

Are Italy and Iran really suffering from COVID-19 epidemic? A controversial study

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Abstract. – The number of global COVID-19 infected cases is increased rapidly to exceed 370 thousand. COVID-19 is transmitted between humans through direct contact and touching dirty surfaces. This paper aims to find the similarity between DNA sequences of COVID-19 in different countries, and to compare these sequences with three different diseases [HIV, Hand-Foot-Mouth disease (HFMD), and Cryptococcus]. The study used pairwise distance, maximum likelihood tree, and similarity between amino acid to find the results. The results showed that different three main types of viruses namely, COVID-19 are found. The virus in both Italy and Iran is not similar to COVID-19 in China and USA. While, two viruses were spread in Wuhan (before and after December 26, 2019). Besides Cryptococcus and HFMD are found as dominant diseases with Group 1 and Group 3, respectively. Authors claim that the current virus in Italy and Iran that killed thousands of people is not COVID-19 based on the available data.

Key Words:

COVID-19, HIV, HFMD, Cryptococcus, Maximum likelihood tree.

Introduction

CoVID-19 is a new generation of infectious coronavirus diseases that originated from animals¹. Recently, several researches were conducted to study the similarity between CoVID-19 and other diseases. It is found that the nucleocapsid (N) protein of CoVID-19 is 90% similar to SARS². On the other hand, the first case of CoVID-19 was found in Wuhan, China, where several diseases were found and spread in Wuhan before. One of the popular infectious diseases that spread in China to other countries globally between the year of 2010 and 2016 is Hand-Foot-Mouth disease (HFMD)². The symptoms of CoVID-19 are mainly fever, cough, myalgia, dyspnea with or without diarrhea². Similar

to CoVID-19 patients, HFMD patients suffer from high fever that exceeds 39°C, shortness of breath, phlegm rale, moist rale, tachycardia, high blood pressure, pale face, and cyanosis³. Besides, HFMD patients have rash and herpes. The similarity between CoVID-19 and HFMD is in the symptoms of upper respiratory tract infection, fever and the symptom of nervous system damage. However, it was found that several diseases have almost similar symptoms like CoVID-19 [i.e., human immunodeficiency virus (HIV), SARS, etc.]. HIV is a disease that infect humans and by time it can cause Acquired Immunodeficiency Syndrome (AIDS)⁴. Infection with HIV can cause flu-like illness symptoms (i.e., fever, chills, sore throat, fatigue, muscle aches, and rash). These HIV symptoms are mainly similar to regular coronavirus symptoms. While HIV can cause both swollen lymph nodes and mouth ulcers. It was reported that some infected cases do not have any kind of symptoms during the early stage of their disease.

On the other hand, *Cryptococcosis* is another kind of diseases that have CoVID-19-like symptoms. This disease can infect both humans and animals and it is caused by inhalation of the fungus. Most of *Cryptococcosis* disease symptoms are similar to CoVID-19 symptoms (i.e., fever, malaise, inflammation, cough, headache, vomiting, and coma, etc.), while few symptoms are different (i.e., vision changes, meningitis, and rash)⁵. Evidently, both viruses and fungus can cause similar symptoms. This is due to the way that immune system follows to defense against infection.

Materials and Methods

This study uses DNA sequences of different patients from seven countries including Spain, USA, China, Italy, Iran, Taiwan and Vietnam.

The study considered different samples based on time and location of the patients to understand the evolution process of COVID-19, besides to compare COVID-19 with different viruses that have similar symptoms. The selected sequences are found in Genbank and denoted using a code sequence. 25 DNA sequences are used with three DNA diseases, including HFMD, HIV, and *Cryptococcus* neoformans.

To understand the similarity between different diseases, a pairwise distance and average distance are calculated between amino acids. The DNA sequences are aligned using MEGA X and filtered using Gblock to remove the gaps before building Maximum likelihood tree and amino acid sequences. The filtered aligned DNA sequences are used to build amino acid sequences to understand the evolution process in COVID-19

and to find the similarity between COVID-19 viruses and three different diseases including HFMD, HIV, and *Cryptococcus* neoformans, besides to understand the evolution between different COVID-19 genomes in different countries. After creating amino acids of different diseases, a comparison between different groups are applied to find the similarity. To validate the results, Maximum likelihood tree with 100 replicas, and cut off of 70% are used.

