Short Review

COVID19 alert
Do we know our enemy?

Katerina Antoniou[1],
Maria Bolaki[1],
Eleni Bibaki[1],
Eirini Vasarmidi[1],
Athina Trachalaki[2],
Eliza Tsitoura[1],
Demosthenes Bouros[3]

[1]Department of Respiratory Medicine, University General Hospital of Heraklion, Laboratory of Molecular and Cellular Pneumonology, Medical School, University of Crete, Heraklion, Crete, Greece
[2]Interstitial Lung Disease Unit Royal Brompton Hospital, London, United Kingdom
[3]Athens Medical Center and 1st Department of Respiratory Medicine, "Sotiria" Hospital for Diseases of the Chest, National and Kapodistrian University of Athens, Greece

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Correspondence to:
Katerina Antoniou
E-mail: katerinaantoniou@yahoo.gr,
kantoniou@med.uoc.gr

ABSTRACT
SARS-coronavirus 2 (SARS-CoV-2), the etiologic agent of the new lung disease COVID-19 is closely related to SARS-CoV, and together with MERS-CoV are three new human coronaviruses that emerged in the last 20 years. Clinical presentations range from asymptomatic or mild symptoms to severe illness. The prevalent cause of mortality is pneumonia that progresses to ARDS. Such a devastating health burden worldwide has imposed intensive international scientific interest to be focused on the emergence of new therapeutic regimens. Pending the availability of a vaccine, there is a critical need to identify effective treatments and a number of clinical trials have been implemented worldwide. Trials are based on repurposed drugs that are already approved for other infections, have acceptable safety profiles or have performed well in animal studies against the other two deadly coronaviruses. In this review, we summarize the main points of clinical papers published in the current literature employed in epidemiology, clinical trials and intensive care unit (ICU) in COVID-19 disease.
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SARS-coronavirus 2 (Severe Acute Respiratory Syndrome Coronavirus 2, SARS-CoV-2), the etiologic agent of the new lung disease COVID-19[1] is closely related to SARS-CoV, and together with MERS-CoV (Middle East respiratory syndrome, MERS) are three new human coronaviruses that emerged in the last 20 years. The three viruses are associated with increased risk of acute lung injury[2]. As of 15th of April more than 2 million people have been infected worldwide in 200 countries resulting in a death toll that surpasses 135,000 people in this ongoing pandemic[3-5]. SARS-CoV-2 is an enveloped, positive sense, single stranded, non-segmented RNA virus of the beta coronavirus family[3-5]. A large epidemiological study including 32583 patients investigated the characteristics of patients with laboratory confirmed COVID-19 in Wuhan as well as the temporal associations of multiple public health interventions with control of the COVID-19 outbreak[6,7]. The institution of interventions

including cordons sanitaire, traffic restriction, social distancing, home quarantine, centralized quarantine, and universal symptom survey was temporally associated with reduced effective reproduction number of SARS-CoV-2 (secondary transmission) and the number of confirmed cases per day across age groups, sex, and geographic regions. These findings may provide great information about public health in other regions of the world to fight the global pandemic of COVID-19[6,7]. It seems that monitoring infection rates and effective reproduction numbers continuously makes nonpharmaceutical interventions a valuable tool for controlling COVID-19. Moreover, future studies that will be focused in genetic analysis of infected patients will be crucial, in order to further analyze the genetic background of different populations. For example, in a population-based study in Iceland, children under 10 years of age and females had a lower incidence of SARS-CoV-2 infection than adolescents or adults and males. The proportion of infected persons identified through population screening did not change substantially during the screening period, which was consistent with a beneficial effect of containment efforts[8].

THERAPEUTIC ISSUES

On March 11 2020, the World Health Organization (WHO) declared the SARS-CoV-2 outbreak a pandemic. On March 18th the World Health Organization launched the SOLIDARITY trial and soon after an add-on trial, a European initiative of the Reacting consortium, the DISCOVERY trial was announced[9,10]. Currently, there are no approved therapies specific for any human CoV. Trials are based on repurposed drugs that are already approved for other diseases, have acceptable safety profiles or have performed well in animal studies against the other two deadly coronaviruses, which cause SARS and MERS. SOLIDARITY includes research looking at four possible therapeutics with direct antiviral actions: remdesivir; chloroquine and hydroxychloroquine; lopinavir plus ritonavir; and lopinavir plus ritonavir and interferon-beta while chloroquine will not be included in the DISCOVERY trial. Additionally, the DISCOVERY trial will include a placebo arm with standard of care while the SOLIDARITY trial will not be blinded and patients will know they received a treatment that would cause a placebo effect as stated by Ana Maria Henao Restrepo, a medical officer at WHO's Department of Immunization Vaccines and Biologicals. Additional information regarding lung imaging and blood gases will be monitored in the DISCOVERY trial besides data on hospitalization length and requirement for oxygen or ventilation tthat will be collected by the SOLIDARITY trial[9-11].

Important considerations in the successful testing and use of currently available and future therapies for COVID-19 are the timing of the treatment, the viral load of the patient and markers predictive of lung injury. Antiviral treatment is more efficient as a prophylactic measure and at earlier times during the infection, when virus replication is at its peak. Conversely, immunomodulatory and anti-inflammatory treatments may be more effective later and may be combined with careful monitoring of the patient viral loads.

OUTCOME IN THE ICU

Unfortunately a large proportion of infected patients need intensive care admission and management however, the knowledge about the clinical characteristics of those patients is generally limited. Grasselli et al reported the largest case series of patients with COVID-19 and severe illness who required admission to the ICU in Lombardy Region, Italy[12]. The majority of patients (68%) had at least 1 comorbidity and 49% had hypertension. 99% needed respiratory support (88% mechanical ventilation and 11% noninvasive ventilation) and the ICU mortality was 26%[12]. However, the above study has different limitations, such as a large number of patients reported were still intubated at the publication date.

The number of critically ill patients presenting to hospitals highlights the fragility of health care systems to care for the most severely ill patients in even the wealthiest countries. Fortunately, pandemics do not affect all locations with the same intensity at the same time. The pandemic burden may be attenuated only when an effective multifaceted response with collaboration and support is demonstrated by all countries. Patients with severe disease not considered suitable for escalation to intensive care, i.e. those who are frail or have multiple comorbidities, are at very high risk of dying, with an estimated death rate of 15–22%[12,13]. We have a moral obligation to provide good symptom control to prevent avoidable suffering. Thus, comprehensive care of the patient with COVID-19 requires identification of patients at increased risk of dying, who would benefit from a parallel approach to management. This encompasses optimal symptom management for those with severe disease but who will

survive, and expert symptom management and end of life care for those that are deteriorating and in their last days–hours of life.

Health care professionals often face fear and anxiety during this period. The 8 sources of anxiety after asking them can be organized into 5 requests from health care professionals to their organization: hear me, protect me, prepare me, support me and care for me. It is important that leaders understand the sources of concern and assure them that their concerns and their daily fight with the invisible enemy are recognized. Health care workers want to see that their leaders make an effort to develop approaches that mitigate those concerns to the extent that they are capable of[14].

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