

Review Article

The Proportion of Asymptomatic Cases Among SARS-CoV-2 Infected Patients: A Systematic Review

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Abstract: Even though some reports unveiled that coronavirus 2019 (COVID-19) cases can be manifested as asymptomatic, there is limited information on how much these cases are significant. Understanding the possible proportion of asymptomatic cases among confirmed patients might help in re-considering of who should be tested for the SARS-CoV-2 infection. Therefore, this study was aimed to summarize the proportion of asymptomatic cases among SARS-CoV-2 infected people since the outbreak of COVID-19. *Methods:* Different studies were searched from databases (PubMed, Medline) by using searching terms. Finally, all eligible articles were selected by using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2009 flow diagram. *Results:* A total of 14 articles that reported asymptomatic cases of COVID-19 were included in this systematic review. The sample size of the studies was ranged from 8 to 2143. Out of the total cases, the overall proportion of asymptomatic cases was 25.9% that ranged from 3.23% to 78%. This systematic review also summarized that there was 17.6%, 4.8%, and 3.23% to 62.2% of asymptomatic cases among pregnant mothers, children, and the adult general population, respectively. *Conclusion and Remarks:* This review showed that the proportion of asymptomatic SARS-CoV-2 infected people is high. Hence, to tackle COVID-19, all concerned bodies should strengthen the screening of asymptomatic cases as part of contact tracing efforts.

Keywords: Asymptomatic Cases, COVID-19, Proportion, SARS-CoV-2, Systematic Review

1. Introduction

Coronaviruses belong to a large family of single-stranded RNA (ssRNA) viruses that are causative agents of the common cold and severe respiratory infections, which include Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS), [1-5]. On December 31, 2019, an outbreak of pneumonia caused by an unknown agent appeared in Wuhan, China [6]. First, the pathogen of the disease was called a novel coronavirus, and now, given the name severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Subsequently, the infection caused by SARS-CoV-2 was officially designated 'coronavirus disease 2019' (COVID-19) by World Health Organization (WHO), [7]. As of June 08, 2020, WHO reported that the disease has spread to 213 countries and territories, and caused about 7 million confirmed cases and

about 40,000 deaths globally [8].

Different studies revealed that the main ways of SARS-CoV-2 transmission are through droplets and fomites during close unprotected contact between an infected and healthy individual, the familial transmission of 78%-85% [9, 10] and nosocomial [11]. Concerning the stage of transmission, several studies indicated that the virus is transmittable during its incubation and asymptomatic period [12-15]. Even though, different reports showed that some of the SARS-CoV-2 infected individuals are asymptomatic, and the potential sources of the infection, different setups are limited to testing individuals based on predetermined conditions such as clinical symptoms and/or exposure history. On the other hand, Zhu et al stated their doubt that there is unclear evidence of whether asymptomatic infection exists for

COVID-19 [16].

Even if the primary focus to combat COVID-19 is prevention by case isolation, quarantine, and careful infection control, the existence of asymptomatic cases is not aggressively seen at different levels. Therefore, by identifying these gaps, we are interested to conduct a systematic review of the proportion of asymptomatic cases among infected people. Since these asymptomatic cases are playing a significant role in transmitting the virus, providing research-based evidence on the prevalence of cases without any clinical feature may be helpful inputs for preventing and controlling of the SARS-CoV-2 infection timely. Hence, the study was

conducted to summarize the proportion of asymptomatic cases among SARS-COV-2 infected people since the outbreak of COVID-19.

2. Methods

2.1. Protocol

Searching of articles followed the recommendations forwarded by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [17].

