Foreword: Current laboratory aspects of COVID-19

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FOREWORD

At the time of writing this foreword for the “COVID-19” thematic issue of the eJIFCC, over half a billion Coronavirus Disease 2019 (COVID-19) positive cases and more than 6.3 million COVID-19 related deaths have been recorded worldwide emphasizing the global impact of this pandemic. We have already witnessed initial waves of the infection, and the vaccination campaigns in most countries have topped the near maximum number of immunized individuals, who opted to receive at least one dose of vaccine. On the other hand, we cannot predict recurrence of dramatic increases in the number of new (severe) cases in the future.

Since the beginning of the pandemic, huge efforts have been made for the development of effective diagnostic tools and strategies 1) to identify and isolate SARS-CoV-2-infected patients to control the pandemic, 2) to limit the risk of contamination, 3) to perform differential diagnosis between COVID-19 and other viral infections, such as seasonal flu, and 4) to treat patients effectively with any respiratory symptoms.
to avoid serious consequences. Many biomedical companies and research laboratories have been working hard to develop competent and approved methods for the rapid detection of SARS-CoV-2 ribonucleic acid (RNA), antigens and antibodies [1].

The efficacy of diagnostic laboratory tests to detect SARS-CoV-2 infection strongly depends on the timing of the testing [2]. Both molecular and serology tests are not useful in the early period (i.e., in the first week) of the supposed infection, because the virus is still in its incubation phase without sufficient levels of viral RNA, proteins or induced antibodies in the circulation. Therefore, the moment of the suspected infection, symptoms, medical history, and detailed physical examination need to be considered before testing to achieve the highest sensitivity of laboratory examinations. In the case of molecular tests, the highest chance for positivity can be reached after two weeks of the onset of infection, but we must know that there are no commercially available diagnostic tools with a sensitivity of 100%, especially in those asymptomatic cases the viral load is low. Repeated nasopharyngeal swabs on 2-3 consecutive days may be effective in overcoming the window period of SARS-CoV-2 incubation. Nonetheless, the positivity ratio is reduced over time due to the elimination of the virus and the remission of the disease [3].

Regarding serological tests, SARS-CoV-2 specific IgM and IgG antibodies become detectable after one month following the presumed infection, but the level of IgG remains elevated for at least 6-8 months in most cases [4]. Finally, increased level of viral proteins in nasopharyngeal swabs can be measured for the early diagnosis of COVID-19 infection by rapid antigen test, however, RT-PCR should be performed in those suspicious cases when this test was negative [1].

Approved, regularly used laboratory techniques for the diagnosis of SARS-CoV-2 infection are depicted in Figure 1A. Besides conventional laboratory methods, additional diagnostic tools have also become available in this field. Virus culturing and next-generation sequencing (NGS) methods have been applied to identify the novel coronavirus and to characterize its molecular structure [1]. Currently, droplet digital PCR, clusters of regularly interspaced short palindromic repeats/Cas (CRISPR/Cas)-based methods, electron microscopy, biosensor, etc., can support the diagnosis of COVID-19 infection, which are under validation in routine laboratory and research settings [1]. These other diagnostic methods and the still research-related tools are depicted in Figure 1B.

Recently, the importance of clinical laboratory tests has also emerged 1) to manage the hospitalization of patients with COVID-19 related disorders, 2) to distinguish severe and non-severe clinical states and 3) to predict the outcome of the disease. For the aforementioned purposes huge amount of clinical data has accumulated and is elegantly summarized by Tomo et al [5]. Several serum and plasma biomarkers have been identified as independent risk factors to assess disease severity and to predict unfavorable outcome of COVID-19, such as elevated activity of total lactate dehydrogenase (LDH) isoenzymes [6], high soluble ACE2 activity [7] and increased D-dimer [8]. In addition, serological tests aid in the evaluation of the humoral response following different types of vaccines [9], but they can also estimate the incidence of SARS-CoV-2 infection in those patients with newly diagnosed malignancy and under anti-cancer therapy [10].

This current thematic issue of the eJIFCC is constituted by a series of manuscripts submitted from various parts of the world and provides an overview on various laboratory aspects of COVID-19. The topics of the manuscripts range from recent clinical data from the laboratory considerations for reporting cycle threshold value in RT-PCR tests via the detailed analysis of routinely available laboratory parameters in
Figure 1  Routinely available, approved diagnostic methods (A) and other laboratory tools with, as yet, research-related techniques (B) in the diagnosis of SARS-CoV-2 infection

The figure was created using BioRender.com.
hospitized COVID-19 patients as new prognostic biomarkers up to the comparison of different serological assays for the evaluation of humoral immune response. Based on the findings of previously published scientific literature and those presented in this thematic issue, it can very well be emphasized that there are no effective diagnostic procedures and therapeutic interventions without the 24/7 active role of routine clinical laboratories worldwide.

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