ORIGINAL ARTICLE

The Importance of Asymptomatic Coronavirus Disease-19 Patients: Never Trust a "Silent Customer"

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ABSTRACT

The asymptomatic infectious case is a "silent client," one of the most complex and damaging types of client: It is someone who does not provide information; of which we have no information. The silent client, as in the asymptomatic infection, can undermine the business by apparently not being able to address the problem. So how do you manage silent clients, asymptomatic cases? Identifying the points where asymptomatic (silent) cases occur and addressing the situation from a comprehensive perspective. This includes: (1) Preventing contagion and interrupting the transmission process immediately after contact with the virus: Test system, trace, and public health measures: Polymerase chain reaction testing on as many people as possible who have been in contact with infected people which allows the isolation of infected and the tracking and quarantine of their contacts; (2) universal public health measures: Wear a mask in public, wash your hands regularly, stay home when sick, keep a physical distance, and avoid meeting people outside of your home; (3) being so strict with negative cases as with positive ones: The consequences of high rates of false negatives are serious because they allow asymptomatic – and symptomatic – people to transmit diseases; follow-up is recommended, from a clinical point of view – epidemiological, as strict to negative cases as to positive ones; (4) trace back the contacts of the positive cases: search the source of a new case, together with the contacts of that person; and (5) massive and opportunistic tests for the detection of general and specific populations: Rapid response tests for coronavirus disease-19 available to everyone, especially those without symptoms, carried out as mass population screening, to certain groups such as health workers and students, as detection opportunistic in the general practitioner's consultation, and even self-administered by anyone.

Key words: Coronavirus disease-19; severe acute respiratory syndrome coronavirus-2; asymptomatic infections; epidemiological characteristic; public health; infectious diseases; community medicine; health promotion and prevention; general practice

INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the causative agent of CoV disease (COVID-19)[1] that has spread rapidly between people. The effectiveness of control measures depends on several key epidemiological parameters, including the duration between the onset of symptoms of successive cases in a transmission chain and the incubation period (time between infection and onset of symptoms).[2] In consequence, a fundamental issue in the COVID-19 pandemic is asymptomatic cases and their role in the transmission of SARS-CoV-2. At present, there is not only evidence that indicates that asymptomatic people from COVID-19 may be the source of the infection but also that a significant number of CoV infections do not cause symptoms.[3]

Hence, the possibility that inadvertent and asymptomatic cases have been and are an important source of contagion is weighed. Considering that the majority of asymptomatic individuals with COVID-19 are likely to go unnoticed by

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healthcare workers and continue to reside within communities, they could act as an essential driving force for the spread of COVID-19 in the community and for the continuous state of pandemic. It has been reported at the beginning of the pandemic, with respect to cases in China, that around four out of five did not present symptoms of the disease.[4] Other data suggest 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. Hence, researchers are divided on whether asymptomatic infections act as a "silent driver" of the pandemic.[5]

The risk of an asymptomatic person transmitting the virus to others in their household is considered to be about a quarter of the risk of transmitting from a symptomatic person.[6] However, there is a lower risk of transmission from asymptomatic people, they could still present a significant public health risk because they are more likely to be in the community than isolated at home. The real public health burden of this massive group of "asymptomatic" interacting in the community probably suggests that a considerable part of transmission events stem from asymptomatic transmissions.[5]

In this scenario, this article, which is a personal view, based on an unsystematic or opportunistic search for information and the author's experience is intended to reflect and underline the different challenges that general practitioners have to face in relation to approach strategies of patients with SARS-CoV-2 but asymptomatic.

METHODS

For the literature review, a pragmatic approach was used that was based on a non-systematic or opportunistic narrative review considered the bibliographic references of selected articles and opportunistic searches on the internet. This article to be understood as a personal view, based on the author's experience and the literature review as described above.