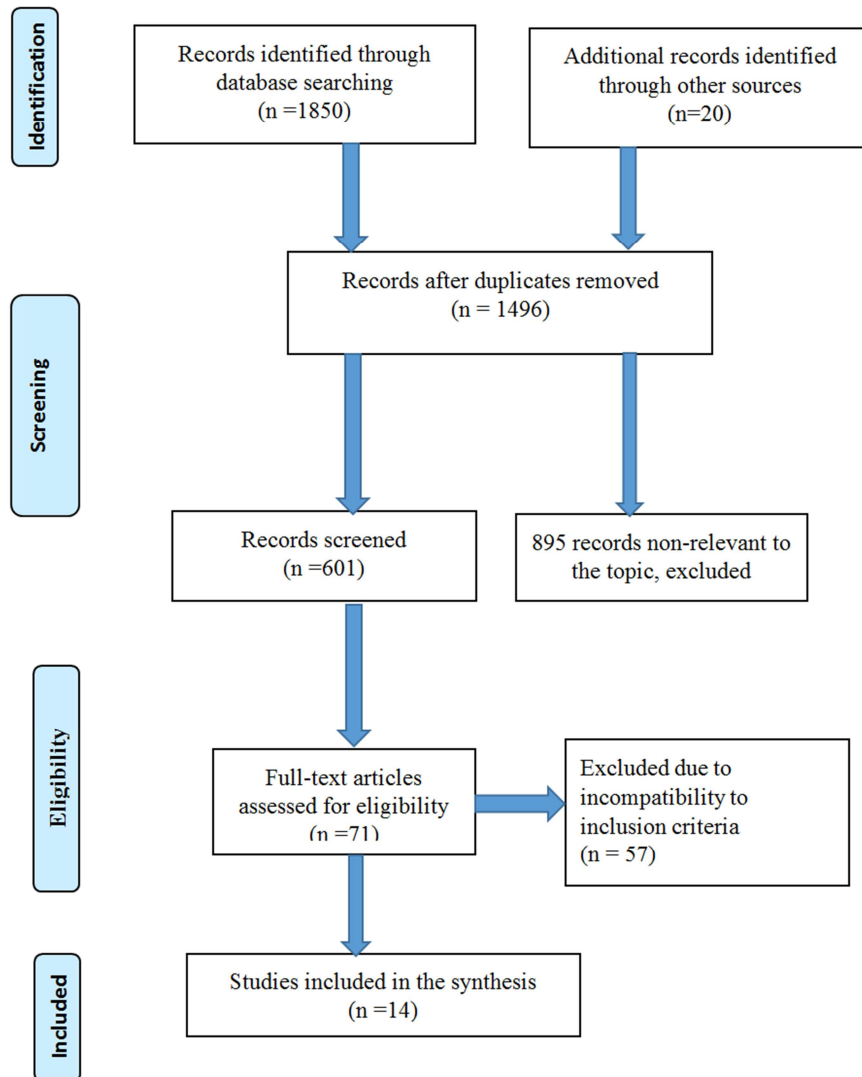


Figure 1. Diagram of PRISMA 2009 Flow for extraction of eligible studies.

2.2. Eligibility Criteria

All peer-reviewed published and pre-print articles that reported asymptomatic cases among confirmed SARS-CoV-2 infection were searched. Regarding the study design and time frame, case series, survey, time series, and retrospective cohort/observational studies conducted from late December 2019 up to May 28, 2020, were included in the study. All of the studies were conducted on human subjects and published

in the English language. Concerning the target population, the study included articles conducted on adults, children, pregnant mothers, and health professionals. Reviews, opinions, and letters that did not present the originality of the primary data were excluded.

2.3. Literature Searching Procedure

The literature search was conducted on June 03 to June 09,

2020, using two databases (PubMed, Medline) with the search terms of ['proportion' or 'percentage' and 'Asymptomatic'] AND ['COVID-19' OR 'COVID-19' OR 'novel coronavirus' OR 'SARS-COV-2' OR 'SARS COV 2']. A total of 1870 studies were retrieved through a thorough search from the two databases by using the date of publications one year. Of retrieved studies, after the full-text screening, 1,309 of the studies were excluded. Finally, out of the left 561 studies, after screening the abstract and full-text of the studies, 14 studies were included in the review.

