

# Symptoms associated with nucleic acid turning-negative-time in COVID-19 patients?

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## Abstract

**Objective:** To explore on the association between nucleic acid turning-negative-time and traditional Chinese medicine (TCM) symptoms in coronavirus disease 2019 (COVID-19) patients with the Omicron variant.

**Method:** For this retrospective cross-sectional study, we enrolled 189 patients with COVID-19 (age 20–90 years) were included. multiple linear regression models were used to investigate the TCM symptoms affecting the nucleic acid turning-negative-time of COVID-19 patients, during the process of data analysis, taking with nucleic acid turning-negative-time as the dependent variable, and TCM symptoms as independent variables, and at the same time, sex, age, hypertension, diabetes, and coronary heart disease were as confounding variables.

**Results:** The study found that the most common TCM symptoms of COVID-19 patients with Omicron were cough, dry throat, expectoration, fever, sore throat, pharyngeal itching, running nose, and nasal congestion. Regression analysis showed that the fit regressive equation showed a significant difference ( $F = 4.286$ ,  $P < 0.001$ ,  $R = 0.400$ , the adjusted  $R^2 = 0.123$ , and three variables in the regression equation showed significant difference ( $P < 0.05$ ). The results showed that nucleic acid turning-negative-time was mostly related to constipation, fever, and expectoration. If the patients had the symptoms of constipation, fever, and expectoration; that is, if patients showed these symptoms, the turning-negative-time of nucleic acid in patients with Omicron will be prolonged.

**Conclusions:** Treatment based on symptoms for patients with constipation, fever, and expectoration may have important clinical significance for the COVID-19 patients with Omicron.

**Keywords:** COVID-19, Omicron, TCM symptoms, nucleic acid turning-negative-time

To the editor:

Coronavirus disease 2019 (COVID-19) is an acute respiratory infectious disease, classified as an “epidemic disease” in traditional Chinese Medicine (TCM). Since its outbreak in 2019, has swept the globe, causing great damage to people worldwide. Currently, symptomatic treatment is the primary management strategy for COVID-19 patients. In China, TCM treatment is also added to the treatment, with significantly positive clinical results. For example, TCM treatment has been shown to shorten the nucleic acid turning-negative-time in COVID-19 patients<sup>[1]</sup>.

The emergence of different variant strains of the novel coronavirus has provided a great challenge the epidemic prevention. Omicron is a mutant strain of COVID-19<sup>[2]</sup>;

although highly infectious it has relatively weak toxicity, and most patient manifest with cold symptoms. In this study, we aimed to analyze the association between the nucleic acid turning-negative-time and TCM symptoms in COVID-19 patients with Omicron. This study aimed to identify which TCM symptoms could affect nucleic acid turning-negative-time, as this may provide some ideas for TCM treatment against COVID-19 patients with Omicron.

A retrospective analysis was performed including 189 COVID-19 patients comprising 109 common cases, and 80 moderate cases between January 9, 2022, and January 27, 2022. There were 77 males and 112 females, accounting for 40.7% and 59.3%, respectively. They age range was 20 to 90, and the average age was  $46.4 \pm 15.45$  years. Among all the patients, there were 127 healthy patients, 43 with hypertension, 12 with diabetes, 8 with coronary heart disease, and fewer other diseases. Inpatient medical records were reviewed, and nucleic acid turning-negative-time and TCM symptoms were recorded. All data used in this study were from COVID-19 patients infected with Omicron in Tianjin Haihe Hospital. The inclusion criteria were a diagnosis with COVID-19 (Omicron) with an available diagnostic type (mild or standard symptoms). The software SPSS 22.0 for multiple linear regression analysis. Taking nucleic acid turning-negative-time as the dependent variable, and TCM symptoms as independent variables, with the potential confounders (age, sex, and some common diseases) included in the model, a regression equation was established to analyze the TCM symptoms affecting the nucleic acid turning-negative-time of COVID-19 patients. First, multiple collinear tests were performed,

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and the stepwise regression method was selected for the analysis. The average turning-negative-time of nucleic acid was  $13.1 \pm 2.87$  days. In this study, we investigated 17 common clinical TCM symptoms, among which cough, dry throat, expectoration, fever, sore throat, pharyngeal itching, running nose, and nasal obstruction were the main clinical manifestations, accounting for 76.19%, 53.44%, 50.26%, 46.03%, 34.92%, 26.98%, and 24.87% of cases, respectively (Table 1).

In the multiple linear regression analysis, nucleic acid turning-negative-time was set as the dependent variable, the 17 TCM symptoms (fever, cough, expectoration, sore throat, nasal congestion, running nose, dry throat, pharyngeal itching, chills, constipation, abdominal pain, diarrhea, fatigue, anosmia, hoarseness, muscle soreness, headache) as the independent variables, and sex, age, hypertension, diabetes, and coronary heart disease as confounding variables. Regression analysis showed that the fit regressive equation showed significant difference ( $F = 4.286, P < 0.001$ ),  $R = 0.400$ , the adjusted  $R^2 = 0.123$ , while three variables in the regression equation showed significant difference ( $P < 0.05$ ). The analysis revealed that the nucleic acid turning-negative-time was most strongly related to constipation, fever, and expectoration. If patients had these symptoms, the turning-negative-time of nucleic acid in COVID-19 patients with Omicron will be prolonged (Table 2).

