Risk Factors for Readmission in the Patients with COVID-19 Admitted to Hospital

Mohammad Nematshahi
Sabzevar University of Medical Sciences

Mahboubeh Neamatshahi
Sabzevar University of Medical Sciences

fahimeh attarian (✉ attarian581@gmail.com)
Iran University of Medical Sciences  https://orcid.org/0000-0001-9752-0480

Faeze Rahimi
Sabzevar University of Medical Sciences

Davood Soroosh
Sabzevar University of Medical Sciences

Research note

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Abstract

**Objective**: COVID-19 has been introduced by the World Health Organization as a health emergency worldwide. Although more than 5% of the patients with COVID-19 require hospitalization, there are still no clear guidelines on patients’ discharge time and factors influencing post-discharge outcomes. This study aimed to determine risk factors for readmission in the patients with COVID-19 admitted to hospital. In this prospective study, 416 discharged patients with a minimum follow-up of one month and the need for readmission were recorded. Evaluated characteristics included age, gender, CT scan, RT-PCR test and treatment modalities. After describing the data, any relationship between the patients’ characteristics and readmission was assessed and predictive factors of readmission risk were estimated using regression model. The data were analyzed through STATA and P value less than of 0.05 was considered significant.

**Results**: Regarding readmission, 51 patients were readmitted during the study period. The median follow-up time was 20 days (IQR: 7-120) and the mean follow-up time was 61±11.2 days. The mean duration of first hospitalization was 5.5 days and the rate of readmission of the patients between 30 and 60 days after discharge was 7.6% and 8.1%, respectively. The median age of these patients was 67 years (IQR: 53-78). About 65% of readmitted patients had underlying disease. The difference in readmission time was based on blood creatinine level and lung involvement. The odds ratio of readmission in the patients with abnormal creatinine levels (higher and equal to 1.2 mg/dl) and diabetes was equal to 2.15 and 3.43, respectively. Also, the odds ratio of readmission in the patients with basal lung involvement was 4.16. The highest readmission rate was 30 days after discharge. Age over 60 years, underlying disease especially diabetes, high creatinine level and lung involvement were the most important predictors of readmission in the patients with COVID-19.

**Introduction**: Coronavirus Disease 2019 (COVID-19) was declared by the World Health Organization (WHO) as a global health emergency on January 30, 2020 (1, 2). There is currently a high prevalence of COVID-19 in the human population, as a consequent rising demand for hospitalization (3), however, the pathogenicity and severity of the disease are not high and most people recover following COVID-19 (4), but in 5% of cases, hospitalization is essential to keep on the treatment process. Old age and underlying disease are the most important factors related to the need for hospitalization (5). Therefore, in most societies due to the aging population and high prevalence of diabetes and hypertension, there is an increase in demand for hospital beds and over-hospitalization (6, 7). The clear guidelines for the management of the patients with COVID-19 and the time of discharge have not yet been determined based on clinical evidence (3, 8). Physicians may be cautious and the patient may be hospitalized for long periods of time unnecessarily, or conversely, with early discharge, the patient may be readmitted or have unwanted complications or a worsening prognosis (9, 10). According to the Centers for Disease Control and Prevention (CDC), up to 9% of the patients with COVID-19 may be readmitted to the same hospital within 2 months of discharge (9), so it is important to pay attention to the clinical aspects of readmission in these patients (11–14).

Mostly male gender, old age and the presence of underlying disease or history of malignancy are associated with poor prognosis and readmission in this group of patients (11, 12, 15). Paying too much attention to COVID-19 pandemic has caused deception to pay attention to other serious diseases such as neoplasms or cardiovascular diseases, which leads to increased mortality in populations and based on the experience of previous respiratory pandemics, the effective use of hospital beds should be an essential goal in the pandemic (4, 16–18). Therefore, identifying the reasons for readmission and the characteristics of the patients at risk for readmission can lead to better decision-making and management at discharge or more accurate clinical follow-up after discharge. The
present study aimed to determine the risk factors for readmission in the patients with COVID-19 admitted to the hospital.

