Scientific Foundation SPIROSKI, Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2020 May 05; 8(T1):1-2.
https://doi.org/10.3889/oamjms.2020.4773
eISSN: 1857-9655
Category: *T1 - Thematic Issue "Coronavirus Disease (COVID-19)"*
Section: *Letter to the Editor*

COVID-19: The Need of Non-traditional Techniques to Screen for the Virus

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Edited by: Mirko Spiroski
Citation: Borroni D, Gadhvi K. COVID-19: The Need of Non-traditional Techniques to Screen for the Virus. Open-Access Maced J Med Sci. 2020 May 05; 8(T1):1-2. https://doi.org/10.3889/oamjms.2020.4773
Keywords: COVID-19; Coronavirus; Metagenomics
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Received: Apr-11-2020
Revised: Apr-18-2020
Accepted: Apr-25-2020

Funding: Publication of this article was financially supported by the Scientific Foundation SPIROSKI, Skopje, Republic of Macedonia
Competing Interests: The authors have declared that no competing interests exist

Abstract

BACKGROUND: At the present moment, the etiological diagnosis of SARS-CoV-2 is based on the polymerase chain reaction (PCR). False negative cases are increasingly reported in several studies using reverse transcription-PCR (RT-PCR). For example, the positive rate of RT-PCR for throat swabs was reported to be about 60% in early stage of COVID-19.

AIM: We aimed to present metagenomic next-generation sequencing (mNGS) as a potential tool to detect pathogens.

METHODS: In the recent year, mNGS is shown the potential to detect pathogens without the need of hypothesis guided approach and is proven to be highly effective.

RESULTS: A recent prospective study in the United States compared the diagnostic performance of routine diagnostic tests with mNGS and showed that mNGS detected a bacteria or virus in the CSF of 13 of 58 patients presenting with meningoencephalitis who were negative for or not assessed with routine diagnostic test including PCR. NGS also has the advantage to cover entire viral genomes.

CONCLUSION: As viral metagenomics has significantly improved in recent years and become more cost effective, we think that a change in the approach toward a shot-gun metagenomic testing should be explored and could potentially aid the diagnosis of COVID-19 cases and the management of this pandemic.

Dear editor,

We, along with the international community, are gravely concerned by the recent international outbreak of the coronavirus SARS-CoV-2 (coronavirus disease 2019; previously 2019-nCoV). SARS-CoV-2 was declared a pandemic by the World Health Organization (WHO) on March 13, 2020, following spread from the Hubei Province of the People's Republic of China. Europe has now overtaken China, becoming the epicenter of the infection and the incidence of new cases plus deaths from COVID-19 in Italy is now greater than in China. To date, 19 genomic strains of the virus have been identified in infected patients [1].

The WHO recommends a combination of measures to tackle spread of the virus including rapid diagnosis, immediate isolation of cases, rigorous tracking, and precautionary self-isolation of close contacts [2]. Rapid diagnosis has been key in managing this pandemic and has worked effectively in many countries such as South Korea and in China which have seen a decline in the number of new infections. However, many individuals with SARS-CoV-2 infection remain undiagnosed because testing efforts are currently ineffective or not widely available. At the present moment, the etiological diagnosis of SARS-CoV-2 is based on the polymerase chain reaction (PCR). Both the WHO and the US centers for disease control and prevention, along with other national and international scientific organizations, have released detailed information for in-house development of reverse transcription-PCR (RT-PCR) tests. These are being implemented by many reference laboratories worldwide and are undergoing clearance by many regulatory agencies. Unfortunately, false negative cases are increasingly reported in several studies using RT-PCR [3]. For example, the positive rate of RT-PCR for throat swabs was reported to be about 60% in the early stage of COVID-19. This is an area of major concern and has huge impacts on the efficacy of testing and isolation processes. False negative RT-PCR patients are less likely isolate, propagating viral spread and means the results of RT-PCR should be interpreted with caution [4].

However, an alternative to RT-PCR may already exist. In the recent year, metagenomic next-generation sequencing (mNGS) is shown the potential to detect pathogens without the need of hypothesis guided approach [5] and is proven to be highly effective [5], [6], [7]. As an example, a recent prospective study in the United States compared the diagnostic performance of routine diagnostic tests with mNGS and showed that mNGS detected a bacteria or

virus in the CSF of 13 of 58 patients presenting with meningoencephalitis who were negative for or not assessed with routine diagnostic test including PCR. NGS also has the advantage to cover entire viral genomes. This carries the added benefit of helping to understand if individual mutations or strain may be responsible for the variable pattern of spread and illness we are witnessing worldwide.

As viral metagenomics has significantly improved in recent years and becomes more cost effective, we think that a change in the approach toward a shot-gun metagenomic testing should be explored and could potentially aid the diagnosis of COVID-19 cases and the management of this pandemic.

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