

COVID-19 revolution: a new challenge for the internist

The COVID-19 pandemic: is it really just a flu?

Focus on epidemiology

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ABSTRACT

As the main title ‘*COVID-19 revolution: a new challenge for the internist*’ states, the global coronavirus infection disease 2019 (COVID-19) pandemic represented a new challenge for the internists. This paper is part of a series of articles written during the difficult period of the ongoing global pandemic and published all together in this fourth issue of the *Italian Journal of Medicine*, with the aim of sharing the direct experiences of those who were the first to face this severe emergency, expressing each point of view in the management of COVID-19 in relation to other diseases. Each article is therefore the result of many efforts and a joint collaboration between many colleagues from the Departments of Internal Medicine or Emergency Medicine of several Italian hospitals, engaged in the front line during the pandemic. These preliminary studies therefore cover diagnostic tools available to health care personnel, epidemiological reflections, possible new therapeutic approaches, discharge and reintegration procedures to daily life, the involvement of the disease not only in the lung, aspects related to various comorbidities, such as: coagulopathies, vasculitis, vitamin D deficiency, gender differences, *etc.*. The goal is to offer a perspective, as broad as possible, of everything that has been done to initially face the pandemic in its first phase and provide the tools for an increasingly better approach, in the hope of not arriving unprepared to a possible second wave.

This paper in particular deals with the epidemiology of COVID-19.

Steps of pandemic

On 31st of December 2019, Chinese health authorities reported a cluster of pneumonia cases of unknown etiology in Wuhan city, Hubei province, China.

A potential transmission from live animals was suspected: many cases reported a history of exposure to Wuhan’s South China Seafood City market.¹

On the 9th of January 2020, the Chinese Center for Disease Control and Prevention (China CDC) identified a novel coronavirus as the causative agent of these cases. Chinese health authorities also confirmed human-to-human transmission of the virus, officially named COVID-19 (coronavirus infection disease 2019) by the World Health Organization (WHO).

COVID-19 virus was classified and designated as SARS-CoV-2 by the Coronavirus Study Group (CSG) of the International Committee on Taxonomy of Viruses, which also formally associated this virus with *severe acute respiratory syndrome coronaviruses* (SARS-CoVs), thus designating it as *severe acute respiratory syndrome coronavirus 2* (SARS-CoV-2).

On the 30th of January 2020, the World Health Organization (WHO) declared the international SARS-CoV-2 outbreak a Public Health Emergency of International Concern (PHEIC), and on the 11th of March 2020 declared that the COVID-19 outbreak could be considered as a pandemic involving more than 150 countries, with a predominant disease load in Italy, South Korea, Iran, Hong Kong, Macau, and Vietnam. A significant number of deaths have been re-

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ported in old individuals and patients with multiple comorbidities.²

By the end of June 2020, more than 9,454,051 cases were confirmed worldwide since the start of the pandemic and 483,686 deaths; Italy was the first western country concerned, with approximately 239,961 officially confirmed cases and some deaths exceeding 34,000 (data updated to the 26th of June). In Spain, France, and Germany, the growth of the epidemic exploded after about a week with initially very similar values of confirmed cases per million inhabitants. The delay in dissemination was even more significant for the US and UK. Some authors have compared³ the evolution of COVID-19 in the six countries (United States, Spain, Italy, Germany, France, and the United Kingdom) with the highest number of confirmed cases of contagion and deaths, using temporal translations to overcome the difficulty to analyze nations with different levels of evolution of the epidemic: the trends in the different countries show a mean overlap despite the significant differences in the policies adopted, in the organization of the various States, in social habits and climatic conditions.

Transmission and infectiousness

Understanding of the transmission risk is incomplete. Epidemiologic investigation at the beginning of the outbreak identified an initial association with a seafood market that sold live animals, where most patients had worked or visited. Subsequently, person-to-person spread became the primary mode of transmission. It is thought to occur through close-range contact, mainly *via* respiratory droplets (which typically do not travel more than two meters) when a person with infection coughs, sneezes, or talks; infection can also occur if a person touches an infected surface and then touches his or her eyes, nose, or mouth. SARS-CoV-2 has also been detected in non-respiratory specimens, including stool, blood, ocular secretions, and semen, but the role of these sites in the transmission is uncertain.⁴ The precise interval during which an individual with COVID-19 can transmit the infection to others is uncertain. It appears that SARS-CoV-2 can be transmitted before the development of symptoms and throughout the illness, particularly early in the course, from about 2 days prior to symptom onset, within about seven days.⁵ Also, viral RNA levels from upper respiratory specimens appear to be higher soon after symptom onset compared with later in the illness. However, detection of viral RNA does not necessarily indicate the presence of an infectious virus, and thus prolonged viral RNA detection following the resolution of illness does not necessarily indicate infectiousness. The duration of viral RNA shedding is variable and may depend on the severity of illness.⁶