Methods And Materials

In this prospective study, a cohort of 508 patients admitted with a diagnosis of COVID-19 in Vasei hospital was studied between March 1, 2019 and May 20, 2020. Vasei hospital is located in Sabzevar city in the west of Khorasan Razavi province. all patients were admitted to this hospital with a definite or clinical diagnosis of COVID-19. Informed consent form was obtained from all patients. Of the total cohort, 34.78%, 75.49%, 100% of the patients were hospitalized by the end of the first month, second month, end of the first trimester from the beginning of the pandemic. COVID-19 was assessed by Polymerase chain reaction (PCR) and imaging finding. In this study, 92 patients (18.18%) who died during hospitalization were excluded from the study and 416 patients (81%) were recovered, discharged and followed up for at least 6 months after discharge to assess the rate of readmission. Assessed characteristics include age, gender, biochemical findings, CT scan and RT-PCR test results, and underlying disease such as diabetes, hypertension and pregnancy or other underlying diseases, and length of hospital stay. Readmission was evaluated as the main dependent outcome and the risk of readmission for each of the related factors was estimated at a time interval of 3 to 180 days after discharge using regression model (20). The data were analyzed through STATA and P value less than of 0.05 was considered significant.

Results

In this study, 416 patients were followed, the median and mean follow-up of discharged patients were 20 days (IQR: 7-120) and 61 ± 11.2 days. Fifty-one discharged patients \ were readmitted, of which 13 patients (25%) one week after discharge (readmission rate = 3.1%) and 32 patients (62%) up to 30 days after discharge (readmission rate = 7.6%) and 34 patients (66%) up to 60 days after discharge (readmission rate = 8.1%) and the rest of the patients (readmission rate = 12.25%) up to 40 weeks after discharge were readmitted.

The age of readmitted patients were range from 29 to 94 years old (median = 67, IQR: 53–78), and mean age was 65 ± 15.42, however the median age of the recovered patients was 58 (IQR: 42–68), with mean age 56 ± 18.2 years old (p < 0.001). Regarding gender, there was no significant difference among readmitted patients (Table 1).

35% of readmitted patients had underlying disease. The results showed that there was a significant relationship between underlying disease and readmission (p < 0.001). It is important to note that none of the pregnant women were readmitted (Table 1).

Of the total readmitted patients, 31 patients (64.5%) had a negative PCR result, although 84.3% of readmitted patients had abnormal chest imaging results in the first hospitalization. Also, the mean blood creatinine level in the patients who were readmitted was significantly higher than patients without readmission (p < 0.001). The median duration of hospitalization for the first time was 5 days (IQR: 3–9) in readmitted patients and 4 days (IQR: 3–6) in other discharged patients (p < 0.001). There was no significant difference between readmitted and discharged patients in respect of the others assessed characters (Table 1).
Table 1
Clinical, biochemical and therapeutic characteristics of the recovered and readmitted patient

| Variable                      | Total Number | Non-readmitted, 365(87.7) | Readmitted, 51(12.2) | P value |
|-------------------------------|--------------|---------------------------|-----------------------|---------|
| Gender (n = 416)              |              |                           |                       |         |
| Male                          | 228(54.0)    | 203 55.6                  | 25 49.0               | 0.78*   |
| Female                        | 188(45.0)    | 162 44.4                  | 26 51.0               |         |
| PCR (n = 368)                 |              |                           |                       |         |
| Negative                      | 227 (61.6)   | 169 61.2                  | 31 64.6               | 0.19*   |
| Positive                      | 141(38.4)    | 124 38.8                  | 17 35.4               |         |
| Comorbidity (n = 416)         |              |                           |                       | <0.001**|
| No                            | 224(53.8)    | 206 56.4                  | 18 35.3               |         |
| Diabetes                      | 42(10.1)     | 29 8.0                    | 13 25.5               |         |
| Hypertension                  | 61(14.7)     | 55 15.0                   | 6 11.7                |         |
| Others                        | 83(20.0)     | 69 18.9                   | 14 27.4               |         |
| Pregnancy                     | 6(0.14)      | 6 1.64                    | 0 0                   |         |
| Dry Cough (n = 416)           |              |                           |                       |         |
| No                            | 154(37.0)    | 131 35.9                  | 23 45.1               | 0.20*   |
| Yes                           | 262(63.0)    | 234 64.1                  | 28 54.9               |         |
| Fever (n = 416)               |              |                           |                       |         |
| No                            | 162(38.9)    | 137 37.5                  | 25 49.0               | 0.11*   |
| Yes                           | 254(61.1)    | 228 62.4                  | 26 51.0               |         |
| CT- Result (n = 416)          |              |                           |                       |         |
| Normal                        | 87(20.9)     | 79 21.7                   | 8 15.7                | 0.32*   |
| Abnormal                      | 329(79.1)    | 286 78.3                  | 43 84.3               |         |
| Lymph-degree (n = 398)        |              |                           |                       |         |
| Lymphocytosis > 3000          | 22(05.5)     | 17 4.9                    | 5 9.8                 | 0.34*   |
| Normal 1100–3000              | 219(55.0)    | 193 55.6                  | 26 51.0               |         |
| Lymphopenia < 1100            | 157(39.5)    | 137 39.5                  | 20 39.2               |         |
| HR-degree (n = 410)           |              |                           |                       |         |
| Tachycardia > 100             | 144(35.1)    | 121 33.7                  | 23 45.1               | 0.12**  |
| Normal 60–100                 | 256(62.4)    | 230 64.0                  | 26 51.0               |         |
| Bradycardia < 60              | 10(02.4)     | 8 2.2                     | 2 3.9                 |         |
| D-dimer (n = 416)             |              |                           |                       |         |
| No                            | 85(19.7)     | 78 21.4                   | 7 13.7                | 0.20*   |
| Yes                           | 331(80.3)    | 287 78.6                  | 44 86.3               |         |
| Age (year)                    |              |                           |                       |         |
| ≤ 60                          | 226(54.3)    | 205 56.2                  | 21 42.1               | 0.04*   |
| > 60                          | 190(45.7)    | 160 43.8                  | 30 58.9               |         |