Results

To align DNA sequences, a MEGA software is used and then the data are filtered using a Gblock. The aligned and filtered data are used to build amino acid and likelihood tree

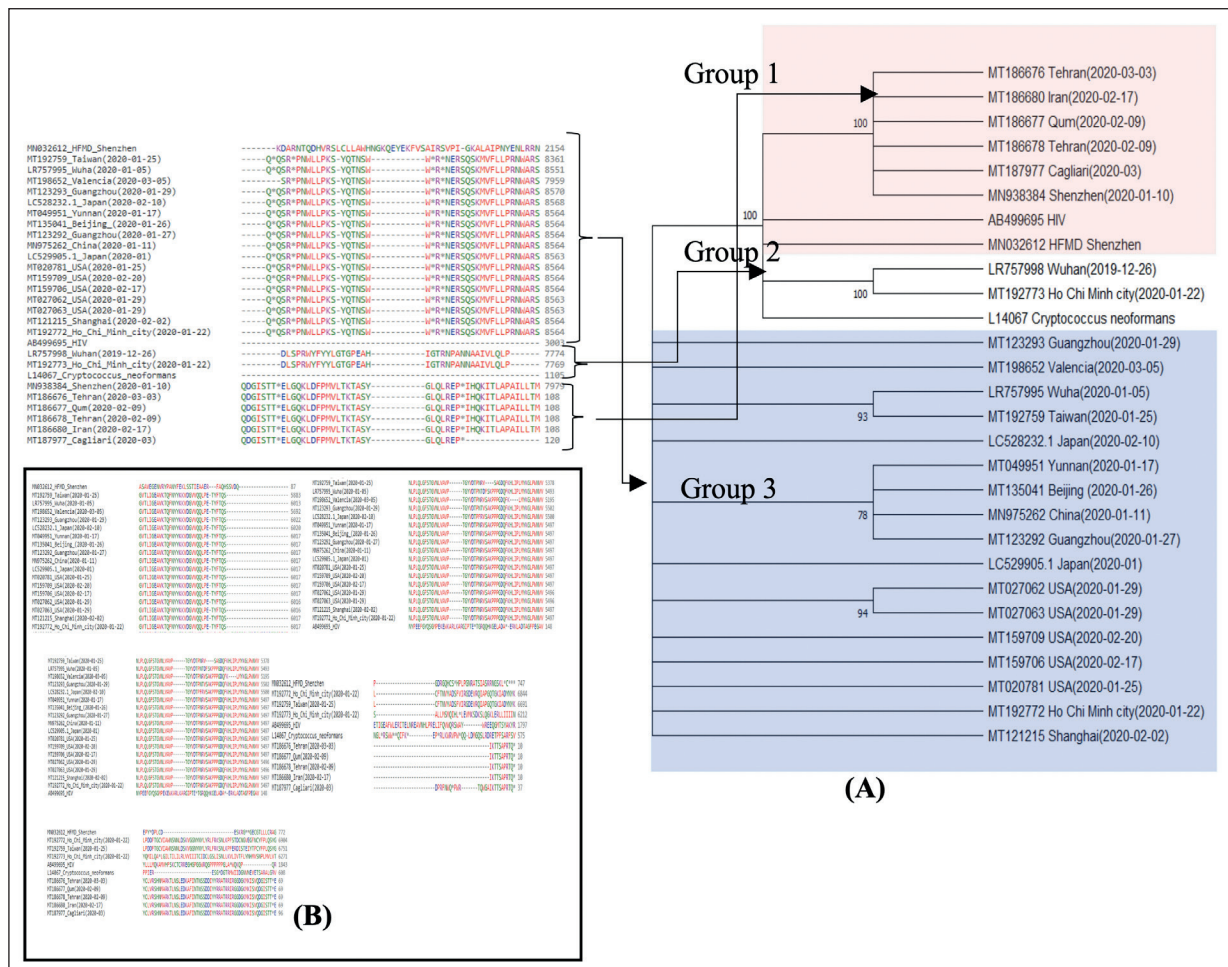


Figure 1. Structure of COVID-19, HIV, HFMD, and *Cryptococcus* neoformans. **A**, Maximum likelihood tree (condensed tree, cutoff value is 70%) of sequences. Bootstrap support values (%) based on 100 replicates. **B**, Matching HFMD-Groups 1 and 2, HIV-Groups 1 and 2, Cryptococcus-Groups 1 and 2, Cryptococcus-Group 3, and HIV-Group 3.

