The incidence of the novel coronavirus SARS-CoV-2 among asymptomatic patients: a systematic review

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Highlights

- The true incidence of SARS-COV-2 is much higher than the reported number of cases.
- Large sample size studies showed 1.2-12.9% incidence of SARS-COV-2 among asymptomatics.
- Studies with a small sample size showed up to 87.9% incidence among asymptomatics.
- Asymptomatic individuals could be a potential source of infection to the community.
Abstract

**Background:** the recent outbreak of the coronavirus disease 2019 (COVID-19) has quickly spread globally since its discovery in Wuhan, China, in December 2019. A comprehensive strategy, including surveillance, diagnostics, research, and clinical treatment is urgently needed to win the battle against COVID-19. Recently, numerous studies reported the incidence of SARS-CoV-2 in asymptomatic patients. Yet, the incidence and viral transmission from the asymptomatic cases are not apparent yet. **Aim:** this study aims to systematically review the published literature on SARS-CoV-2 in the asymptomatic patients to estimate the incidence of COVID-19 among asymptomatic cases, as well as describe its epidemiological and clinical significance. **Method:** the literature was searched through four scientific databases: PubMed, Web of Science, Scopus, and Science Direct. **Results:** a total of 63 studies satisfied the inclusion criteria where the majority of the reported studies were from China. However, there was a lack of SARS-CoV-2 epidemiological studies from several countries worldwide, tracing the actual incidence of COVID-19, especially in asymptomatic patients. Studies with a large sample size (n>1000) estimated that percentage of people contracting SARS-CoV-2 and are likely to be asymptomatic ranges from 1.2-12.9%. However, the other studies with a smaller sample size reported a much higher incidence and indicated that up to 87.9% of COVID-19 infected individuals could be asymptomatic. Most of these studies indicated that asymptopatics are a potential source of infection to the community. **Conclusion:** this review highlighted the need for more robust and well-designed studies to better estimate COVID-19 incidence among asymptomatic patients worldwide. The early identification of the asymptomatic cases, as well as monitoring and tracing close contact, could help in mitigating the spread of COVID-19.

**Keywords:** COVID-19, SARS-CoV-2, Asymptomatic carrier, Viruses, Incidence
1. Introduction

Infectious diseases impose a major health threat globally, leading to 15 million deaths annually [1]. Although the percentage of mortality due to infectious diseases has declined, numerous new infectious diseases have been identified and reported recently. The novel coronavirus disease (COVID-19), caused by the SARS-CoV-2 virus, was firstly identified in Wuhan, China, in late December 2019 as an outbreak of unusual viral pneumonia [2]. Later, the World Health Organization (WHO) declared a public health emergency worldwide, and the total number of infected cases reached 4.4 million by May 2020 [3]. Consequently, educational institutions, business centers, public transport, and other social interaction were locked down points to prevent the spread of COVID-19 and ease the burden on health facilities. SARS-CoV-2 is an enveloped positive-sense single-stranded RNA virus with six open reading frames (ORFs) that codes for structural proteins, including surface (S), envelope (E), membrane (M), and nucleocapsid N proteins [4]. Based on the genomic structures and phylogenetic analysis of SARS-CoV-2, the virus belongs to genera Betacoronavirus, which includes SARS-CoV and MERS-CoV. Yet, SARS-CoV-2 has differences in its genomic that can influence its pathogenesis.

The most effective approach to prevent and mitigate the adverse consequences of this viral pandemic requires the development of effective surveillance programs, incorporated with laboratory preparedness. Diagnostic laboratory tests play a significant role in the rapid and accurate detection of new viruses [5, 6]. Currently, real-time reverse-transcription polymerase chain reaction (RT-PCR) testing is the main technique used for the diagnosis of COVID-19. However, false-negative RT-PCR results occur in up to 30% of COVID-19 patients [7-9]. This could be due to the collection of inappropriate or insufficient sample, inaccurate conditions of sample transportation and storage, as well as collecting the sample too late in the disease process.
On the other hand, serology testing could cover this gap since detecting SARS-CoV-2 IgG antibodies could indicate recovery or immunity from COVID-19 infection. Besides, IgM could be detected in the acute phase of infections. Although, manual enzyme-linked immunoassay (ELISA) kits could be subjected to non-specific binding and cross-reactivity with other coronaviruses such as MERS-CoV and SARS-CoV-1, most commercially available antibodies utilize lateral flow assays (LFA) [10]. However, recently ELISA and automated-based assays were also introduced. The diagnostic performance, including sensitivity and specificity, of these assays, were better than the LFA [11]. It worth mentioning that there is a high percent of COVID-19 asymptomatic patients who could transmit the infection to all communities. For instance, the asymptomatic ratio of COVID-19 was estimated to be 41.6% of Japanese individuals who were evacuated from China [12]. Similarly, 72% of people infected with COVID-19 on board the Diamond Princess cruise ship were asymptomatic [13]. However, the extent of viral transmission from the asymptomatic cases is not clear yet. The positive RT-PCR results only imply the potential infectivity. A prospective study was published on March 28 in which the viral load and clinical manifestations of 2,147 close contacts of symptomatic and asymptomatic COVID-19 cases were followed up [15]. The study concluded that the virus infection rate of close contacts with asymptomatic patients was 4.11%.