* Pearson χ2, ** Fisher's exact, *** t-test
| Variable                          | Total Number | Non-readmitted, 365(87.7) | Readmitted, 51(12.2) | P value |
|----------------------------------|--------------|----------------------------|----------------------|---------|
|                                  | N            | Mean(CI %95)               | N                    | Mean(CI %95) | P value |
| Quantitative variables           | N            |                           | N                    |                |        |
| Systolic blood pressure (mmHg)   | 415          | 119.8 (117.6, 122.0)      | 51                   | 117.3 (112.6, 122.0) | 0.42    |
| Diastolic blood pressure (mmHg)  | 416          | 73.8 (72.6,75.1)          | 51                   | 74.2 (71.3, 77.2) | 0.80    |
| SPO2                             | 407          | 89.3 (88.4, 90.2)         | 51                   | 88.2 (86.3, 90.1) | 0.40    |
| Creatinine (mg/dl)               | 372          | 1.1 (1.1, 1.2)            | 46                   | 1.5 (1.2, 1.9) | <0.001  |
| Hospitalization (day)            | 415          | 5.2 (4.7, 5.7)            | 51                   | 7.0 (5.5, 8.5) | <0.001  |
| ICU (day)                        | 52           | 4 (2.75, 5.24)            | 9                    | 3.4 (0.36, 7.25) | 0.72    |
| Mechanical ventilation (day)     | 11           | 1.6 (0.75, 2.7)           | 2                    | 1 (1, 1)     | 0.53    |

* Pearson χ², ** Fisher's exact, *** t-test

Most readmitted patients (82.3%) who had positive PCR and abnormal creatinine levels (82%) were admitted to the hospital up to 30 days after discharge. There was no difference in the time of readmission of the patients based on age, underlying disease or history of hospitalization in ICU. However, 84.3% of readmitted patients had a history of abnormal CT scan. In general, the time of readmission was related to the results of CT scan and involvement site of the lung (Table 2).
Table 2  
Comparison of readmission time of patients based on clinical and laboratory characteristics and CT scan