as shown in Figure 1. The average distance between all the amino acid is equal to 0.54, where the range of distances is from 0.000 to 0.938. Amino Acid sequences of all countries showed that COVID-19 viruses are divided into three groups, including Group 1 (i.e., Italy and Iran), Group 2 (i.e., Wuhan December 26, 2019 and Vietnam Jan 22, 2020) and Group 3 (the rest of cases). All groups showed completely very high dissimilarity between Amino acid sequences. To check the similarity of viruses, Maximum likelihood tree is built. The evolutionary history was inferred by using the Maximum Likelihood method and Tamura-Nei model. The tree with the highest log likelihood (-162757.67) is shown in Figure 1A. The percentage of trees in which the associated taxa clustered together is shown next to the branches. Initial tree(s) for the heuristic search were obtained automatically by applying Neighbor-Join and BioNJ algorithms to a matrix of pairwise distances estimated using the Maximum Composite Likelihood (MCL) approach, and then, selecting the topology with superior log likelihood value. This analysis involved 28 nucleotide sequences. Codon positions included were 1st+2nd+3rd+ Non-coding. There was a total of 28200 positions in the final dataset. Tree showed that groups 1 and 2 can be inserted in the same level, where group 3 has higher distance compared with groups 1 and 2. To compare COVID-19 with HFMD, HIV and *Cryptococcus neoformans*, amino acid sequences are studied and the higher similarity with one group of amino acids is considered. The results found that there is a similarity between groups 1 to 3 and HFMD, HIV and *Cryptococcus neoformans*, where the ranges are 1%-23%, 1%-5% and 12.5%-20%, respectively as shown in Figure 1B. The results indicated that the obtained amino acid sequence either is for a new generation of COVID-19 or represents another kind of unknown diseases. Besides, some symptoms and mysterious infection cases of CoVID-19 can be inherited from one or more studied diseases (i.e., HFMD, HIV and *Cryptococcus neoformans*). The infection reasons may be caused from the inherited diseases, such as nasal secretions or throat discharge, saliva, fluid from blisters, human stool, birds droppings, tree hollows, and decaying wood. In addition, symptoms of COVID-19 can be inherited, such as sensitivity to light, confusion or changes in behavior, loss of appetite, irritability in infants and toddlers and skin lesions.

Understanding the similarity between different diseases could help researchers and doctors to predict the symptoms, the infection reasons, expected treatment, medications, and time for treatment. The results revealed that COVID-19 which spread in Wuhan on December 26, 2019 is similar to that which spread in Vietnam on Jan 11, 2020. It was found that USA, Taiwan, Vietnam, and China after December 26, 2019 have the similar sequences. This indicates that those countries were infected from the main source, where the rest of countries are infected directly from the center of infection in China (Wuhan). Spain has both sequences (group 1 and group 2), thus, this could prove that Spain was infected from different sources and regions.

Controversially, different sequences have been found in both Iran and Italy. It is found that the difference between both viruses in (Iran and Italy) and (China and the rest) is relatively high. While, the COVID-19 that spread in Iran might be direct/indirect reason of infecting Italy and spreading the disease there.

Conclusions

Analyzing different DNA sequences of different countries could find the original source for the disease and it would help in understanding the nature of this disease, thus, mitigate of COVID-19. The main findings of this paper can be summarized as follow:

- Italy and Iran have another kind of disease, which is not COVID-19 that spread in China, and USA based on amino Acid analysis.
- COVID-19 in USA, Spain, Vietnam, China, and Taiwan have genetically inherited information from HFMD, and *Cryptococcus*. While, CoVID-19 in Italy and Iran have genetically inherited information from *Cryptococcus* only.
- Use Amino acid sequences with date and location could build a map to trace how the country is infected.
- The authors claim that there are different viruses spread globally under the name of COVID-19.

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Conflict of Interest

The Authors declare that they have no conflict of interests.

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