In TCM theory, COVID-19 is classified into the category “epidemic disease.” In ancient TCM documents, a significant amount of information about the plague has been recorded, thereby providing significant theoretical and practical experience for modern researchers. Facing the COVID-19 epidemic situation, it is necessary for us to constantly practice and innovate using the basis of

TCM theory. In this study, the COVID-19 patients with Omicron infection in Tianjin mainly presented with upper respiratory symptoms including cough, pharyngeal stem, expectoration, fever, sore throat, pharyngeal itching, running nose, and nasal congestion, accompanied by weakness, muscle soreness, diarrhea, and constipation. According to Chinese medicine, these symptoms are indicative of evil *qi* attacking the exterior and the spleen and stomach, while the disease is located in the upper and middle energizer. This study showed that nucleic acid turning-negative-time is prolonged in patients with constipation, which coincides with the classical theory of TCM “lung integrating large intestine”<sup>[3]</sup>. The lung and large intestine are interconnected *via* meridians, forming an exterior–interior relationship. They are thus closely related to each other physiologically and pathologically. The lung is connected with the *qi* activity of the large intestine, so the descending lung-*qi* will lead into descending large intestine-*qi*, and clearing the large intestine will also clear the lung-*qi*. Therefore, patients with constipation can be treated based on symptoms, which may achieve good clinical results. For patients with fever and expectoration, these symptoms may be related to the expansion and congestion of alveolar septal capillaries, fluid exudation in alveolar cavity, and interstitial edema of interlobular septum caused by COVID-19 infection<sup>[4]</sup>. For this, TCM can be used for pathogen development by diffusing the lung and expelling pathogenic factors, eliminating and clearing dampness, as well as clearing heat and detoxifying. TCM has several inherent advantages in the treatment of COVID-19, which is mainly embodied in the underlying concept of wholism and differentiate treatment. The full utilization of Chinese medical data

**Table 1**  
Frequency analysis of common TCM symptoms in COVID-19 patients with Omicron

| Number | TCM symptoms       | Frequency | Percent (%) | Number | TCM symptoms    | Frequency | Percent (%) |
|--------|--------------------|-----------|-------------|--------|-----------------|-----------|-------------|
| 1      | Cough              | 144       | 76.19       | 10     | Muscle soreness | 21        | 11.11       |
| 2      | Pharyngeal stem    | 101       | 53.44       | 11     | Diarrhea        | 16        | 8.47        |
| 3      | Expectoration      | 95        | 50.26       | 12     | Constipation    | 14        | 7.41        |
| 4      | Fever              | 87        | 46.03       | 13     | Hoarseness      | 10        | 5.29        |
| 5      | Sore throat        | 66        | 34.92       | 14     | Fear of cold    | 8         | 4.23        |
| 6      | Pharyngeal itching | 51        | 26.98       | 15     | Anosmia         | 7         | 3.70        |
| 7      | Running nose       | 47        | 24.87       | 16     | Headache        | 6         | 3.17        |
| 8      | Nasal congestion   | 44        | 23.28       | 17     | Abdominal pain  | 5         | 2.65        |
| 9      | Weakness           | 27        | 14.29       |        |                 |           |             |

**Table 2**  
The correlation between nucleic acid turning-negative-time and TCM symptoms in COVID-19 patients with Omicron

| Predictor variable | Unstandardized coefficient |           | Standardized coefficients |         | Collinearity statistics |       |
|--------------------|----------------------------|-----------|---------------------------|---------|-------------------------|-------|
|                    | B                          | Std Error | Beta                      | P-value | Tolerance               | VIF   |
| Independents       | Constant                   | 11.126    | 0.722                     |         | <0.001                  |       |
|                    | Fever                      | 1.123     | 0.399                     | 0.196   | 0.005                   | 0.965 |
|                    | Expectoration              | 0.822     | 0.401                     | 0.144   | 0.042                   | 0.951 |
|                    | Constipation               | 2.545     | 0.769                     | 0.233   | 0.001                   | 0.942 |
| Confounders        | Sex                        | 0.455     | 0.408                     | 0.078   | 0.266                   | 0.953 |
|                    | Age                        | 0.010     | 0.014                     | 0.056   | 0.475                   | 0.775 |
|                    | Hypertension               | 0.365     | 0.536                     | 0.053   | 0.497                   | 0.757 |
|                    | Diabetes                   | 0.579     | 0.892                     | 0.049   | 0.517                   | 0.808 |
|                    | Coronary heart disease     | -0.627    | 1.031                     | -0.044  | 0.544                   | 0.886 |

$R = 0.400, R^2 = 0.160; \text{adjusted } R^2 = 0.123; F = 4.286, P < 0.001.$

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will be of great practical significance in the treatment and prevention of COVID-19.

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### Author contributions

Mingchi Luo assessed and verified the data. Qiang Li contributed to the study design. Qiang Li and Lei Zhang contributed to statistical analysis. Limin Feng, Hongyuan Sun, Xiaoya Liu, Cunzhong Shi, and Yan Ma were involved in the acquisition of data. All authors were involved in interpretation of data. All authors read and approved the final manuscript.

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### Availability of data and materials

All data analyzed during this study are included in the article.

### Ethical approval of studies and informed consent

This study was approved by the First Hospital Affiliated to Tianjin University of Traditional Chinese Medicine (Tianjin, China) (Approved No. TYLL2020[K]006).

### Conflict of interest statement

None of the authors declare any conflicts of interest.

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