Risk of transmission, exposure, and environmental contamination

The risk of transmission from an individual with SARS-CoV-2 infection varies by the type and duration of exposure, use of preventive measures, and likely individual factors (*e.g.*, the amount of virus in respiratory secretions). The risk increases with the closeness and duration of contact: most secondary infections have been described among household contacts, in congregate or health care settings when personal protective equipment was not used,⁷ and in closed settings (*e.g.*, cruise ships). The risk of transmission with more indirect contact (*e.g.*, passing someone with an infection on the street, handling items previously handled by someone with infection) is not well established and is likely low. Virus present on contaminated surfaces may be another source of infection if susceptible individuals touch these surfaces and then transfer the infectious virus to mucous membranes in the mouth, eyes, or nose, mostly in settings where there is heavy viral contamination (*e.g.*, in an infected individual's household or health-care settings). It is unknown how long SARS-CoV-2 can persist on surfaces;⁸ other coronaviruses have been tested and may survive on inanimate surfaces for up to six to nine days without disinfection. Some studies say that disinfectants (including ethanol at concentrations between 62 and 71%) inactivated some coronaviruses related to SARS-CoV-2 within one minute and also sunlight inactivated SARS-CoV-2 in 15-20 minutes.^{8,9} Duration of viral persistence on surfaces also likely depends on the ambient temperature, relative humidity, and the size of the initial inoculum.

Although SARS-CoV-2 infection is thought to have been initially transmitted to humans from an animal host, there is no evidence suggesting animals (including domesticated animals) are a major source of infection in humans. There have been rare reports of animals with SARS-CoV-2 infection (including asymptomatic infections in dogs and symptomatic infections in cats) following close contact with a human with COVID-19.¹⁰ There have been no reports of domesticated animals transmitting SARS-CoV-2 infection to humans.

Antibodies to the virus are induced in those who have become infected. Preliminary evidence suggests that some of these antibodies are protective, but this remains to be definitively established. Moreover, it is unknown whether all infected patients mount a protective immune response and how long any protective effect will last.

Comparison between COVID-19 and flu

The Epicenter site of the *Istituto Superiore di Sanità* (ISS, Italian National Institute of Health)¹¹ esti-

mates about 8000 average annual deaths more or less directly related to the flu, based on some non-virological parameters: only a small part of these deaths has confirmed the presence of the virus. It is not easy, in fact, to establish with absolute accuracy the mortality rate of the flu, or the number of deaths from flu in a given population. By comparing the estimated 8000 average deaths to around 60 million Italian citizens, we obtain a mortality rate of just over 0.01% on average per year. About one death per 10,000 individuals, with much higher peaks in risk categories. For the new coronavirus, we cannot yet have these data. The parameter that we can consider is the so-called lethality rate, which is the number of deaths that occur only in infected patients. The significance of this parameter depends on how many specific tests are performed and, consequently, on how many positive tests can be detected or on how many cases are highlighted based on clinical suspicion only. The more precise you are in identifying cases, the closer you get to the result. It is so difficult to calculate the lethality rate for influenza's virus (the range of values that is obtained when it comes to the lethality of the seasonal influenza virus is very wide; the value that recurs most often is 0.02% but, it is subject to considerable variability in the various studies) and much more difficult it is to do it for the coronavirus at the current epidemic. Recently the Chinese Center for Disease Control and Prevention¹² has published an extensive range of cases: more than 72 thousand cases, of which approximately 45 thousand are virologically confirmed. Considering only the latter cases (the safest ones), it is possible to say that the observed lethality rate is above 2% (2.3%). Even considering cases not confirmed virologically, the lethality rate remains well above 1% (1.5%). These values, observed on such a large series, fall within the range (0.9-1.7%) of the values so far calculated by various mathematical models, which also included possible unregistered cases. As with influenza, peaks above 10% have been observed in older patients. Another consideration is that, unlike the flu, for the coronavirus, we do not yet have a vaccine, and the majority of the population has no defenses and is not protected from infections by previous years, and we do not yet have effective drugs.

The Italian situation

From the beginning of the epidemic to the 30th of June 2020, 240,578 cases of COVID-19 diagnosed by the regional reference laboratories as positive for SARS-CoV-2 have been reported to the Italian surveillance system. 34,767 deaths were reported. The epidemic curve showed an upward trend in new diagnoses until the 20th of March 2020, followed by a steady decrease.