Since the transmission ability of asymptomatic individuals should not be ignored, it was of interest to conduct a systemic review to paint a picture of the current status and incidence of SARS-CoV-2 in asymptomatic patients. Therefore, this study would give significant insights into COVID-19 infection and help health authorities to determine the need for social distancing close contact restrictions in specific areas or populations.

2. Methods
2.1. Search Strategy

We conducted a systematic review of all literature published on COVID-19 in the asymptomatic patients using four databases: PubMed, Web of Science, Scopus, and ScienceDirect. The search covered all literature within the databases up to April 2020. The databases were queried with the keywords: “COVID-19”, “SARS-CoV-2”, “seroprevalence”, and “asymptomatic” to ensure complete coverage of all literature. The four databases were searched without filters. Therefore, results that were letters and commentaries were also included. All retrieved citations were imported into EndNote X8, and duplicates were removed using the EndNote X8 built-in “Find Duplicates” feature. Finally, the titles and abstracts of the remaining citations were screened to remove any irrelevant articles.

2.2. Study Selection

The following inclusion criteria were used in study selection: (i) published in a peer-reviewed journal, letters, case reports, and commentaries (ii) articles studying the COVID-19 infection in asymptomatic patients, and (iii) articles published in English or at least with an abstract in English. A schematic of the search strategy and study selection process is shown in Figure 1. Besides, studies that reported the coinfection of COVID-19 with other viruses as well as comorbidities, such as cancer and cystic fibrosis, were also included in this study. No exclusion criteria were followed unless the studies did not report the incidence of SARS-CoV-2 in asymptomatic patients, published in a non-English language, or do not have full-text access.

2.3. Data Extraction and Analysis

The studies included in this systematic review were analyzed two times by the same individual to ensure accurate capture of the information. The analyzed data included the incidence
of SARS-Cov-2 in the asymptomatic COVID-19 patients, incidence of COVID-19 infection, routes of transmission, laboratory diagnostic tests, laboratory results, as well as CT scan findings.
Figure 1. Flow diagram of the search strategy and article selection.
3. Results

3.1 Search findings

The search yielded 505 studies, of which 370 citations remained after removing duplicates (Figure 1). After screening the titles, abstracts, and keywords, 312 citations were excluded. The removed citations included irrelevant studies. The remaining 67 citations were screened against the eligibility criteria. Of these, one study was removed due to the unavailability of full-text access. Furthermore, three studies were removed two for being published in languages other than English with no English abstract. The remaining 63 studies were included in this study for further analysis, and they consisted of letters to the editor, commentaries, case reports as well as research studies.

3.2 Epidemiological findings

The reviewed studies covered SARS-CoV-2 incidence worldwide. Country-wise, the majority of the studies were from China \((n = 44)\) and included different provinces such as Wuhan, Shenzhen, Guangzhou, Beijing, Shanghai, Hunan, Nanjing, Guangdong, Anhui, Hubei, Zhejiang, Jinan, and Hefei (Table 1). The remaining studies were published in Japan \((n = 2)\), Italy \((n = 3)\), Germany \((n = 1)\), Iran \((n = 2)\), and USA \((n = 6)\), which included studies from Texas, Washington, and New York. However, there was a lack of SARS-CoV-2 epidemiological studies from several countries worldwide, tracing the actual incidence of COVID-19, especially in asymptomatic patients.

Looking at all the included studies with a large sample size \((n>1000)\) cases), these studies (Table 1, highlighted with bold text) estimated that percentage of people contracting SARS-CoV-2 and are likely to be asymptomatic range from \((1.2-12.9\%)\). However, the other studies with a smaller sample size \((n<1000)\) reported a much higher incidence and indicated that up to \(87.9\%\) of COVID-19 infected individuals could be asymptomatic (Table 1). Most of these estimates were based on RT-PCR results. On the other hand, the estimated seroprevalence of antibodies to SARS-CoV-2 was reported to be higher. For instance, a study that was performed on 2,857 blood donors from Rio de Janeiro showed 23.7\% of IgM positive cases, 11.4\% of IgG positive cases,
while both IgM and IgG was detected in 64.9% [16]. This is could due to the limitation of the nasal swab since the PCR diagnostic could be negative though antibody detection is positive. In fact, this finding was reported in a study where four subjects out of 317 asymptomatic participants had negative PCR diagnostic, while antibody testing was positive [17]. Therefore, relying only on molecular testing could significantly underestimate the seroprevalence SARS-CoV-2, especially in asymptomatic individuals.
4. Discussion

