Asymptomatic Covid-19: A Model Kit

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ABSTRACT

Actions on asymptomatic SARS-CoV-2 infections are a fundamental piece of a "model kit" against COVID-19. It has been claimed that up to 40% of infections can be asymptomatic. Without a doubt, the transmission of SARS-CoV-2 from people without symptoms contributes to the spread of the pandemic acting as a "silent driver." Presymptomatic and asymptomatic transmission significantly reduces the effectiveness of control measures that start with the onset of symptoms, such as isolation and follow-up of contacts. In a community transmission scenario, what is desired is to know is whether a patient is contagious. The antigen test is the most powerful tool we have to find out it. So, the focus of testing programs for SARS-CoV-2 should be expanded to include people who do not have COVID-19 symptoms. It is not clear whether the screenings performed so far have worked well, but it is possible that in the coming months the efficacy of the use of antigens for mass testing will improve. Even antigen tests can have an individual use; almost a home use. Having cheap, fast, and self-executing antigens, they may become mandatory for risky activities: traveling by plane, dining in a restaurant, or hanging out with a group of friends for a few days.

Keywords: COVID-19; SARS-CoV-2; Asymptomatic Infections; Epidemiological Characteristic.

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Introduction

COVID-19 is a new disease, and obviously many things about it are not yet known for sure. Gaps in understanding limit the development of optimal public health strategies to control the pandemic.[1] It is needed to clarify concepts and put together the available pieces of a puzzle (which, however, will remain incomplete yet).

The number of asymptomatic SARS-CoV-2 infections, in which people do not show any symptoms, remains questionable and uncertainty remains about how much they have contributed to the pandemic. Although there have been more than 75,000 peer-reviewed and preprint publications on SARS-CoV-2 and COVID-19 since January, 2020, the size and characteristics of the persistently asymptomatic subpopulation remain poorly understood.[1]

It has been claimed that up to 40% of infections can be asymptomatic.[2] In a paper that analyzed almost a hundred studies on this subject, it was estimated that the number of patients who did not develop symptoms during the entire infection was around 20%, with a wide range that ranged

from 3 to 67%; if the population bias is analyzed, the percentage of asymptomatic patients rose to 31%.[3] In a small study In the context of general medicine in Toledo (Spain), the prevalence of asymptomatic patients was 23% and of subclinical disease (sum of true and presymptomatic asymptomatic patients) 36%; being an asymptomatic COVID-19 patient vs. symptomatic, it was associated with being younger and having more exposure to known contacts, mainly family and social.[4] These data are not far from what seroprevalence studies say: one third of patients do not develop symptoms.[5]

On the other hand, another review, of more than 2,500 studies, found percentages of asymptomatic patients between 4 and 41%, and concluded that the real figure was between 14 and 20%.[6] However, three methodological issues have been described that make attempts to estimate this proportion difficult:

1. Incomplete assessment of symptoms probably overestimates the asymptomatic fraction.

2. Studies with inadequate follow-up misclassify presymptomatic individuals.

3. Serological studies could identify people with a previously unrecognized infection, but dependence on ill-defined antibody responses and retrospective assessment of symptoms can lead to misclassification.[1]

In any case, we must bear in mind that what has been accepted so far is: 1) people are really highly infectious from the beginning and that emphasizes that we need much faster tests and immediate results in order to prevent further transmission; 2) most studies agree that baseline viral loads are similar between symptomatic and asymptomatic people; 3) asymptomatic people have a shorter viral shed, which means that they can be infectious but for a shorter period; 4) transmission in asymptomatic people generally occurs between households.[7,8]

Transmission of SARS-CoV-2 from people without symptoms contributes to the spread of the pandemic, but the extent of transmission from persistent asymptomatic people is unknown.[1] Yet there are surprising discrepant data. According to Cao et al.[9], "of 1,174 close contacts of the asymptomatic positive cases that were traced, all tested negative for COVID-19" This study is important, but as the exception which proves the rule. The researchers have said that their findings did not show that the virus could not be transmitted by asymptomatic carriers and did not suggest that their findings were generalizable. They said that strict measures, such as the use of masks, hand washes, social distancing and confinement, managed to reduce the virulence of SARS-CoV-2 in Wuhan and that asymptomatic people in Wuhan may have low viral loads. This means that the finding cannot be applied to countries where outbreaks have not been successfully controlled. Conversely, there is a lot of evidence elsewhere showing that people infected with COVID-19 can be temporarily asymptomatic and infectious, before developing symptoms.[10]

Now, evidence suggests that about one in five infected people will experience no symptoms and will transmit the virus to significantly fewer people than to someone with symptoms. But researchers are divided on whether asymptomatic infections act as a

