



Misclassification of Asymptomatic Infections of COVID-19

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Authors' contributions

This work was carried out in collaboration between both authors. Author VNO designed the study and wrote the first draft of the manuscript. Author DML contributed to the design of the study and managed the literature searches. Both authors read and approved the final manuscript.

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ABSTRACT

Introduction: Several cases of asymptomatic infections of COVID-19 being reported by several countries in this pandemic and with the recent conflicting information of asymptomatic transmission of COVID-19, it is important to look critically on the true nature of these reported asymptomatic infections. There is a possibility most of the reported asymptomatic infections of COVID-19 are not truly asymptomatic but are either presymptomatic, mild infections or infections in the post-symptomatic phase.

Results: These infections misclassified as asymptomatic infections can result in misleading findings in studies attempting to understand asymptomatic transmission of COVID-19.

Conclusion: It is therefore crucial that rigorous and detailed data be collected during contact tracing to accurately identify and classify asymptomatic infections COVID-19.

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1. INTRODUCTION

Asymptomatic infection is very common in patient with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the novel type coronavirus responsible for COVID-19 [1] With over ten million infections globally, a significant number of these are asymptomatic with the exact prevalence still very much varied as some report 75% and 80% in epicenters in Italy and China respectively while a smaller cohort of 3,711 people of the Diamond Princess Cruise Ship reported a 17.9% of asymptomatic infections [2,3,4,5].

Many countries are reporting large numbers of their active COVID-19 cases as asymptomatic infections identified through contact tracing or screening of high risk group or communities [1,6]. While the definition of asymptomatic infection for COVID-19 is quite straight forward like for all infectious diseases, the transmission dynamics and the novelty of COVID-19 makes the identification of asymptomatic infections quite tricky [1]. While the identification of COVID-19 positive patients with real-time reverse-transcription-polymerase-chain-reaction (RT-PCR) assay, with no symptoms or signs indicate asymptomatic infection [7], there is the possibility

that errors can be made concerning the accuracy in establishing the absence of symptoms.

When asymptomatic infections are reported it is important to note that these infections might be from other categories of COVID-19 that can be misclassified as asymptomatic infections. The natural history of COVID-19 presents with different phases that can be misclassified as asymptomatic infection (Fig. 1). The reported asymptomatic infections might be correctly classified, meaning they are truly free from symptoms and will never develop symptoms. There is also a possibility that these reported asymptomatic infections are actually in the pre-symptomatic phase of infections eventually developing symptoms [7]. Some infected people with mild symptoms might be misclassified as asymptomatic infection [8], while some who might have recovered from mild symptoms might also be misclassified as asymptomatic [9]. Thus reported cases of asymptomatic infections of COVID -19 might include those accurately classified as asymptomatic cases and those with, presymptomatic infections, mild symptoms and those in their post symptomatic phase of infection who are wrongly classified as asymptomatic infections.

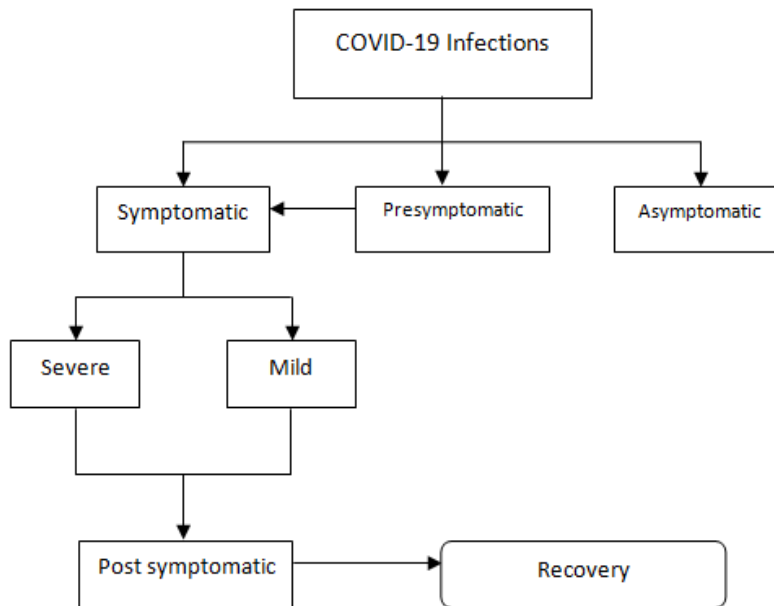


Fig. 1. Natural history of COVID-19 infection

2. ASYMPTOMATIC AND SYMPTOMATIC INFECTIONS

Asymptomatic infection is a common term when describing infectious diseases but recently with the advent of COVID -19, the term presymptomatic infection has been added [10]. Technically both asymptomatic and presymptomatic infections are related and at some point, are the same, since they both have no symptoms at the time of identification during contact tracing or screening of high risk groups or communities [11]. Whilst asymptomatic infections remain without symptoms, presymptomatic become symptomatic at some point [11]. Therefore misclassification can occur when the asymptomatic infections identified are not followed up to see if they will develop symptoms. It is important to note that, it is impossible to identify presymptomatic infections without a follow up [11]. While it is very likely that countries are reporting asymptomatic infections accurately, a subset of these asymptomatic infections maybe presymptomatic. The distinction between asymptomatic and presymptomatic infection is necessary to fully understand the transmission dynamics of COVID-19 as there are reports that both categories are actively involved in the transmission of infection [1,6].

3. MILD INFECTION

The possibility that most infections of COVID-19 recorded as asymptomatic infections, are cases of mild infections exists [8]. Most times during contact tracing or mass screening exercise, cases of mild infections are encountered but erroneously misclassified as asymptomatic infection because the respondents deny having symptoms probably because of the intermittency of their symptoms. The absence of fever in COVID-19 positive individuals who are apparent healthy looking, might be mistaken for asymptomatic infections, despite the presence of occasionally coughing or sneezing which might be considered insignificant [12]. Even WHO stated that majority of the reported asymptomatic cases are actually mild infections [8] Some studies have described asymptomatic persons as persons who are mildly ill [13,14] The absence of fever should not mean asymptomatic infection, for mild infections can still have subtle symptoms of cough and sneezing which facilitates transmission.

4. POST-SYMPTOMATIC PHASE OF INFECTION

Another category of COVID-19 infections that can be misclassified as asymptomatic infections are those in the post-symptomatic phase. Encountering post-symptomatic infections during contact tracing is not impossible as some persons might have recovered from a short period of mild illness, without hospital care or management. Many of the COVID-19 infection might go undetected and some might be detected after recovery from mild symptoms, still testing positive for COVID-19 with RT-PCR [9]. The absence of symptoms at the time of identification, might cause them to be categorized as asymptomatic infections. A proper data collection at the time of contact tracing, having in mind the existence of this group of infections can help identify them accurately. The disease transmission of this group is still in doubt despite the ability to still test positive [15,9].

5. CONCLUSION

Misclassification of asymptomatic infections might be hampering a better understanding of the asymptomatic transmission of COVID-19. Epidemiological investigation on the ability of asymptomatic infections to cause transmission might include some of the other categories, misclassified as asymptomatic infections, resulting in misleading interpretations, which might be responsible for the recent confusion on asymptomatic transmission. It is necessary therefore, that detailed information during contact tracing must be obtained to ensure accurate classification of the truly asymptomatic infections. With the experiences learned throughout the pandemic, some methodologies for asymptomatic patient classification should be changed and pre-symptomatic patients' follow-up should be improved.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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