The spread of COVID-19 is an emerging condition with pandemic potential that threatens all countries. Over the last four months, more than three million cases of COVID-19 have been confirmed worldwide. Numerous epidemiologic investigations identified an association with respiratory droplet transmission. Yet, understanding of the transmission risk is incomplete. It worth mention that COVID-19 asymptomatic individuals may pose a significant public health threat. The majority of these patients might be unaware of their disease and, therefore, not isolate themselves or seek treatment. Consequently, unknowingly transmit the virus to others. To the best of our knowledge, this is the first systematic review study that investigated the incidence of SARS-CoV-2 in asymptomatic patients.

A total of 63 out of 505 screened studies reporting COVID-19 asymptomatic patients were included in this review. Epidemiological data, clinical laboratory results, CT image findings, as well as the medical and contact history of the patient are critical knowledge that should be carefully studied when a new infectious disease emerged [59]. Although asymptomatic patients with SARS-CoV-2 were uncommon, studies showed that the prevalence of SARS-CoV-2 in asymptomatic patients is underestimated and might increase. For instance, a review paper showed the rate of asymptomatic individuals with the Middle East Respiratory Syndrome coronavirus (MERS-CoV) ranged from 0% to 28.6% [60]. Besides, it was reported that 75% of COVID-19 infected individuals could be asymptomatic [55].

COVID-19 infection ranges from asymptomatic to severe respiratory distress. Yet, clinically is shows a milder infection in children, and many studies reported children patients with asymptomatic COVID-19 infection. For instance, a study in China (Guangzhou) reported an asymptomatic 3-years old male who tested positive for SARS-CoV-2, yet, had normal lymphocyte
counts and chest CT images [19]. Similarly, a study reported in China (Wuhan) showed a 3-years old male asymptomatic patient with positive RT-PCR for SARS-CoV-2 and normal lymphocyte counts and chest CT images [20]. It is unknown yet the reason of having a benign clinical course and low incidence of COVID-19 in children compared to adults. A proposed hypothesis suggested that it might be due to the low expression of ACE2 receptors, high plasticity of their immune system, or to the exposure of other coronaviruses which are generally common in kids [61, 62]. Besides, children may play a major role in community-based viral transmission. For instance, it was reported that viral shedding in the stool sample could persist for several weeks after diagnosis [63, 64]. Consequently, it poses a threat of viral transmission through the fecal-oral route, particularly for infants and children who are not toilet trained. Most of the reported COVID-19 cases in children were due to close contact with family members with SARS-CoV-2 infection (Table 1). Many experts believe that undetermined asymptomatic cases of COVID-19 infection could be an important source of contagion [41]. Therefore, the early identification of the asymptomatic cases, as well as monitoring and tracing close contact, could help in mitigating the spread of COVID-19 infection.

Another factor that increases the asymptomatic rate of COVID-19 is the inaccuracy of diagnostic testing. For instance, a recent article highlighted key important steps to be considered when designing seroprevalence studies, as well as experts’ opinion on the recent studies. A major concern raised about the recently published results was the type of antibody test used since most of them inaccurate to support the conclusions [65]. It was reported that the manual ELISA kits are subject to cross-reaction with other coronaviruses such as SARS-CoV-1 and MERS-CoV [10]. This depends on the type of antibody or antigen used to coat the plates. For instance, a recent study used previously developed ELISA method based on bat SARS-CoV Rp3 N protein since it does
not cross-react with other human coronaviruses except SARS-CoV [66]. The method successfully detected IgM and IgG antibodies against SARS-CoV-2 in early cases of COVID-19. Yet, various studies, such as the studies included in this review, used Chinese manufactured tests kit that are not approved by Chinese authorities or the US Food and Drug Administration (FDA). Besides, until to date, a seroprevalence population-based study was carried in Santa Clara County, USA and suggested that over 30% of positive cases are missed by the PCR test and results in an underestimation of the incidence. The most significant implication of their findings is that the true infection rate is much higher than the reported number of cases. For instance, the study showed that the infection was 50 to 85-fold higher than confirmed positive cases by PCR [67]. Besides, although most of the included articles in this study used RT-PCR to confirm asymptomatic cases, no serological or other tests were performed to accurately estimate the incidence of SARS-CoV-2 in asymptomatic patients. In other words, PCR is considered the gold standard for diagnosis. Yet, if the sample was collected after 14 weeks or more after infection, the viral genome/antigen might not be detected. Therefore, it could underestimate the prevalence of the infection.

Besides, some of the included studies reported that the patients were positive for SARS-CoV-2 IgG, which suggested that the patient was an asymptomatic SARS-CoV-2 carrier. The differential use of serology for confirming acute infection is not appropriate without the additional collaboration of results. Therefore, combining both molecular and serological testing would be the best approach to accurately estimate the prevalence of COVID-19 infection, especially if the patient is at later stages of the infection and does not show symptoms [68].

