBC, median (IQR) | 5.80 (0.67) | 7.15 (3.18) | 6.82 (3.11) | 0.095 |
| Lymphocytes, median (IQR) | 27.95 (10.20) | 9.90 (10.50) | 11.20 (13.40) | 0.014 |
| ESR, mean±SD | 14.00±7.07 | 65.63±20.47 | 55.30±28.38 | 0.010 |
| CRP, mean±SD | 5.97±7.83 | 14.00±7.07 | 7.15 (3.18) | 0.006 |
| Ferritin, median (IQR) | 161.1±111.0 | 237.4±150.3 | 126.3±100.2 | 0.023 |
| K, mean±SD | 4.12±0.44 | 4.54±0.68 | 4.45±0.65 | 0.161 |
| ALT, median (IQR) | 18.50 (15.50) | 27.00 (20.00) | 27.00 (20.00) | 0.414 |
| AST, median (IQR) | 20.00 (9.50) | 32.00 (26.00) | 31.00 (32.00) | 0.110 |

\(\text{Table 7: Management provided to patients infected with 2019-nCoV}\)

| Covariate | Statistics | Level | Group | P*     |
|-----------|-----------|-------|-------|--------|
| ICU       | N (Col %) | Yes   | n=23  | 13 (61.9) | <.001 |
| Ventilator| N (Col %) | Yes   | n=21  | 7 (33.3)  | 0.003 |
| Antibiotics| N (Col %) | Yes   | n=23  | 21 (100) | <.001 |
| Antiviral | N (Col %) | Yes   | n=23  | 21 (100) | <.001 |
| Hydroxylorquine | N (Col %) | Yes | n=23  | 4 (19.0) | 0.028 |
| Tocilizumab | N (Col %) | Yes   | n=23  | 8 (38.1) | 0.001 |
| Corticosteroids | N (Col %) | Yes   | n=23  | 13 (61.9) | <.001 |
| Anticoagulants | N (Col %) | Yes   | n=23  | 20 (95.2) | <.001 |
and neutralizing antibodies are observed at high levels in a high proportion of individuals who recovered from SARS-CoV-2 infection, they start to decrease within 2–3 months after infection.\[8\]

Further observations regarding demographic characteristics between the two groups found that the mean age for moderate and severe disease group (65) was higher than that of the mean age for mild disease group (6) which is in line with other studies\[11\] but inconsistent with the study done by Bryan et al\[12\]. Saudi nationals and smokers were found to be significantly higher in the moderate and severe disease group patients compared to the mild disease patients group. Moreover, more men were found in the moderate and severe disease group patients than in the mild disease patients group.

Pre-existing conditions, diabetes, and hypertension were more in the moderate and severe disease group compared to the mild
disease group with a \( P \) value of <.001 between the two groups for both conditions.

Common symptoms at presentation, cough and fever, were significantly higher in the moderate and severe disease patients group compared to the mild disease patients group which is in line with the results of other studies (\( P \) value <.001 and 0.004, respectively). Moreover, shortness of breath (SOB) was also significantly higher in the severe disease group than in the mild disease group (\( P \) value of 0.002). Consequently, SpO2 was significantly lower in the severe disease patient group compared to the mild disease patient group (\( P \) value of <.001).

In terms of laboratory results, ESR, CRP, Ferritin, LDH, and creatinine were all significantly higher in the severe disease patients group than in the mild disease patients group. However, lymphocytes were lower in the severe disease group than in the mild disease group. \( P \) value was significant with a value of 0.014.

As expected, the usage of all management modalities including ICU admission, use of ventilators, and pharmacotherapy was found to be significantly higher in the moderate and severe disease group patients compared to the patients in the mild disease group.

Conclusion

This is a case series of 44 patients belonging to the mild and severe COVID-19 disease showed that the IgG antibody level was higher in the severe disease group than in the mild disease group. Also, it showed significant differences between the two groups in terms of demographic, clinical, and management variables. The higher antibody level correlates with more severe symptoms, higher inflammatory markers, laboratory abnormalities, and more need for medication and interventions.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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