The studies selected in this systematic review were conducted in China, Japan, America, South Korea, and the European region (Figure 1). We also searched for the references included in the introduction.

2.4. Additional Analysis

We have calculated the overall proportion of asymptomatic

cases among laboratory-confirmed SARS-COV-2 infected people. The proportion of asymptomatic cases was calculated by using asymptomatic cases of SARS-COV-2 as the numerator and all people who have been positive for SARS-CO-2 as the denominators.

$P = \text{no. of asymptomatic cases} / \text{total no. of SARS-COV-2 infected people} \times 100\%$. Where P stands for proportion.

3. Results

Out of 14 selected articles, nine were conducted on adult people, two on pediatrics, one on pregnant mothers, and two on healthcare workers. The total number of patients included in the studies was 3945 that is ranged from 8 to 2143. The studies revealed that out of 3945 laboratory-confirmed SARS-COV-2 infected people, the overall proportion of asymptomatic cases was 739 (18.7%) ranging from 3.23% to 78% (table 1).

Table 1. The proportion of asymptomatic cases among SARS-COV-2 infected patients from fourteen articles between 18 January 2019 and May 28, 2020.

First author	Time horizon	Country	Sample size (N)	Asymptomatic cases (%)	Study Design	Target population	Reference
Chen R. et al	1 March 2020	Wuhan, China	17	3 (17.6)	Case series	Pregnant mothers	[18]
Chen J. et al	20 Jan, Feb 6, 2020	Shanghai, China	249	7 (28)	Retrospective Cohort	Adults	[19]
			634				[20]
	Before 13, Feb 2020		218	35 (16)			
	February 15, 2020		285	73 (25.6)			
Mizumoto K et al	February 16, 2020	Japan	355	111 (31.3)	Time series		
	February 17, 2020		454	181 (39.9)			
	February 18, 2020		542	246 (45.4)			
	February 19, 2020		621	341 (54.9)			
	February 20, 2020		634	320 (50.5)			
Spiteri G et al	Jan24-21Feb, 2020	European regions	31	2 (6.4)	Survey report	Adults	[21]
Gostic K et al	February 20, 2020	Japan	355	111 (31.2)	Survey report	Adults	[22]
Xing Y et al	March 12, 2020	China	62	2 (3.23)	Survey	Health Care workers	[23]
Hasan A et al	March 31, 2020	China	2143	94 (4.4)	Review	Pediatrics	[24]
Li K et al	January 18, February 7, 2020	China	78	7/(9)	Retrospective Cohort	Adults	[25]
Day M	April 1, 2020	China	166	130 (78)	Survey report	Adults	[26]
Qiu H <i>et al</i>	Jan 17 to March 1, 2020	China	36	10 (28)	Observational	Children	[27]
Nishiura H <i>et al.</i>	February 4, 2020	Japan	8	5 (62.2)	Modeling	Passengers	[28]
Arons MM et al	May 28, 2020	America	48	27 (56%)	Survey	Healthcare workers	[29]
Kim SE et al.	April 28, 2020	South Korea	71	10 (14.1%)	Cross-sectional	Adults	[30]
Ma Y et al.	April 27, 2020	China	47	11 (23.4%)	Cross-sectional	Adults	[31]

Regarding the study areas, eight (57.1%) and three (21.4%) studies were conducted in China and Japan respectively, and the remaining three (21.4%) studies were conducted in Europe region, America and South Korea (one study in each area) in the different study settings (table 2).

Table 2. The overall proportion of asymptomatic cases among SARS-COV-2 infected people from selected fourteen articles (N=3,945) from January 18, 2019, to May 28, 2020.

Study area	No. articles	Total sample size	Total asymptomatic cases	The overall proportion of asymptomatic cases
China	8	2798	264	9.4%
Japan	3	997	436	43.7%
European regions	1	31	2	6.4%
America	1	48	27	56%
South Korea	1	71	10	14.1%
Total	14	3945	739	18.7%

4. Discussion

This systematic review was aimed at reviewing the proportion of asymptomatic cases among SARS-CoV-2 infected patients. Accordingly, fourteen studies from different countries that fulfilled the eligibility criteria were included. The review showed that the overall proportion of asymptomatic cases was notably high.