Although governments in many countries are planning to conduct largescale seroprevalence surveys, many laboratories try to rely on well-established and validated lab tests, rather than rapid tests. The latter is based on blood collected from finger pricks to detect SARS-
CoV-2 antibodies. Yet, the test performance and efficacy are not up to the required level, and many false results were detected. Both specificity and sensitivity are essential in detecting SARS-CoV-2 to prevent false positive and negative results. It is not reliable to examine the test performance and efficacy of rapid tests based on finger-prick blood compared to the ELISA test, which utilizes collect venous blood. Consequently, preventing the underestimation of asymptomatic COVID-19 infection rate.

Such positive cases may contribute to the silent spread of the virus. Yet, one of the significant limitations of many studies reporting asymptomatic cases is the difficulty of differentiating between asymptomatic or pre-symptomatic, who are asymptomatic at the time of testing and later on they developed symptoms. Citing data from China WHO officials said on April 1 “some cases of asymptomatic carriers have been confirmed by finding and testing people who were in close contact with COVID-19 patients. For those who tested positive without symptoms, follow-up exams confirmed that about 25% continued to show no signs”. For instance, a clinical study with a small sample size from china, done in March 2020, followed up 24 asymptomatic positive PCR patients, 60% of them were pre-symptomatic and showed COVID-19 symptoms after 1-3 weeks [31]. More follow-up studies should be done to determine whether these cases continue to be asymptomatic or eventually develop symptoms. Whether these asymptomatic or pre-symptomatic individuals can spread the infection, a question remained to be answered with further follow-up studies.
5. Conclusion

COVID-19 is a new infectious disease that infected more than three million people in many countries all over the world. The severity and clinical manifestation of COVID-19 varies, and some individuals were reported as asymptomatic. Based on the results of this study, many of the COVID-19 infected cases show no symptoms, and that the infection could be transmitted during the incubation period. Consequently, asymptomatic patients are considered carriers and a potential source of infection to the community. Therefore, additional research studies on the epidemiological significance of COVID-19 asymptomatic cases are required.

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References

1. Fauci, A.S., N.A. Touchette, and G.K. Folkers, *Emerging infectious diseases: a 10-year perspective from the National Institute of Allergy and Infectious Diseases.* Emerging infectious diseases, 2005. 11(4): p. 519-525.

2. Mousavizadeh, L. and S. Ghasemi, *Genotype and phenotype of COVID-19: Their roles in pathogenesis.* Journal of Microbiology, Immunology and Infection, 2020.

3. WHO, *Coronavirus disease (COVID-19) Pandemic.* 2020.

4. Khailany, R.A., M. Safdar, and M. Ozaslan, *Genomic characterization of a novel SARS-CoV-2.* Gene Reports, 2020: p. 100682.

5. Song, Z., et al., *From SARS to MERS, Thrusting Coronaviruses into the Spotlight.* Viruses, 2019. 11(1).

6. Parreira, R., *Laboratory Methods in Molecular Epidemiology: Viral Infections.* Microbiol Spectr, 2018. 6(6).

7. Wikramaratna, P., et al., *Estimating false-negative detection rate of SARS-CoV-2 by RT-PCR.* medRxiv, 2020.

8. Breslin, N., et al., *COVID-19 infection among asymptomatic and symptomatic pregnant women: Two weeks of confirmed presentations to an affiliated pair of New York City hospitals.* Am J Obstet Gynecol MFM, 2020: p. 100118.

9. Qin, C., et al., *18 F-FDG PET/CT findings of COVID-19: a series of four highly suspected cases.* European Journal of Nuclear Medicine and Molecular Imaging, 2020: p. 1-6.

10. Al Kahlout, R.A., et al., *Comparative serological study for the prevalence of anti-MERS coronavirus antibodies in high- and low-risk groups in Qatar.* Journal of immunology research, 2019. 2019.

11. Amanat, F., et al., *A serological assay to detect SARS-CoV-2 seroconversion in humans.* Nature medicine, 2020: p. 1-4.

12. He, D., et al., *The relative transmissibility of asymptomatic COVID-19 infections among close contacts.* International Journal of Infectious Diseases, 2020. 94: p. 145-147.

13. London School of Hygiene and Tropical Medicine. *Almost 75% of people on board Diamond Princess with COVID-19 may have been asymptomatic.* 2020 16/6/2020]; Available from: https://www.lshtm.ac.uk/newsevents/news/2020/almost-75-people-board-diamond-princess-covid-19-may-have-been-asymptomatic.