DISCUSSION

Several characteristics of SARS-CoV-2 make controlling the ongoing epidemic a challenge. One of them is the existence of asymptomatic infections (and pre-symptomatics) that contribute to transmission.[7,8] Probably significant pre-symptomatic transmission reduces the effectiveness of control measures that begin with the appearance of symptoms, such as isolation, follow-up of contacts.[2]

The dominant scientific view of asymptomatic patients is that their immune systems are especially well tuned. This could explain why children and young adults make up the majority of people without symptoms because the immune system naturally deteriorates with age. It is also possible that the immune system of the asymptomatic has been primed by a previous infection with a milder CoV, such as those that cause the common cold.[9] Furthermore, the absence of COVID-19 symptoms in people infected with SARS-CoV-2 does not necessarily imply the absence of harm. Asymptomatic infection can be associated with slight changes in biochemical and inflammatory variables and subclinical pulmonary abnormalities can occur, detected by computed tomography.[10,11]

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. It has been claimed that up to 40% of infections can be asymptomatic.[10,11] In a study 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%.[12] These data are not far from what seroprevalence studies say: One-third of patients do not develop symptoms.[13] On the other hand, another review, of more than 2500 studies, found percentages of asymptomatic patients between 4% and 41%, and concluded that the real figure was between 14% and 20%.[14]

Asymptomatic or subclinical SARS-CoV-2 infections are often underreported, meaning that confirmed case counts may not accurately reflect the underlying epidemic dynamics. Furthermore, the epidemiological and clinical characteristics and immune responses of asymptomatic individuals infected with SARS-CoV-2 have not been well described.[15]

A few studies have described the clinical characteristics of asymptomatic patients; however, some of these patients were asymptomatic at the time of diagnosis, but developed symptoms later, so they cannot really represent the clinical characteristics of asymptomatic patients.[16] Therefore, it is useful to distinguish between people who are infected and who never develop symptoms ("completely asymptomatic" individuals) and those who have not yet developed symptoms, but do develop them within a few days (pre-symptomatic). Consequently, symptomatic and asymptomatic cases must be studied separately to understand the dynamics of infection.[17]

Data from the few cohort studies with longitudinal reports suggest that a small fraction of asymptomatic people may eventually develop symptoms. In the Italian and Japanese cohorts, 0% of the asymptomatic people became symptomatic. In the Greece and New York cohorts, 10.3% of asymptomatic people became symptomatic. However, in general, there is great variation in the published data on the frequency of pre-symptomatic. A conservative estimate of all these data would be that of a prevalence of 30% or more for the mixture of pre-symptomatic and true asymptomatic.[10]

Estimates of how these asymptomatic infections influence vary, but mathematical models suggest that 30–60% of spread occurs when people have no symptoms.[18] While current data suggest that asymptomatic people can transmit SARS-CoV-2, the relative contribution of asymptomatic people to the spread of SARS-CoV-2 remains an area of controversy. The previous reports have indicated that low values for the number of cycles required to detect the virus (Ct), indicating higher levels of virus, can occur in pre-symptomatic and asymptomatic patients. While many factors beyond viral load can contribute to infectivity, viral loads have been reported to be similar between asymptomatic (including pre-symptomatic) and symptomatic patients. Furthermore, viral loads tend to decrease more slowly in asymptomatic patients.[19]

The most likely source of asymptomatic infections is close contacts of patients who have been diagnosed, predominantly in the family groups.[20] Asymptomatic infections are more common in populations of young individuals (and specifically, women with frequencies between 60% and 70% are even more likely than men not to show signs of the disease), and in middle age (average age according to different studies, between 26 and 49 years). Age can play an important role in the severity of COVID-19, and this is related to different immune responses.[10,20-23] The frequency of children carrying asymptomatic SARS-CoV-2 infection has been suggested to be higher than among adults. It is also suggested that asymptomatic children enhance viral spread and may be a potential source of contagion in the SARS-CoV-2 pandemic.[24,25]

It has been hypothesized that young people without symptoms initiate much of the COVID-19 outbreaks and are driving the spread of the pandemic.[26,27] However, the prevalence figures for SARS-CoV-2 in asymptomatic children and adolescents are highly variable and difficult to interpret, among other things due to the variable concept of the age considered. Possibly prevalence rates of children and adolescents with SARS-CoV-2 are between 20% and 50% and are correlated with those of the local community.[20,28]

The silent client

In marketing, the term "silent customer" is used to refer to one of the most complex and damaging types of customer. This is someone who does not provide information; we have no information. Therefore, it is not easy to know how his experience has been and, consequently, it is difficult to improve the relationship of the company with him. It is not a dissatisfied customer, in which the problem can be identified.