| Variable                           | Cat        | Total n% | Readmission                      | Log-rank test |
|------------------------------------|------------|----------|----------------------------------|---------------|
|                                    |            |          | 3–7 days | 8-30days | 31-60days |          |          |
|                                    |            |          | N       | Failure Function | N       | Failure Function | N       | Failure Function | P = 0.28 |
| PCR (n = 48)                       | Negative   | 31(64.5) | 8       | 0.25     | 16      | 0.51     | 18      | 0.58     |          |
|                                    | Positive   | 17(35.5) | 5       | 0.29     | 14      | 0.82     | 14      | 0.82     |          |
| Age (n = 51)                       | 60≥        | 21(41.2) | 4       | 0.19     | 13      | 0.61     | 14      | 0.66     | P = 0.72 |
|                                    | 60<        | 30 (58.8)| 9       | 0.30     | 19      | 0.63     | 20      | 0.66     |          |
| Comorbidity (n = 51)               | No         | 18 (35.2)| 4       | 0.22     | 11      | 0.61     | 12      | 0.22     | P = 0.69 |
|                                    | DM         | 13(25.5) | 4       | 0.30     | 9       | 0.69     | 9       | 0.69     |          |
|                                    | HTN        | 6 (11.8) | 2       | 0.33     | 4       | 0.66     | 4       | 0.66     |          |
|                                    | Others     | 14 (27.5)| 3       | 0.21     | 8       | 0.57     | 9       | 0.64     |          |
| Creatinine (mg/dl)                 | < 1.2      | 16 (35.6)| 3       | 0.18     | 9       | 0.56     | 18      | 0.58     | P = 0.84 |
|                                    | ≥ 1.2      | 29(64.4) | 9       | 0.29     | 14      | 0.82     | 14      | 0.82     |          |
| History admission ICU (n = 51)     | No         | 42(82.3) | 10      | 0.23     | 26      | 0.61     | 28      | 0.66     | P = 0.77 |
|                                    | Yes        | 9 (17.7) | 3       | 0.33     | 6       | 0.66     | 6       | 0.66     |          |
| Mechanical Ventilation (n = 51)    | No         | 49(96.8) | 12      | 0.24     | 30      | 0.61     | 39      | 0.65     | P = 0.20 |
|                                    | Yes        | 2(3.92)  | 1       | 0.50     | 2       | 1.0      | -       | -        |          |
| History of CT result (n = 51)      | Normal     | 8 (15.7) | 1       | 0.12     | 2       | 0.25     | 3       | 0.37     | P = 0.04 |
|                                    | Abnormal   | 43 (84.3)| 12      | 0.27     | 30      | 0.69     | 31      | 0.72     |          |
| Ground Glass Opacity (n = 43)      | No         | 6(13.95) | 2       | 0.33     | 3       | 0.50     | 3       | 0.50     | P = 0.65 |
|                                    | Yes        | 37(86.05)| 10      | 0.27     | 27      | 0.72     | 28      | 0.75     |          |
| Site of lesions (n = 43)           | Multiple lobes | 4(9.30) | 3       | 0.75     | 4       | 1.0      |          |          | P = 0.04 |
|                                    | Peripheral | 20(46.51)| 6       | 0.30     | 15      | 0.75     | 16      | 0.80     |          |
|                                    | Lung bases. | 14(32.56)| 3       | 0.21     | 10      | 0.71     | 10      | 0.71     |          |
|                                    | Peribronchovascular distribution | 2(4.65) | -       | -       | -       | -       | -       | -        |          |
|                                    | Central    | 3(6.96)  | 0       | 0        | 1       | 0.33     | 1       | 0.33     |          |
| Bilateral                          | No         | 12(27.91)| 4       | 0.33     | 4       | 0.33     | 4       | 0.33     | P = 0.002|
|                                    | Yes        | 31(72.09)| 8       | 0.25     | 26      | 0.83     | 27      | 0.87     |          |
| Pleural effusion                   | No         | 39(90.7) | 10      | 0.25     | 26      | 0.66     | 27      | 0.69     | P = 0.38 |
|                                    | Yes        | 3(7.30)  | 1       | 0.33     | 16      | 0.51     | 16      | 0.51     |          |
Discharged patients older than 60 years were 1.12 times more likely to be readmitted than other patients. Patients who had a dry cough and fever for the first time or had a positive PCR test were at lower risk of readmission ($p > 0.05$). Lung involvement and involvement site were most important factors related to readmission, so that patients with Lung involvement 1.48 times and with peribronchovascular distribution or central involvement had 4.5 times more likely to be readmitted ($p < 0.05$). Also, the odds ratio of readmission in the patients with basal lung involvement was 4.16 times greater than those with multiple lobes involvement. After controlling the effect of other variables, the odds ratio of readmission in the patients with abnormal creatinine level and diabetes was 2.15 and 3.43 times other patients. (Table 3).
Table 3
Relationship between demographic, clinical, biochemical and therapeutic characteristics and readmission of COVID-19 patients