14. Mizumoto, K., et al., *Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020.* Eurosurveillance, 2020. 25(10).

15. Chen, Y., et al., *The epidemiological characteristics of infection in close contacts of COVID-19 in Ningbo city.* Chinese Journal of Epidemiology, 2020. 41(0): p. 0-0.

16. Amorim Filho, L., et al., *Seroprevalence of IgG and IgM anti-SARS-CoV-2 among voluntary blood donors in Rio de Janeiro, Brazil.*

17. Korth, J., et al., *SARS-CoV-2-specific antibody detection in healthcare workers in Germany with direct contact to COVID-19 patients.* Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology, 2020. 128: p. 104437-104437.

18. Ling, Z., et al., *Asymptomatic SARS-CoV-2 infected patients with persistent negative CT findings.* European Journal of Radiology, 2020. 126.

19. Pan, X., et al., *Asymptomatic cases in a family cluster with SARS-CoV-2 infection.* The Lancet Infectious Diseases, 2020. 20(4): p. 410-411.

20. Li, C., et al., *Asymptomatic and Human-to-Human Transmission of SARS-CoV-2 in a 2-Family Cluster, Xuzhou, China.* Emerging infectious diseases, 2020. 26(7).
21. Chan, J.F.-W., et al., *A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster*. The Lancet, 2020. 395(10223): p. 514-523.

22. Meng, H., et al., *CT imaging and clinical course of asymptomatic cases with COVID-19 pneumonia at admission in Wuhan, China*. Journal of Infection, 2020.

23. Luo, Y., et al., *Asymptomatic SARS-CoV-2 Infection in Household Contacts of a Healthcare Provider, Wuhan, China*. Emerg Infect Dis, 2020. 26(8).

24. Ouyang, W., et al., *Alert to Potential Contagiousness: A Case of Lung Cancer with Asymptomatic SARS-CoV-2 Infection*. J Thorac Oncol, 2020.

25. Jiang, X., et al., *Asymptomatic SARS-CoV-2 infected case with viral detection positive in stool but negative in nasopharyngeal samples lasts for 42 days*. J Med Virol, 2020.

26. Wang, X., et al., *Clinical characteristics of non-critically ill patients with novel coronavirus infection (COVID-19) in a Fangcang Hospital*. Clin Microbiol Infect, 2020.

27. Wang, Z., et al., *Household transmission of SARS-CoV-2*. Journal of Infection, 2020.

28. An, P., et al., *Asymptomatic Patients with Novel Coronavirus Disease (COVID-19)*. Balkan medical journal, 2020.

29. Zhang, Y.H., et al., *[2019 novel coronavirus infection in a three-month-old baby]*. Zhonghua Er Ke Za Zhi, 2020. 58(3): p. 182-184.

30. Zhou, X., et al., *Follow-up of asymptomatic patients with SARS-CoV-2 infection*. Clinical Microbiology and Infection, 2020.

31. Hu, Z., et al., *Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China*. Science China Life Sciences, 2020.

32. Mao, Z.Q., et al., *The enlightenment from two cases of asymptomatic infection with SARS-CoV-2: is it safe after 14 days of isolation?* International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases, 2020.

33. Lu, S., et al., *Alert for non-respiratory symptoms of Coronavirus Disease 2019 (COVID-19) patients in epidemic period: A case report of familial cluster with three asymptomatic COVID-19 patients*. Journal of Medical Virology, 2020.

34. Lu, D., et al., *Asymptomatic COVID-19 infection in late pregnancy indicated no vertical transmission*. J Med Virol, 2020.

35. Qiu, H., et al., *Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study*. The Lancet Infectious Diseases, 2020.

36. Huang, L., et al., *Rapid asymptomatic transmission of COVID-19 during the incubation period demonstrating strong infectivity in a cluster of youngsters aged 16-23 years outside Wuhan and characteristics of young patients with COVID-19: A prospective contact-tracing study*. J Infect, 2020.

37. Ma, Y., et al., *Characteristics of asymptomatic patients with SARS-CoV-2 infection in Jinan, China*. Microbes and Infection, 2020.

38. Dong, Y., et al., *Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China*. Pediatrics, 2020.

39. Luo, S.H., et al., *A confirmed asymptomatic carrier of 2019 novel coronavirus (SARS-CoV-2)*. Chinese medical journal, 2020.

40. Ye, F., et al., *Delivery of infection from asymptomatic carriers of COVID-19 in a familial cluster*. Int J Infect Dis, 2020.

41. Day, M., *Covid-19: four fifths of cases are asymptomatic, China figures indicate*. BMJ (Clinical research ed.), 2020. 369: p. m1375.
42. Yongchen, Z., et al., Different longitudinal patterns of nucleic acid and serology testing results based on disease severity of COVID-19 patients. Emerging Microbes & Infections, 2020(just-accepted): p. 1-14.

43. Surveillances, V., The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19)—China, 2020. China CDC Weekly, 2020. 2(8): p. 113-122.

