



## Commentary

# SARS-COV-2 PANDEMIC IN THE MEDITERRANEAN AREA: EPIDEMIOLOGY AND PERSPECTIVES

Claudio Costantino<sup>1,2</sup>, Emanuele Cannizzaro<sup>1</sup>, Davide Alba<sup>1</sup>, Arianna Conforto<sup>1</sup>, Livia Cimino<sup>1</sup>, Walter Mazzucco<sup>1,2</sup>

1. Department of Health Promotion, Maternal and Infant Care, Internal Medicine and Medical Specialties (PROMISE), University of Palermo, Palermo, Italy

2. Clinical Epidemiology and Cancer Registry Unit, COVID-19 Western Sicilian Regional Reference Laboratory, Palermo University Hospital (AOUP) "P. Giaccone", Palermo, Italy

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### ABSTRACT

In December 2019, a disease caused by a novel Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) was identified in Wuhan, Hubei Province, China. In March 2020, the World Health Organization declared the pandemic due to SARS-CoV-2. At the end of May 2020, SARS-CoV-2 confirmed cases and deaths due to novel Coronavirus disease (COVID-19) were about 6.5 million and 380,000, worldwide. In this commentary the authors argue on the impact of SARS-CoV-2 pandemic in different epidemiological settings within the Mediterranean area, discussing any possible association with higher or lower virus spread according to climatic factors, pollutants, characteristics of general population, and organization of health care services.

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Since the declaration of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) pandemic by the World Health Organization (WHO) [1, 2], novel Coronavirus disease (COVID-19) has been continuously spreading towards continents, moving from Asia to Europe.

More recently, while the epidemic seems to be under control in most Australasian and European countries, an increasing incidence trend on the American continent is being documented, with the United States of America and Brazil having dramatically moved to the top of the global ranking [3].

Globally, at the end of May 2020, SARS-CoV-2 confirmed cases and deaths were about 6.5 million and 380,000, respectively, and in more than 200 countries, areas and territories cases of the epidemic occurred [3].

To date in the Mediterranean area, 814,801 confirmed cases and 97,739 deaths associated to COVID-19 occurred, respectively, with a greater epidemiological impact on the southern European populations as compared to remaining countries bordering the Mediterranean sea [3].

Both SARS-CoV-2 incidence and mortality for COVID-19 have been associated with advanced age and pre-existing chronic health conditions (i.e. cardiovascular, cerebrovascular diseases, cancer, diabetes, etc.), being that fragile populations are at higher risk of developing severe health consequences [4, 5].

These are all factors that have probably contributed to the excess in mortality related to COVID-19, as reported for high income countries documenting high proportions of elderly residents, such as Italy, Spain and France. In contrast, despite Croatia and Greece are considered at higher vulnerability to COVID-19 as well, better epidemiological outcomes were registered to date [6].

Severe epidemic situations were reported in Egypt and Algeria, while underreporting of SARS-CoV-2 cases should be considered for the epidemic progression in Northern Africa [7].

Of interest, some countries of the Eastern Mediterranean region (EMR) were called to develop and enact extraordinary public health measures in order to face the additional unique challenge related to major religious mass gathering events and to this end they were supported by EMR WHO Regional Office [8, 9].

\* Corresponding author: Davide Alba, [davide.alba@unipa.it](mailto:davide.alba@unipa.it)

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The approach of Israel resulted in effective control of the COVID-19 impact thanks to a rapid response during the prevention phase of the SARS-CoV-2 pandemic, among a strong community and primary health care system, and to public health measures tailored to vulnerable cultural minority populations [10].

On the other side, while entering the second phase of the pandemic, concerns have raised in high income areas for non COVID-19 patients according to the limitations and a delayed access to care and secondary prevention services, such as the colorectal cancer screening [11-14]

Italy was the first Country within the Euro-Mediterranean area to dramatically experience the pandemic and to progressively put in place increasingly preventive measures according to WHO interim guidelines [15], including social distancing, community and communication [16] strategies, as non-pharmaceutical interventions to mitigate the contagion [17], escalating in a lockdown on the 8 of March, 2020 [18].

Having one of the highest life expectancies in the world, Italy has documented one of the highest number of deaths (more than 33,000 to date) and one of the worst lethality by country worldwide, with a north to south gradient ranging the worst outcomes in Lombardy region [19, 20]. This excess of mortality has been explained by age and high density population, but in this context some criticisms have also been reported with regard to an unpunctual contact tracing system in place, an insufficiently developed community and primary health care response in place for COVID-19 patients, and to the lack of specific clinical risk management procedures against SARS-CoV-2 for long term care facilities [21-23].

In addition, some epidemiologists have pointed out the attention on the evidence that, similar to Wuhan, the Italian regions most affected by COVID-19 outbreak were situated in a hyper-industrialised and highly polluted area corresponding to the Po valley [24, 25].

Therefore, the role of environmental pollution on boosting the spread of the COVID-19 epidemic has been postulated and recent studies have showed a correlation between particulate and COVID-19 incidence and death rates [26,27].

Of interest, air pollution represents one of the most well-known causes of prolonged inflammation, eventually leading to an innate immune system hyper-activation [27].

Moreover, preliminary evidences suggested that particulate matter (PM) can also be a possible carrier of SARS-CoV-2, thus supporting the hypothesis that air sampling used for air pollution monitoring could provide indicator of epidemic recurrence [28].

