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MAIN COVID-19 DIAGNOSTIC METHODS: recommendations and perspectives

COVID-19 PRINCIPALES MÉTODOS DE DIAGNÓSTICO: recomendaciones y perspectivas PRINCIPAIS MÉTODOS DIAGNÓSTICOS DA COVID-19: recomendações e perspectivas

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Recently, the world was surprised by the emergence of a new disease, called COVID-19 (Coronavirus Disease-2019), originated from infection by a type of coronavirus, SARS-CoV-2. This new infectious pathology was identified

in December 2019, when an outbreak of pneumonia, of unknown causes at the time, spread in Wuhan, China, a densely populated city, putting its entire population at risk due to the rapid contagion and spread disease. After the emergence of cases in several countries, the World Health Organization (WHO) took a stand and declared COVID-19 a pandemic in March 2020⁽¹⁾.

This pandemic changed the world scenario in a profound way and quickly became a public health emergency, with more than 3 million cases and 250,687 thousand confirmed deaths worldwide so far - data obtained on 05/04/2020 at $18: 32h^{(2)}$. In Brazil, the numbers are around 105thousand confirmed cases and 7,288 deaths and a fatality rate of 7.0%. The Southeast region is the most affected, with around 49 thousand cases, which represents 46.9% of the country's total numbers - data captured on 05/04/2020 at $16: 30h^{(3)}$.

Coronaviruses are part of a large group of viruses present in several vertebrates. In the 1960s, the first coronaviruses capable of infecting people were identified and, since then, seven different strains have been recognized as human pathogens: HCoV-OC43, HCoV-HKU1, HCoV-229E and HCoV-NL63, which usually result in respiratory disorders mild, MERS--CoV (Middle East Respiratory Syndrome), and SARS-CoV and SAR-S-CoV-2 (Severe Acute Respiratory Syndrome), which can cause severe forms of respiratory infections^(1,4).

Different mortality rates are associated with infections caused by coronavirus. Epidemiological data indicate a lethality of around 10% when analyzing SARS-CoV and up to 35% in the case of MERS-CoV^(4,5). Mortality rates induced by SARS-CoV-2 infection are still contradictory and vary widely between the various regions affected, but a lethality of up to 27% in individuals over 85 years old has been previously described⁽⁶⁾. Although the three most serious forms are potentially important threats, it is necessary to consider the clinical evolution that each coronavirus subtype can induce. Such an individualized analysis has the potential to directly interfere in the strategic planning of public health policies, as well as in decision-making and conducting the scenario that is in place.

It is essential that communication between public authorities, the scientific community and the population is carried out in an effective, clear and up-to-date manner. The production and dissemination of knowledge significantly affects the clinical management of the various manifestations of the disease and its problems. Especially nowadays, ensuring broad access to health guidelines is causally related to the promotion of quality care, as well as ensuring greater tranquility and confidence for professionals working in direct care for patients.

The entire crisis arising from CO-VID-19 resulted in an unprecedented union of the scientific community and health professionals. Although it is surprising to observe such a quick response in the face of the pandemic, the immense volume of data that was made available so quickly can make it difficult, especially for professionals working in the front line, to access the content necessary for making assertive clinical decisions in pandemic times. In this scenario, finding information about the diagnostic protocols and tests that guide these professionals can be an arduous task, especially for those who work directly in the effort to contain the disease and are already burdened with the high workload. Thus, this study aims to briefly expose some information about the tests for COVID-19 currently available in Brazil, as well as some recommendations regarding its use, which will be discussed below.

Diagnostic Exams and Guidelines

In Brazil, the number of rapid tests approved by Anvisa has been growing rapidly. The approval of the diagnostic tests for COVID-19 follows Resolution RDC No. 348, of March 2020, which defines temporary and extraordinary criteria and procedures due to a public health emergency⁽⁷⁾.

The gold standard diagnostic method is RT-PCR in real time using samples that can be obtained in three different ways: nasopharyngeal aspirate (ANF), combined swab (nasal/ oral) and lower respiratory secretion (sputum, tracheal lavage or bronchus lavage) alveolar). The collection of the material must be carried out up to 10 days after the appearance of the first symptoms (preferably between the 3rd and 5th days) by professionals professionally trained and trained to perform the procedure. Refrigeration of the samples (4-8 ° C) is essential, and these should be analyzed between 24-72 hours after collection. If it is not possible to send the sample within the established period, it is recommended that the material be stored at -70 ° C until shipping is provided. It is worth mentioning that damaged samples, with little biological material or improperly handled / stored, as well as samples collected early (less than 3 days after the onset of symptoms) or late (more than 10 days after the onset of symptoms) may have a false negative result of infected individuals⁽⁸⁾. It is realized that many factors can interfere with the effectiveness and result of the test. Thus, it is essential that the professionals involved are attentive and strictly follow the suggested protocol, in order to guarantee the reliability of the results and avoid as much as possible the waste of a resource that has been shown to be scarce.

The diagnosis of COVID-19 can also be performed by serological methods. In Brazil, only the immunochromatographic assay for rapid and qualitative detection of SARS--CoV-2 IgG/IgM antibodies is available, carried out from a sample of whole blood, serum, or human plasma. The sample for the immunological test should be obtained, in general, from the 8th day of the onset of symptoms, ensuring the time necessary for the immune system to produce antibodies in sufficient quantity for detection in the test⁽⁸⁾. This method has the advantage of providing a quick result, however, due to the risk of false negatives, it should be used only for screening and diagnostic assistance, leaving the interpretation to a doctor who has complementary clinical and laboratory data. The serological test with a positive result should not be used as the only indicator of the presence of infection, and a negative result does not exclude the possibility of the patient being infected. This information is of great importance, since false negative results can induce an infected individual to erroneously leave home isolation, resulting in the spread of the virus. This possibility illustrates the relevance both of using other methods and of caution when interpreting the results⁽⁸⁾.

Imaging exams, which must be performed following the necessary measures for the prevention and control of contagion, are also important allies in the diagnosis of this disease, due to the speed of performance and obtaining the results. Chest radiography is recommended for all patients with suspected pneumonia and in general, unilateral (25% of patients) and bilateral (75% of patients) pulmonary infiltrates are seen in the images. Computed tomography (CT) of the chest is indicated for patients with involvement of the lower respiratory tract, bilateral lobular and subsegmental areas with a ground-glass aspect, are usually present in most of those affected by the disease. It is noteworthy that evidence of the presence of viral pneumonia on CT may be present before a positive RT-PCR for SARS-CoV-2. Asymptomatic patients may have altered imaging tests, just as individuals can test positive even without the presence of significant findings on computed tomography⁽⁷⁾. As with serological tests, imaging tests should be used as an auxiliary method, and it is not possible to confirm the presence of COVID-19 infection only with CT and / or chest radiography. It is worth emphasizing that, during

the exams, the protocols that prevent the transmission of diseases during the procedure must be followed.

It is noticed that the diagnostic tests have different advantages and disadvantages. Serological tests and imaging tests are quick to perform and produce results; however, they can show false negatives and should not be used alone in the diagnosis. The RT-PCR is ideal; however the collection, handling and storage of the samples must be supervised and follow strict standards to guarantee reliable results; the long waiting time is also a limiting factor of this method. It is vital to stress that the indication, use and interpretation of each diagnostic test must be performed with caution and following the established guidelines and standards. Only tests approved and registered by Anvisa must be purchased and used as instructed by each manufacturer. As noted, all tests have limitations, and should be used together, so that their full potential is used.

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