44. Pan, Y., et al., Epidemiological and clinical characteristics of 26 asymptomatic SARS-CoV-2 carriers. J Infect Dis, 2020.

45. Jiang, X.L., et al., Transmission potential of asymptomatic and paucisymptomatic SARS-CoV-2 infections: a three-family cluster study in China. J Infect Dis, 2020.

46. Bai, Y., et al., Presumed Asymptomatic Carrier Transmission of COVID-19. Jama, 2020.

47. Imai, K., et al., Clinical evaluation of an immunochromatographic IgM/IgG antibody assay and chest computed tomography for the diagnosis of COVID-19. Journal of Clinical Virology, 2020: p. 104393.

48. McGinnis, G.J., et al., Rapid Detection of Asymptomatic COVID-19 by CT Image-Guidance for Stereotactic Ablative Radiotherapy. J Thorac Oncol, 2020.

49. Arons, M.M., et al., Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility. N Engl J Med, 2020.

50. Kimball, A., et al., Asymptomatic and Presymptomatic SARS-CoV-2 Infections in Residents of a Long-Term Care Skilled Nursing Facility - King County, Washington, March 2020. MMWR Morb Mortal Wkly Rep, 2020. 69(13): p. 377-381.

51. Gandhi, M., D.S. Yokoe, and D.V. Havlir, Asymptomatic Transmission, the Achilles’ Heel of Current Strategies to Control Covid-19. N Engl J Med, 2020.

52. Mayor, S., Covid-19: Nine in 10 pregnant women with infection when admitted for delivery are asymptomatic, small study finds. BMJ (Clinical research ed.), 2020. 369: p. m1485.

53. Albano, D., et al., INCIDENTAL FINDINGS SUGGESTIVE OF COVID-19 IN ASYMPTOMATIC PATIENTS UNDERGOING NUCLEAR MEDICINE PROCEDURES IN A HIGH PREVALENCE REGION. J Nucl Med, 2020.

54. Poli, P., et al., Asymptomatic case of Covid-19 in an infant with cystic fibrosis. Journal of Cystic Fibrosis, 2020.

55. Day, M., Covid-19: identifying and isolating asymptomatic people helped eliminate virus in Italian village. BMJ (Clinical research ed.), 2020. 368: p. m1165.

56. Rothe, C., et al., Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany. The New England journal of medicine, 2020. 382(10): p. 970-971.

57. Asadollahi-Amin, A., et al., Lung Involvement Found on Chest CT Scan in a Pre-Symptomatic Person with SARS-CoV-2 Infection: A Case Report. Trop Med Infect Dis, 2020. 5(2).

58. Samsami, M., et al., COVID-19 Pneumonia in Asymptomatic Trauma Patients; Report of 8 Cases. Arch Acad Emerg Med, 2020. 8(1): p. e46.

59. Rodriguez-Morales, A.J., et al., Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. Travel medicine and infectious disease, 2020: p. 101623-101623.

60. Al-Tawfiq, J.A. and P. Gautret, Asymptomatic Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection: extent and implications for infection control: a systematic review. Travel medicine and infectious disease, 2019. 27: p. 27-32.

61. Cruz, A.T. and S.L. Zeichner, COVID-19 in children: initial characterization of the pediatric disease. Pediatrics, 2020.

62. Jia, H.P., et al., ACE2 receptor expression and severe acute respiratory syndrome coronavirus infection depend on differentiation of human airway epithelia. J Virol, 2005. 79(23): p. 14614-21.

63. Cai, J., et al., A Case Series of children with 2019 novel coronavirus infection: clinical and epidemiological features. Clinical Infectious Diseases, 2020.
64. Xiao, F., et al., *Evidence for gastrointestinal infection of SARS-CoV-2*. Gastroenterology, 2020. 158(6): p. 1831-1833. e3.

65. Offord, C. *How (Not) to Do an Antibody Survey for SARS-CoV-2*. 2020 1/5/2020; Available from: https://www.the-scientist.com/news-opinion/how-not-to-do-an-antibody-survey-for-sars-cov-2-67488?utm_campaign=TS_OTC_2020&utm_source=hs_email&utm_medium=email&utm_content=87227297&_hsenc=p2ANqtz--OX79Py05lz3KB_wqDMHJfcVa3bRgNFKwz-ImL1fxCEQ_f2wMR1zxNctcNqGZAYwBFm8PrGdjQib1gWD3oZ0NWpLCEaw&_hsmi=87227297.

66. Zhou, P., et al., *A pneumonia outbreak associated with a new coronavirus of probable bat origin*. Nature, 2020. 579(7798): p. 270-273.

67. Bendavid, E., et al., *COVID-19 Antibody Seroprevalence in Santa Clara County, California*. medRxiv, 2020: p. 2020.04.14.20062463.