On the contrary, in the case of the silent client, there is no feedback. There is simply no information about him or his motivations when making the purchase process. In the silent client, nothing can be done to solve the possible weaknesses that, as a company, may be weighing down our clients. Apparently, a client (a virus -silent, i.e., to say asymptomatic) does not harm us. This client may even seem better than a dissatisfied customer (than a virus that always expresses itself with serious symptoms...). However, it is the opposite: The silent client, as the asymptomatic infection, it can undermine the company by apparently not being able to manage the problem; the virus that causes many asymptomatic infections is more difficult to control. That is the case with SARS-Cov-2. So how do you manage silent clients? Identifying the points where asymptomatic (silent) cases are occurring by approaching the situation from a complete perspective.[29,30]

Approaching asymptomatic cases from a comprehensive perspective [Table 1]

In addition to the usual "Test system and trace" approach and public health measures, some particularly important situations should be taken into account with regard to the management of asymptomatic cases.

Prevent contagion and interrupt the transmission process immediately after contact with the virus: Test system and trace

The prevalence rate of people testing positive but without symptoms (who can infect others), confirms the assumption that intervention must take place before symptoms appear. It is therefore a priority to prevent contagion and interrupt the transmission process immediately after contact with the virus. The test is our window to the pandemic and how it is spreading. Without evidence we have no way of understanding the pandemic. One of the keys to slowing the spread of the virus is to perform polymerase chain reaction (PCR) testing on as many people as possible who have been in contact with infected people. The tests allow us to identify infected people, guiding the medical treatment they receive. It allows the isolation of the infected and the tracking and quarantine of their contacts. Moreover, it can help allocate medical and staff resources more efficiently.[31] In this context, the GP will play a key role in controlling outbreaks of the COVID-19 pandemic: Detecting suspected cases as early as possible and conducting tests to confirm new infections so that transmission chains can be shortened.[32]

Universal public health measures (for the entire population, including asymptomatic people and those who have had a negative test of any type of test)

In any case, a pure test, trace and isolation strategy is probably not feasible, nor totally useful in isolation from other public health measures: Wearing a mask in public (a model suggests that universal mask wearing could save more than 100,000 US lives in the next 4 months), washing hands regularly, staying home when sick, maintaining a physical distance, and avoiding meeting with people outside your home (simulation modeling reveals that timing of social distancing measures has major effects on number of COVID-19 cases). These

Table 1: Addressing asymptomatic cases from a full perspective

Approaches/Strategies	Concept
Prevent contagion and interrupt the transmission process immediately after contact with the virus: Test system and trace	PCR testing on as many people as possible who have been in contact with infected people. It allows the isolation of the infected and the tracking and quarantine of their contacts
Universal public health measures (for the entire population, including asymptomatic people and those who have had a negative test of any type of test)	Public Health Measures: Wear a mask in public, wash your hands regularly, stay home when sick, keep a physical distance, and avoid meeting people outside your home
Being as strict with negative cases as with positive ones	The consequences of high false negative rates are serious as they allow asymptomatic (and symptomatic) people to transmit disease. Follow-up is recommended, from a clinical-epidemiological point of view, as strict for negative cases as for positive ones
Backward follow-up of contacts of positive cases	Find the source of a new case, along with that person's contacts; spend more time understanding where someone got infected and finding other people in the same group; this can help find more drive chains
Mass and opportunistic tests for the detection of general and specific populations	Rapid response tests for COVID-19 available to everyone without symptoms, carried out as mass population screening, to certain groups such as health workers and students, as opportunistic detection in the GP consultation, and even self-administered by anyone