| Variable                      | Crude OR (95% CI) | Adjusted OR (95% CI) |
|-------------------------------|-------------------|----------------------|
| Age                           |                   |                      |
| 60≥                           | 1                 | 1                    |
| > 60                          | 1.83 (1.00, 3.31)*| 1.12 (0.52, 2.47)    |
| Gender                        |                   |                      |
| Male                          | 1                 |                      |
| Female                        | 1.30 (0.72, 2.34) |                      |
| Dry Cough                     |                   |                      |
| No                            | 1                 |                      |
| Yes                           | 0.68 (0.37, 1.23) |                      |
| Fever                         |                   |                      |
| No                            | 1                 |                      |
| Yes                           | 0.62 (0.34, 1.12) |                      |
| Comorbidity                   |                   |                      |
| No                            | 1                 |                      |
| DM                            | 5.27 (2.34, 11.89)*| 3.43 (1.13, 8.37)*   |
| HTN                           | 1.28 (0.48, 3.39) | 0.72 (0.21, 2.47)    |
| Others                        | 2.38 (1.13, 5.05)*| 1.24 (0.46, 3.27)    |
| D-dimer (ng/ml)               |                   |                      |
| No                            | 1                 |                      |
| Yes                           | 1.70 (0.74, 3.94) |                      |
| PCR                           |                   |                      |
| No                            | 1                 |                      |
| Yes                           | 0.86 (0.46, 1.63) |                      |
| Creatinine, mg/dL             |                   |                      |
| < 1.2                         | 1                 | 1                    |
| ≥ 1.2                         | 2.84 (1.48, 5.43)*| 2.15 (1.00, 4.59)*   |
| Duration of Hospitalization   |                   |                      |
| < 6                           | 1                 | 1                    |
| ≥ 6                           | 1.93 (1.06, 3.51)*| 2.00 (0.94, 4.27)    |
| Admission to ICU              |                   |                      |
| No                            | 1                 |                      |
| Yes                           | 1.60 (0.73, 3.52) |                      |
| Ct result                     |                   |                      |
| Normal                        | 1                 |                      |
| Abnormal                      | 1.48 (0.67, 3.28) |                      |
| Site of lesion(s)             |                   |                      |
| Multiple lobes                | 1                 | 1                    |
| Peripheral                    | 3.36 (1.10, 10.19)*| 2.40 (0.75, 7.67)    |
| Lung bases.                   | 4.41 (1.38, 14.05)*| 4.16 (1.23, 14.05)*  |
| Peribronchovascular distribution | 4.55 (0.72, 28.4) | 4.43 (0.65, 30.51)  |
| Variable | Crude OR (95% CI)         | Adjusted OR (95% CI) |
|----------|--------------------------|---------------------|
| Central  | 20.5 (3.10, 135.5)*      | 6.15 (0.66, 56.93)  |

**Discussion**

In this prospective study, the results of clinical, laboratory and radiological examinations were used to identify the factors associated with readmission. Diabetes, abnormal blood creatinine levels, lung involvement, and duration of first-time hospitalization were the most important predictors of readmission. The readmission rate was 3.1% for one week after discharge, 7.6% for one month after discharge, and 8.6% for two months after discharge.

In this study the rate of readmission at similar time intervals was consistent with other studies (9), in which readmission in the first week after discharge was between 2 and 4% (13, 14 22) and was reported 10% for two months after discharge (9). In the follow-up of 279 discharged patients in Rhode Island of the United States, 30 days after discharge, readmission rate was reported 6.7% (11). In a study done in Turkish study, 7.1% of discharged patients were readmitted (15). The readmission rate of 106,543 COVID-19 patients discharged from the hospital two months after discharge was 9% in the United States (9). Donnelly et al followed up 1,775 discharged patients in the United States and reported readmission in 20% of the patients two months after discharge (19). In another study, 10.3% of discharged patients were readmitted to hospital 80 days after discharge (23). However, in different findings in the Korean study, the readmission rate of the patients with COVID-19 after discharge was 4.3% (12) and in Spanish study, the readmission rate was 4.4% up to three weeks after discharge (10).