68. Younes, N., et al., *Challenges in Laboratory Diagnosis of the Novel Coronavirus SARS-CoV-2*. Viruses, 2020. 12(6): p. 582.
| Country   | Type of the study | Total case number | Number of asymptomatic patients | Age/mean age | Gender | Clinical features | Chest CT findings | Reference |
|-----------|-------------------|-------------------|---------------------------------|--------------|--------|------------------|-------------------|-----------|
| China     | Correspondence    | 295               | 45 (15.2%)                      | -            | -      | RT-PCR positive for SARS-CoV-2. 30 patients started to show few clinical symptoms (after 3-14 days). | Persistent negative CT findings. 15 patients had CT scan positive (after 3–6 days) for COVID-19 pneumonia. | [18]     |
| (Guangzhou) |                |                   |                                 |              |        |                  |                   |           |
| China     | Correspondence    | 5                 | 2 (40%)                         | 3-years old male | 1 male | Normal lymphocyte counts. | Normal chest CT images | [19]     |
| (Guangzhou) |                |                   | 33-years old woman              |              |        |                  |                   |           |
| China     | Research letter   | -                 | 7                               | Age range: 21-56-year-old | 4 males 3 females | Positive for SARS-CoV-2 by RT-PCR | The 56-year old patient showed multiple ground-glass-like high-density shadows on both lungs. | [20]     |
| (Guangzhou) |                |                   |                                 |              |        |                  |                   |           |
| China     | Research article  | 5                 | 1 (20%)                         | 10-year-old  | Male   | RT-PCR positive for SARS-CoV-2. Lymphopenia, thrombocytopenia, and increased | Ground-glass lung opacities | [21]     |
| (Guangdong) | (familial cluster) |                   |                                 |              |        |                  |                   |           |
| Country   | Type                | Age | Gender | Symptoms                                                                 | Imaging Features                                                                 | Reference |
|-----------|---------------------|-----|--------|--------------------------------------------------------------------------|--------------------------------------------------------------------------------|-----------|
| China (Wuhan) | Research article | 58  | 26 male and 32 females | After a short-term follow-up, 16 patients (27.6%) presented symptoms with lower lymphocyte count and higher CRP, mainly including fever, cough, and fatigue | Ground glass opacity (GGO) in 55 (94.8%) with peripheral in 44 (75.9%) distribution, unilateral location in 34 (58.6%) and mostly involving one or two lobes in 38 (65.5%) | [22] |
| China (Wuhan) | Research letter | 5   | 2 females | Throat swab specimens tested for SARS-CoV-2 were positive by PCR except for one patient, who tested negative on 4 consecutive throat swab specimen tests for SARS-CoV-2 but whose stool specimen was positive for SARS-CoV-2 | Abnormal chest CT scans showing features consistent with SARS-CoV-2 infection in one of the twins | [23] |
| China (Wuhan) | Case report        | 56  | Male   | RT-PCR of SARS-CoV-2 and IgM were negative, while his serological IgG antibody to SARS-CoV-2 were positive | CT scan was negative | [24] |
| Country        | Type              | N    | Positive RT-PCR for SARS-CoV-2 | CT findings                                      | Reference |
|---------------|------------------|------|-------------------------------|-------------------------------------------------|-----------|
| China (Wuhan) | Case report       | 1    | No clinical symptoms or decreased lymphocyte count. Positive for SARS-CoV-2 IgG. | Normal chest CT image | [25] |
| China (Wuhan) | Research article  | 1012 | Positive RT-PCR for SARS-CoV-2. During follow up from admission to the end, fever occurred in 6, with cough in 8, myalgia in 3, dyspnoea in 2, nasal congestion in 1, and abdominal pain in 1. 14 of 1012 patients (1.4%) remained asymptomatic during the whole follow up | Small patchy opacities (38.7%) and ground-glass opacities (55.4%) | [26] |
| China (Wuhan) | Research article  | 155  | Positive RT-PCR for SARS-CoV-2 | CT showed no signs of viral pneumonia | [27] |
| China (Hubei) | Letter to the Editor | 25  | 16 of the patients recovered without any symptoms. Nine patients developed a mild cough and/or other symptoms. | Two-thirds of the patients had involvement of a single lobe, and two-thirds had only a ground-glass density shadow. The least common CT finding was | [28] |
interlobular septal thickening
| Country (Province) | Type of Report | Total | Percentage | Description |
|--------------------|----------------|-------|------------|-------------|
| China (Hubei)      | Case Report    | 1     | 100%       | Male, no nasal congestion and snot, no cough, no shortness of breath, no cyanosis, no nausea, vomiting, and diarrhea, good mental response, and crying sound. All blood, liver, and kidney tests were normal. RT-PCR positive for SARS-CoV-2. Chest X-ray showed a slightly thicker texture of the right lung. |
| China (Shanghai)   | Letter to the Editor | 328 | 13 (3.9%) | Mean age was 51.8 years (range: 25-80 years). 6 males and 7 females. Leucocytes were below the normal range in two patients (15.4%). Ten patients (76.9%) had differing degrees of elevation of the ESR. Liver function, renal function, and coagulation function were within the normal range. No fever. Positive RT-PCR for SARS-CoV-2. A patient has developed signs, such as pneumonia on chest CT. |
| China (Nanjing)    | Research Article | 24 screened due to close contact with COVID-19 patients | 8 males and 16 females. Five cases (20.8%) developed symptoms (fever, cough, fatigue, etc.) during hospitalization. 5 (20.8%) presented stripe shadowing in the lungs. Twelve (50.0%) cases showed typical CT images of the ground-glass chest. |
### Cases without symptoms after diagnosis (n=19)