Further, a recent study provided preliminary evidence about a partial suppressing effect on the COVID-19 pandemic with increases in temperature and humidity [29].

This body of evidence is in line with previous studies documenting a link between atmospheric pollutants, temperature, humidity, and season and incidence of other air-borne infectious diseases like measles, SARS-CoV-1, avian and other influenza viruses [30-34], and may suggest public health measures to control the spread of COVID-19, acting against the source of infection and blocking the transmission [29].

Consequently, lower average ages, population density and anthropic pollution on one side, and higher temperature and relative humidity on the other side, could explain the differences in the epidemiological trends and the lower impact of COVID-19, as documented in the African populations [35].

In the same direction, a recent study highlighted how, between February and March 2020, a 4–12 °C isotherm zone extending mostly from Central China toward Iran, Turkey, and up to West-Mediterranean Europe, showed a collinearity with the geographic regions most affected by the pandemic in that same period, while the Tropical zone and the large part of the southern hemisphere could avoid an extreme impact of the pandemic because of the sufficiently annual warm weather and of the lower median age of the resident populations [36].

In contrast, other findings about the comparison between the number of confirmed cases in the worst affected European countries and the west African countries with confirmed COVID-19 cases did not clearly support the hypothesis of the virus spreading slower in areas with warmer climates [36, 37], so that with this perspective, underreporting of cases and deaths should be taken into account.

Of interest, as a consequence of nosocomial transmission, healthcare workers (HCW) globally resulted in a core group for SARS-CoV-2 risk exposure and infection [38, 39], as further confirmed in Italy where to date 27,952 (12.9% of the total cases) health care professionals were SARS-CoV-2 positive [40]. HCW and medical staff members are particularly vulnerable because of exposure to more viral particles than the general public and because of shortages of personal protective equipment (PPE) while the number of patients rapidly increases during a pandemic [41]. As the correct use and management of PPE and infection control has been associated with decreased infection risk, the importance of pandemic plans including a specific training for HCW should be highlighted [41].

During the pandemic, training programs on epidemiology and COVID-19 preparedness were implemented in high vulnerability countries from the EMR to increase their capacity of surveillance and rapid response to public health threats [42].

Moreover, distance training should be promoted whereas conventional educational approaches are limited by circumstances and may be effective to efficiently fill the gap in knowledge [43]. Because of the threats to health professionals, the need to investigate the impact of virus circulation in the different healthcare and non-healthcare settings has to be taken into account [44].

To this end, SARS-CoV-2 risk profiling associated to different health professionals should be studied, according to environmental and individual (biological and professional) factors in order to implement specific prevention measures.

Despite that progress has been made in the understanding of the epidemiology of COVID-19, several controversial points are still debated within the international research community, starting from the role of asymptomatic SARS-CoV-2 patients in the seeding of outbreaks [45].

Recent researches indicated that asymptomatic cases could represent 15% to 60% of SARS-CoV-2 infections and that about a quarter could develop delayed symptoms turning out to be presymptomatic patients, so having a role in the epidemic spreading, in particular in the younger age strata [46-48].

These findings imply a focus on the socio-demographic and cultural characteristics of every different population with particular regard to the interactions between youngsters and elder people which are more intense in the southern Mediterranean countries as compared to the ones in the northern European countries and may partly explain the different epidemiological impact of COVID-19 [49].

Moreover, current findings available on COVID-19 documented that SARS-CoV-2 can be shed through the gastrointestinal system and that a subset of COVID-19 patients may continue to have positive SARS-CoV-2 anal/rectal swab and stool test after negative conversion of nasopharyngeal test, suggesting a possible, but controversial, transmission via the fecal-oral route [50].

All of the previous aspects should be considered relevant in the countries bordering the Mediterranean sea characterised by frequent migration flows of young people from Africa or Asia, and where, as a consequence of SARS-CoV-2 epidemics and the well-known intense commercial relationships between China and some African countries, local authorities are again experiencing the increase of an already existing public health concern from the local communities with regard to the serological status of immigrants [51].

Lastly, the role of superspreaders has been taken into account to explain the heterogeneous propagation of SARS-CoV-2 between and within the different countries, where the time that it took for the explosive spread to begin varied greatly [52, 53]. Therefore, heterogeneity and the emergence of super spreading events, where certain individuals are able to infect large numbers of secondary cases, represents a strategic point for prediction and control of future SARS-CoV-2 epidemics [54].

In conclusion, we believe that to counteract the SARS-CoV-2 outbreak in a long-term perspective, all of the key modifiable factors, including the environmental ones, should be promptly identified in the different epidemiological settings in order to share the coexistence with SARS-CoV-2.

However, while at the beginning of the outbreak different strategies have been put in place in different Mediterranean countries, later on effectiveness of non pharmaceutical measures against COVID-19 had to be proven in the field by the different countries [55, 56].

Nevertheless, while waiting for the results of on-going clinical trials on several potential COVID-19 treatments to provide new perspectives in the clinical field [57, 58], preliminary serological testing suggests that populations are very far from reaching herd immunity [59]. Contextually, mandatory vaccination of at-high risk categories against influenza, S.Pneumoniae or diphtheria/tetanus/ pertussis could represent an further public health measure in reducing COVID-19 impact [60 - 63]. Therefore, the development of vaccines against SARS-CoV-2 still represent the main target to counteract the pandemic worldwide [64].

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