The median length of stay in hospitals for the first time was 4 days which was similar to the findings of previous studies in Iran (24, 25). A review of 52 studies estimated the median length of stay in hospitals about 5 days (26), which was similar to the median length of stay in New York hospitals performed on 5,700 patients (13). Length of stay was very different in Korean hospitals (17 days) (12). Also, in the present study, the median length of stay for readmitted and non-readmitted patients was 5 days (IQR: 3–9) and 4 days (IQR: 3–6), respectively, while in the Turkish study, the median length of stay in the patients was 4 days and 3 days, respectively (15).

In the Spanish study, the median length of stay in the readmitted patients with COVID-19 was lower than other patients (6 days vs. 9 days) (10). In a review of 7,590 patients admitted to Korean hospitals, the median length of stay was lower than other patients (10, 12), but since the median length of stay in the patients who were not readmitted was shorter than in readmission patients, most patients were likely to be discharged on time. Hospitalization of patients has some conditions which include the capacity of the medical system, the quality of care and the demand for hospital beds in the pandemic period (15, 16). Different quality of post-discharge care can also have consequences on its effective after the discharge and we should pay attention to it in analyzing the results (14, 23).

Old age and underlying disease, especially diabetes, were two important characteristics of patients who were readmitted. The odds ratio of readmission in the patients over 60 years and diabetics compared to the younger patients and free of underlying disease was 1.83 and 3.43 times higher, respectively. In a study by Jeon et al, the odds ratio of readmission in the patients over 65 years and underlying disease was 2.23 and 4.39, respectively (12). Wu and McGoogan (27) and another study (13) the odds ratio of readmission in elderly patients was higher than in other age groups. Underlying diseases, especially hypertension and diabetes, have also been confirmed in other COVID-19 studies (10, 11, 14, 15). As the response of immune cells to the corona virus decreases with age, so the virus may be able to stay in the body longer. COVID-19 and readmission complications in older patients increase
(28), however these two factors may be strong predictors of readmission in hospitalized patients (29). Highly creatinine level in hospitalized patients was another predictor of the risk of readmission in the COVID-19 patients, so that a creatinine level greater than 1.2 mg/dl, the odds ratio of readmission was 2.15 times higher than in other COVID-19 patients. Patients with a history of ICU hospitalization had higher creatinine levels (23). Findings of previous studies on other diseases also consider creatinine level as an effective factor in hospital readmission of the COVID-19 patients (32 – 30).

In this study, more than 84% of the patients who were readmitted had abnormal chest CT scans. Also, most readmitted patients (64%) had a negative PCR test and the time interval between discharge and readmission was higher in the patients with a negative test than in patients with a positive test. This finding was consistent with the findings of previous studies that introduced abnormal chest imaging results as a predictor of readmission (12, 33), making it a suitable tool for managing COVID-19 patients (34–36). Also, the possibility of a false negative result in PCR test was reported in previous studies (34).

**Conclusion**

In this study, the readmission rate of patients during 30 & 60 days after discharge was 7.6% and 8.1%. Age over 60 years, underlying disease especially diabetes, high creatinine level and lung involvement were the most important predictors of readmission in the patients with COVID-19.

**Limitation**

One of the main limitations in the present study was small sample size which makes it hard to generalize the obtained results.

**Abbreviations**

Coronavirus Disease 2019 (COVID-19)

World Health Organization (WHO)

Centers for Disease Control and Prevention (CDC)

Polymerase Chain Reaction (PCR)

Intensive Care Units (ICUs)

**Declarations**

- **Ethics approval and consent to participate:**

  The protocol of study was approved by Sabzevar University of Medical Sciences (IR.MEDSAB.REC.1399.004) and informed consent form was obtained from all patients.

- **Consent to publish:**
Availability of data and materials:
Not applicable

Competing interests:
There are no financial conflicts of interest to disclose for any authors.

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Authors' Contributions:
- Conceptualization; D.S. and M.N, S.A.J
- Data extraction; D.S., M.N., F.A., M. N, F.R.
- Funding acquisition; M.N.
- Investigation; M. N, D.S, F.A, M.N.
- Methodology; F.A.
- Project administration; D.S and F.A.
- Resources; M.N, D.S, Software; F.A.
- Supervision; D.S.
- Roles/Writing original draft; M.N, D.S, F.A, M.N, F.R.
- Writing - review & editing: F.A, D.S and S.A.J.

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