PCR: Polymerase chain reaction, COVID: Coronavirus disease

measures will continue to some extent until scientists find an effective treatment or vaccine, and possibly also for a certain time afterwards.[33,34]

Being as strict with negative cases as with positive ones

All tests generate some false positives and false negatives. The consequences of false negative rates are more severe since these people can transmit the disease. Up to 30% of people with SARS-CoV-2 infection are not detected by swab-based PCR tests.[35,36] A positive PCR test for the COVID-19 test carries more weight than a negative test due to the high specificity of the test but moderate sensitivity.[37] Monitoring is probably recommended, from the clinical-epidemiological point of view, as strict in negative cases as to the positives. It is already common in asymptomatic contacts, but it should also be done in patients with symptoms and negative PCR, including repeating the test. This should also be done in asymptomatic cases with negative tests. This follow-up is part of the GP's regular continuity of care work.

Backward follow-up of contacts of positive cases

This means that contact trackers must dedicate more time searching for the source of a new case, along with that person's contacts (understanding where someone got infected and finding other people in the same group), than they do on the new case's contacts: If you discover that someone has COVID-19, you can trace their contacts and test or quarantine them; after all, the patient may not infect anyone else, but they probably he or she contracted the virus as part of a group. Backward contact tracing could prevent twice as many infections as forward contact tracing alone. Hence, contact trackers should spend more time understanding where someone got infected and finding other people in the same group.[38,39]

Massive and opportunistic tests for the detection of asymptomatic cases in general and specific populations

Rapid response tests for COVID-19 are available to everyone, especially those without symptoms. These screenings are intended to show that massive asymptomatic testing can help identify many more cases and break the chain of CoV transmission. Participation would be voluntary. Those with a positive result are asked to isolate themselves and contact their GP for contact tracing. Key workers, health and social care personnel, school personnel, and children 11 and older are the primary target, but anyone can get tested. For example, it has been proposed to carry out tests twice a week for all health personnel, to introduce mass tests of students (including self-administered tests), and in each geographic area to analyze 10% of its population per week.[40]

Another upcoming option is the search for opportunistic cases in the GP consultation or in another center: People who come to that place for a reason other than COVID-19 is invited to take a test that otherwise would not have been done or they would not have asked. In this scenario.

However, the strategy of mass testing has been criticized.[41] The qualitative rapid lateral flow antigen test, which can provide results in 30 min, is of doubtful value, with a high false negative rate. That is, it does not have a

high enough sensitivity to rule out COVID-19 (and although the false positive rate is small, this is also a problem in a low prevalence setting). Thus, it can give people the mistaken assurance that, "at least for a limited time, they are unlikely to have the virus and that they are at low risk of transmitting it to others[42]" (However, the asymptomatic case with a false negative with the test that assumes false security and puts others at risk would also incur the same risk without the test; thus we would be in Pascal's wager, an argument in philosophy presented by the 17th-century French philosopher, Blaise Pascal (1623–1662): A rational person should choose to believe in God, because, if it exists, the reward – eternal glory – would be infinite. And if it did not exist, it does not matter much if one chose one or the other belief.[43] On the other hand, it has been suggested that the frequency of testing for SARS-CoV-2 at the population level is more important than the sensitivity of the test in controlling the pandemic. Effective detection is highly dependent on the frequency of the tests and the speed ad of the reports, and only marginally improves with high test sensitivity. Therefore, screening must prioritize accessibility, frequency, and time between sample and response; analytical detection limits should be secondary.[44,45]

It is also said that many asymptomatic people who test positive for COVID-19 on the rapid test are probably relatively non-infectious (although avoiding the risk is possibly adequate, although a small risk), and half may develop symptoms later and be in that moment detected, without the need for the rapid test[46] (although the pre-symptomatic stage seems to be the most contagious; and in the end that patient would also require a PCR test for diagnosis).[2] In any case, users of these tests should be explained the mistaken belief that they "accurately detect infectivity" and that their negative result does not imply that they are released from the restrictions.