"silent driver" of the pandemic.[11] The infectivity during the incubation period for COVID-19 is a big challenge for controlling the disease.[12] The actual public health burden of this massive group of asymptomatic patients interacting in the community suggests that a considerable part of transmission events stem from asymptomatic transmissions.[11] Higher levels of virus can occur in presymptomatic and asymptomatic patients. Viral loads have been reported to be similar between asymptomatic (including presymptomatic) and symptomatic patients. Furthermore, viral loads tend to decrease more slowly in asymptomatic patients.[13]

Presymptomatic and asymptomatic transmission significantly reduces the effectiveness of control measures that start with the onset of symptoms, such as isolation and follow-up of contacts.[14] Additionally, asymptomatic infection can be associated with slight changes in biochemical and inflammatory variables and subclinical pulmonary abnormalities can occur, detected by computed tomography.[2,15]

While more information becomes available every day, many questions about transmission remain. Infected people can transmit the virus both when they have symptoms and when they don't have symptoms. Current evidence suggests that COVID-19 spreads between people through direct, indirect (through contaminated objects or surfaces), or close contact with infected people via mouth and nose secretions. These include saliva, respiratory secretions or secretion droplets. These are released from the mouth or nose when an infected person coughs, sneezes, speaks or sings, for example. People who are in close contact (within 1 metre) with an infected person can catch COVID-19 when those infectious droplets get into their mouth, nose or eyes. There have been reported outbreaks of COVID-19 in some closed settings, such as restaurants, nightclubs, places of worship or places of work where people may be shouting, talking, or singing. In these outbreaks, aerosol transmission, particularly in these indoor locations where there are crowded and inadequately ventilated spaces where infected persons spend long periods of time with others, cannot be ruled out.[16]

Moreover, it is said that rapid antigen tests are effective, inexpensive and could end the pandemic in a few weeks (in theory).[16] It is the frequency that really matters.[17] What has been seen is that where there is frequent testing, outbreaks simply do not occur. The accuracy of a test depends entirely on what its objective is. If the target of rapid antigen tests is infectious people, which is really the most important public health goal (not for medical diagnostic purposes; rapid antigen tests are less accurate if you apply a standard PCR), these tests become extremely accurate, and can help us control the spread of the disease. But on the other hand, under no circumstances can you start implementing antigen tests without providing confirmatory tests along with them to avoid false positives: once someone tests positive, they are not called positive; at that time a confirmation test is performed.[16]

Thus, antigen testing is predicted to change the fight against the pandemic. Rapid antigen testing has been reported to be highly sensitive in detecting the presence of SARS-CoV-2 in nasal or nasopharyngeal swabs

from symptomatic and asymptomatic individuals. Diagnostic performance of the test is particularly good in samples with viral loads associated with a high risk of viral transmission (Ct <25), which show high positive and negative predictive values even when a prevalence as low as 5% is assumed.[18]

In a community transmission scenario, what we want to know is whether a patient is contagious. The antigen test is the most powerful tool we have to find out. "We can give up that sensitivity to win where we had a huge problem, which was the time it took to communicate positives and isolate." Rapid antigen tests would perform particularly well in those cases, "associated with a high risk of transmission." "SARS-CoV-2 can be transmitted before symptoms appear, so by the time a symptomatic case is detected, it may have infected others - which means that conventional testing and tracing is always playing catch".[19]

The indications of numerous international organizations have meant that antigen tests are being used in symptomatic cases, where they were better studied by the manufacturers.[20] But some studies suggest that they could also be used for close contacts without symptoms.[18,20] So, the focus of testing programs for SARS-CoV-2 should be expanded to include people who do not have COVID-19 symptoms.

However, mass testing is still one piece to fit the puzzle. In several countries, from Spain to India to the United Kingdom, massive screening has been done to find positives in places such as a university campus or a neighborhood. If thousands of people are tested, some will be found infected. But it is still a challenging strategy. Firstly, for the false positives; some of the people who test positive are not actually infected - between 10 and 150 people for every 10,000 tested, depending on the specificity of the antigen test and the prevalence of the disease.[21] For example, in Slovakia.[22] they have tested two-thirds of its population and quarantined the 57,000 people who tested positive, although a part will not have the virus. It is not clear whether the screenings performed so far have worked well, but it is possible that in the coming months the efficacy of the use of antigens for mass testing will improve. There is even talk of individual use; almost a home use. Having cheap, fast, and self-executing antigens, they may become mandatory for risky activities: travelling by plane, dining in a restaurant, or hanging out with a group of friends for a few days. Even if the vaccine arrives, the virus will not disappear completely and it will continue to be important to protect ourselves in the best possible way.[23] In any case, users of these tests should certainly be explained the erroneous belief that they "accurately detect infectivity" and that their negative result does not imply that they are released from the restrictions.

Medical decisions are taken in a framework of uncertainty. The probability of disease moves between diagnostic threshold, below which no further tests are needed, and therapeutic threshold, above which we don't need further tests to justify treatment.[24] It is in this "model kit".[25] of asymptomatic people with COVID-19 where the different sequences available must be placed.

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