The eight studies conducted in China disclosed that 9.4% (ranged from 3.23% to 78%) of SARS-CoV-2 infected people were asymptomatic. These studies also reported that the overall proportions of asymptomatic cases among pregnant mothers and children were 17.6% and 4.8% in different corners of China, respectively. The lowest (3.23%) proportion of asymptomatic cases was observed among health care providers after discharged from SARS-CoV-2 hospitalization.

The three studies conducted in Japan showed that out of a total of 997 cases, the overall proportion of asymptomatic cases was 436 (43.7%) that ranged from 31.2% to 62.2% in different settings. Also, a time-series study uncovered that the proportion of asymptomatic cases increased from 16% (before 13 February 2020) to 50% (20 February 2020). The study conducted in the European region found that out of 31 laboratory-confirmed cases, 6.5% were asymptomatic (Tables 1 and 2).

The survey study conducted in America on skilled nurses indicated that out of 48 confirmed cases 27 (56%) were asymptomatic. The cross-sectional study conducted on 71 adult patients in South Korea showed 10 (14.1%) asymptomatic cases.

This systematic review demonstrated that the proportion of asymptomatic cases among SARS-CoV-2 infected people is high. Especially, in China, there was a high proportion of asymptomatic cases that might be due to the attention given to large population detection, contact tracing, and proactive follow-up of any suspected/quarantined people during the incubation period of the virus. This study also revealed that more than 60% of the passengers in Japan were asymptomatic. This high proportion among passengers may be due to that the passengers can be missed from those individuals screened based on symptoms at the portal point. Also, this review indicated that people can be re-infected and become asymptomatic after discharged from the hospital.

Moreover, this systematic review unveiled that all individuals, whether they are children, pregnant mothers, or adults are susceptible to SARS-CoV-2 and develop a COVID-19 or become asymptomatic.

Furthermore, the review indicated that the degree of asymptomatic cases varies among different countries, different study areas of the same country, and target populations. The factors affecting this variation among the different countries and different areas of the same country are most probably the differences in study size, sample size, and study designs. However, the factor responsible for being asymptomatic among different target populations is in the same and or different counties is uncertain and requires investigation.

5. Conclusion

The review demonstrated that 18.7% of COVID-19 cases were asymptomatic. In conclusion, although further studies are warranted to generate weight of evidence, with the limited shred of information, there are a significant number of asymptomatic SARS-CoV-2 infected people.

6. Recommendation

Since prevention should be a priority in combating COVID19, individuals who had an exposure history should be tested as soon as possible regardless of clinical manifestations. Also, besides testing adults for COVID-19, children and pregnant mothers should not be neglected during massive testing, contact tracing, and hospital visits. Moreover, in every country, entry points should be strictly followed by providing a short time-consuming laboratory diagnosis as much as possible. Furthermore, asymptomatic case identification should be carried out as part of contact tracing effort and prevention measures to contain COVID-19. Finally, we recommend that studies that identify the factors responsible for being asymptomatic among SARS-CoV-2 infected individuals should be conducted.

Abbreviations and Acronyms

COVID-19:	Coronavirus Disease 2019
IL-6:	Interleukin six
MERS:	Middle East Respiratory Syndrome
PRISMA:	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
SARS:	Severe Acute Respiratory Syndrome
SARS-CoV-2:	Severe Acute Respiratory Syndrome Coronavirus-2
WHO:	World Health Organization

Authors' Contributions

AB was involved in the study conception, article extraction, analysis, writing, and manuscript drafting. GC and TOF participated in articles extraction, manuscript drafting, and critically editing the manuscript. Finally, all authors read and approved the manuscript to be submitted for publication.

Conflict of Interest Statement

The authors declare that they have no competing interests.

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