In Liverpool, UK, 100,000 asymptomatic people were tested at 34 sites in the first 10 days of mass testing. Of this group, 700 (0.7%) tested positive for COVID-19. Even these rapid tests can be self-administered by anyone; and a quick test can be performed at concerts, at the cinema, in large stores, or at home.[47] In this way, there would be no need to preventively close a venue or an event or a meeting (maintaining the rest of the public health measures: Masks, distancing, capacity limitation, hand washing, and mobility limitation). Even with possible errors, a majority of possible disease vectors would be detected.[48]

In any case, it seems that the advantages outweigh the problems as an approach to asymptomatic patients, and the initial acceptability of these tests is high. Quick, cheap, and frequent mass testing will likely be a vital tool to help control COVID-19 and make life more normal by cutting the chains of transmission.[49-51]

CONCLUSION

The effectiveness of control measures depends on the role of asymptomatic people in the transmission of SARS-CoV-2. Probably 20–30% of infections are asymptomatic. These asymptomatic infections act as a silent driver" of the pandemic. Asymptomatic patients are more likely to be in the community than isolated at home. The most likely source of asymptomatic infections is close contacts of patients who have been diagnosed, predominantly in the family groups. Asymptomatic infections are more common in populations of young individuals (and specifically in women). The frequency of children carrying asymptomatic SARS-CoV-2 infection has been suggested to be higher than among adults. The real public health burden of this massive group of asymptomatic community-interacting patients suggests that a significant portion of transmission events stem from asymptomatic transmissions. Mathematical models suggest that 30–60% of the spread occurs when people have no symptoms. It has been hypothesized that young people without symptoms initiate much of the COVID-19 outbreaks and are driving the spread of the pandemic. Higher levels of virus can occur in pre-symptomatic and asymptomatic patients. Viral loads have been reported to be similar between asymptomatic (including pre-symptomatic) and symptomatic patients. Furthermore, viral loads tend to decrease more slowly in asymptomatic patients. Pre-symptomatic and asymptomatic transmission significantly reduces the effectiveness of control measures that start with the onset of symptoms, such as isolation, follow-up of contacts. Data from the few cohort studies with longitudinal reports suggest that a small fraction of asymptomatic people may eventually develop symptoms. A conservative estimate indicates a prevalence of 30% or more for the mixture of pre-symptomatic and true asymptomatic. Furthermore, the absence of COVID-19 symptoms in people infected with SARS-CoV-2 does not necessarily imply the absence of harm. Asymptomatic infection can be associated with slight changes in biochemical and inflammatory variables and subclinical pulmonary abnormalities can occur, detected by computed tomography.

The asymptomatic infectious case is a "silent client," a term that refers to one of the most complex and damaging types of client: It is someone who does not provide information; of which we have no information. The silent client, as in the asymptomatic infection, can undermine the business by apparently not being able to manage the problem. That is the case with SARS-Cov-2. Hence, how to manage silent clients, asymptomatic cases? Identifying the points where asymptomatic (silent) cases are occurring by approaching the situation from a comprehensive perspective. This includes: (1) Preventing contagion and interrupting the transmission process immediately after contact with the virus: Test system and trace (PCR testing on as many people as possible who have been in contact with infected people. It allows the

isolation of the infected and the tracking and quarantine of their contacts); (2) universal public health measures (Wear a mask in public, wash your hands regularly, stay home when sick, keep a physical distance, and avoid meeting people outside of your home); (3) be as strict with negative cases as with positive ones (The consequences of high rates of false negatives are serious because they allow asymptomatic and symptomatic people to transmit diseases. Follow-up is recommended as strict to negative cases as to positive ones); (4) trace back the contacts of the positive cases (Look for the source of a new case, along with the contacts of that person; and (5) massive and opportunistic tests for the detection of general and specific populations (rapid response tests for COVID-19 available to everyone, especially those without symptoms, carried out as mass population screening, to certain groups such as health workers and students, as opportunistic detection in the general practitioner's office, and even self-administered by anyone).

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