We state that the data are constantly being consolidated and updated, as foreseeable in an emergency, so that some information is incomplete. According to the data provided in the National Update of the 23rd of June 2020 by ISS:¹³

- the symptom start date is currently available only in 180,118 of the 239,709 reported cases. The first symptomatic cases date back to the end of January, with an increasing trend in the number of cases up to the 13th of March 2020. The fact that the peak of the cases for the starting date of symptoms was reached a few days after the adoption of the restriction measures at the national level (lockdown) confirms that these measures have had an impact on reversing the trend of infections;
- the median time between the onset of the symptoms and the diagnosis: about 4 days;
- 109,773 cases are males (45.8%);
- the median age: 61 years (range 0-100);
- in the age groups 0-9, 60-79 years, male cases are more than female cases, while in the age group >90 years, the number of females is more than triple than the number of male subjects, probably due to the demographic structure of the population;
- lethality increases with increasing age¹⁴ of cases and is higher in male subjects in all age groups, with the exception of the 0-9 age group;
- in 34.3% of the reported cases, at least one comorbidity is reported (cardiovascular pathologies, respiratory pathologies, diabetes, immune deficiencies, metabolic pathologies, oncological pathologies, obesity, kidney pathologies, or other chronic pathologies);
- the epidemiological investigations carried out suggest that in almost all cases, the infection was acquired in Italy;
- 164,997 patients healed;
- clinical severity is available for 18,553 confirmed cases, of which 5231 (28.2%) asymptomatic, 2155 (11.6%) paucisymptomatic, 6828 (36.8%) with mild symptoms, 3320 (17.9%) with severe symptoms, 364 (2.0%) with a severely critical clinical picture in the remaining 3.5% of cases the level of severity is unknown;
- information on the place of treatment is available for 160,777 cases (67% of the total), of which 10,781 (6.7%) are hospitalized. Of the latter, 957 (8.8%) are hospitalized in Intensive Care Unit;
- as of the 23rd of June 2020, all Italian provinces have reported at least one case of COVID-19. As regards the incidence and distribution, the cases are concentrated mainly in northern Italy, in particular in Lombardy, Piedmont, Emilia-Romagna, and Veneto (85% of the national total).
- overall, the diagnosed cases in the age group <18 are 2% of the total. Among them, 12.5% are under

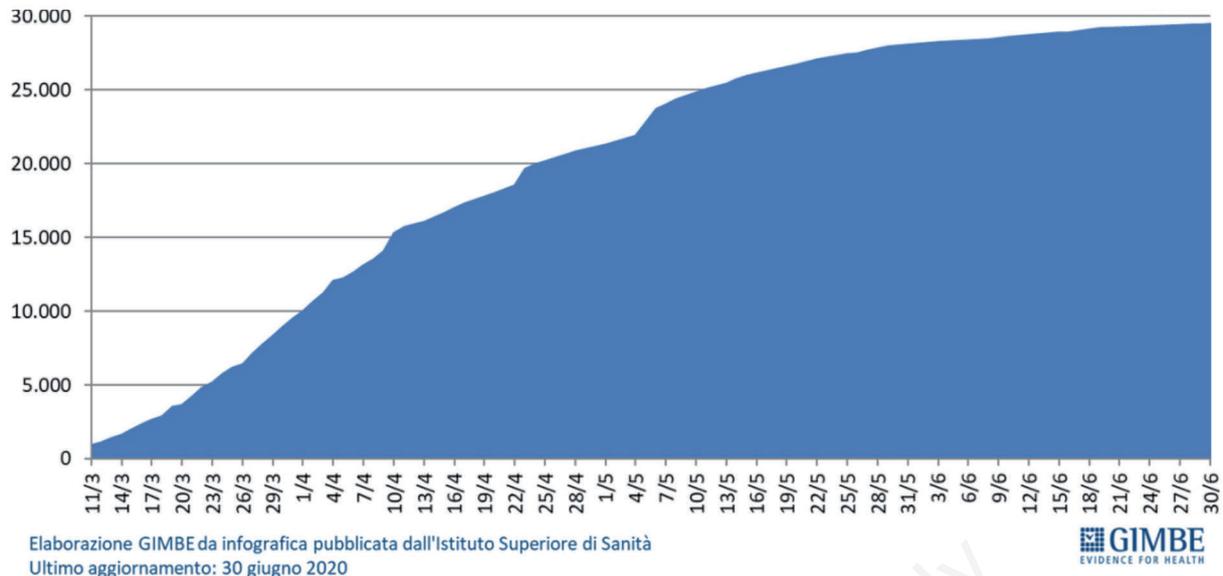


Figure 1. Health workers infected in Italy.¹⁵

the age of one year; 69.5% are aged >6 years. Overall, about 2.1% of cases <18 years are hospitalized. The percentage of hospitalized cases is higher among cases <2 years of age;

- an analysis of the information on the place of exposure, available for 969 / 8.394 cases, diagnosed from the 25th of May to the 23rd of June, showed that 35.1% of the cases contracted the disease in a nursing home or community for the disabled, 24.6% became infected in the family, while 6.6% became infected in hospital or outpatient clinic.

Risk factors (Italy)

Except for the first three reported cases of COVID-19 from China, no other reported cases in Italy communicated a travel history in countries with transmission supported by SARS-CoV-2 during the 14-day incubation period.

According to the data from ISS and from the independent monitoring of the GIMBE Foundation, as of the 30th of June, 29,476 health workers were infected (Figure 1),¹⁵ 12.3% of the 240,578 total national infections.

Lethality among health workers is lower than total lethality, probably because asymptomatic and paucisymptomatic health workers have been more tested than the general population.

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