Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

An epidemiological study on COVID-19 should be carried out: With a serological test, a pharyngeal swab or both?

As stated by the World Health Organization as of 29th July 2020, 16,747,268 confirmed cases and 660,593 deaths of a Novel Coronavirus Disease (COVID-19) were reported throughout the world. In Italy, the first death linked to COVID-19 occurred on 21st February 2020 in Vo' (Veneto).

In China and Europe, the epidemic was successfully contained with drastic social distancing measures like closing schools and workplaces, prohibiting any type of gathering and allowing the quarantined population to leave the house only for extreme necessity reasons. This strategy was based on the isolation of cases and their contacts. On the contrary, in the US, a soft and late lockdown did not produce the effects obtained in other countries. The US have been one of the most severely affected countries in the world and still in the log phase of the pandemic wave.

In Italy, no epidemiological study has been done to verify how many people have been infected. We know that to date we have had 246,488 cases with 35,123 deaths, numbers highlighted by pharyngeal swabs RT-PCR performed on subjects suspected of COVID-19 and their close contacts excluding asymptomatic and paucysymptomatic individuals. Therefore, the real prevalence and mortality rate on the entire population are not known in our country yet. Only in Vo'(Padua, Italy), nasopharyngeal swabs from 2812 subjects were collected, corresponding to 85.9% of the entire Vo' population, a total of 73 individuals were positive and 30 of them (41.1%; 95% CI 29.7–53.2%) who tested positive were asymptomatic [1]. The actual prevalence was 2.6% which would be decreased to 1.5% without asymptomatic cases. In Italy, only people with symptoms have been mainly tested so far, therefore official data greatly underestimate SARS-CoV-2 occurrence in all the population.

Since several doubts currently persist regarding the virus transmission dynamics, principally concerning the influence of asymptomatic subjects on the virus's spread [2], it would be vital to know their number, especially now that people's mobility restrictions are over. This would let us know the real impact of the virus, control its spread and, at the same time, allow the population to maintain public and economic activities.

We should probably estimate the number of infected people through a probability sample representing the population obtained by randomly selecting people from the municipal civil record list, following a sampling strategy. By carrying out the RT-PCR test in association with serology tests we could estimate quite correctly the prevalence of SARS-CoV-2 in the target population. In fact, the gold standard for COVID-19 diagnosis was nucleic acid testing for SARS-CoV-2 by RT-PCR. However, false-negative results may occur due to the presence of amplification inhibitors in the sample or insufficient organisms rising from inappropriate collection, transportation, or handling. On the other hand, serological tests could also lead to several cases of false negatives therefore there might be no evidence of their reliability on asymptomatic patients. There are many serological tests and each of them is differently reliable. An analysis of various serological tests has concluded that both IgM and IgG tests' sensitivity ranges between 72.7% and 100%, while specificity varies between 98.7% to 100% [3]. Furthermore, these tests may give false negative responses in COVID-19 infection's early phase. In fact, the seroconversion of specific IgM and IgG antibodies was observed as early as the 4th day after symptom onset [4] or even after 9 days [5]. This can lead to low sensitivity of serological tests. Actually, in confirmed COVID-19 patients, sensitivity and specificity percentages of IgM to detect disease were 77.3% (51/66) and 100%, while those of IgG were 83.3% (55/66) and 95.0% respectively [4]. In patients with suspected COVID-19, sensitivity and specificity of IgM were 87.5% (21/24) and 100% and those of IgG were 70.8% (17/24) and 96.6% [4]. Therefore, antibodies against SARS-CoV-2 can be detected from mid to late stages of the disease significantly reducing its sensitivity during its early stages. Carrying out the pharyngeal swab RT-PCR and serological tests together could reduce the sensitivity gap of the latter. Other authors agree with the combined use of the two tests since, as already mentioned, viral nucleic acid and antibody concentrations fluctuate in different infection stages. Consequently, using a combination of molecular and serological assays may permit to determine SARS-CoV-2 infection more effectively [6]. In fact, in patients with undetectable RNA in their respiratory tract samples collected during day 1–3, day 4–7, day 8–14 and day 15–39 since onset of SARS-CoV-2 infection, there were 28.6% (2/7), 53.6% (15/28), 98.2% (56/57) and 100% (30/30) had detectable antibody in total Ab assay [7]. Therefore, combining RNA and antibody detections would significantly improve the sensitivity of pathogenic diagnosis for COVID-19, even in the early phase of 1-week since onset thus making an epidemiological study more reliable. Practically, by using the molecular test we can identify subjects with active SARS-CoV-2 infection whereas the serological assays can detect past COVID-19 disease. This would allow us to have data concerning the general population's real incident/prevalence of the infection which would give us the possibility to make future predictions on COVID-19 spread.

In conclusion, descriptive, analytical, clinical epidemiological research based on a significant statistical sample is necessary to understand the real impact of COVID-19 infection on our country and to have clear indications on which to base the definition of swab and serological testing policies, health practices and protocols, methods of managing economics and social activities. The combination of serological and pharyngeal swab RT-PCR tests may improve the reliability of an epidemiological analysis of the spread of COVID-19.

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