- Remaining 7 had no symptoms during hospitalization.
- 4 patients had C-reactive protein level ≥10 mg/liter

### China (Hunan)

| Research article | 78 | 2 (2.5%) | 36-year-old Males | Positive RT-PCR for SARS-CoV-2: Patient 1: Laboratory evaluation showed an elevated myoglobin, ALT, and uric acid level. Patient 2: Laboratory tests including blood routine test, erythrocyte sedimentation rate (ESR), C-reactive protein and three items of myocardial enzyme spectrum were all negative | Chest CT scan was negative for both |
|------------------|----|----------|-------------------|----------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------|
| 19-year-old      |    |          |                   |                                                                                                               |                                                                          |

### China (Guangdong)

| Short communication | - | 3 | Patient 1: not determined | No fever, cough, and expectoration during hospitalization. | Patient 1: multiple patchy and ground glass shadows with uneven density and fuzzy edge in the outer zone of both lungs |
|---------------------|---|---|--------------------------|------------------------------------------------------------|-------------------------------------------------------------------------|
|                     |   |   | Patient 2: female        |                                                             |                                                                         |
|                     |   |   | Patient 3: male          |                                                             |                                                                         |
| Location | Type of Study | Total | Positive Cases (%) | Age Range | Gender | Clinical Symptoms | Imaging Findings | Reference |
|----------|---------------|-------|---------------------|-----------|--------|------------------|-----------------|----------|
| China (Anhui) | Short communication | 1 | - | 22-year-old pregnant woman | Female | No cough, dyspnea, or diarrhea was noted. | CT reexamination showed a small amount of pleural effusion on both sides | [34] |
| China (Zhejiang) | Research article (observational cohort study) | 36 | 10 (28%) | Age range: 0–16 years with mean 8.3 years | - | Decreased lymphocytes, high levels of procalcitonin, D-dimer, and creatine kinase MB | - | [35] |
| China (Hefei) | Prospective contact-tracing study | - | 1 | 22-year-old | Male | - | Lung infiltrates | [36] |
| China (Jinan) | Research article | 47 | 11 (23.4%) | Median age: 23 years, ranging from 1 to 60 years | 6 males 7 females | Pharyngeal swab COVID-19 nucleic acid was positive. The blood cell test results showed that 27.3% (3/11) had decreased white blood cell and 36.4% (4/11) had increased lymphocyte count. High D-dimer levels, C-reactive protein and ESR. | 4 (36.4%) showed bilateral involvement and 3 (27.3%) showed unilateral involvement | [37] |
| China | Research article | 2143 | 94 (12.9%) | Median age: 7 years (range: 2-13) | - | No clinical symptoms and signs, while the 2019-nCoV nucleic acid test is positive. | The chest imaging is normal. | [38] |
| China | Clinical observations | 83 | 1 (1.2%) | 50-year old | Female | Persistent positivity of the virus nucleic acid in her throat swabs and anal swabs for at least 17 days suggested that she was very likely a healthy carrier. |
|---|---|---|---|---|---|---|
| China | Research article (familial cluster) | 5 | 2 (40%) | 28-year-old | Males | Patients were afebrile without any clinical signs. On days 3 through 5 of hospitalization, the 23-years old man developed fever and cough symptoms. Other laboratory examinations showed increasing C-reactive protein. Chest CT images showed no abnormalities. On days 3 through 5 of hospitalization, the 23-years old man chest CT scans showed ground-glass opacities in the lungs. |
| China | News journal article | 166 | 130 (78%) | - | - | - |
| China | Research article | 21 | 5 (20.8%) | 25 (10–61) years | 3 males 3 females | RT-PCR positive for SARS-CoV-2. Only 1 case generated SARS-CoV-2 specific antibody responses. |
| China | Research article | 72,314 | 889 (1.2%) | Most were aged 30–79 years | - | Positive viral nucleic acid test results but without any COVID19 symptoms |
| Country | Study Type | Sample Size | Median Age | Gender | Test Result | Observations | Reference |
|---------|------------|-------------|------------|--------|-------------|--------------|-----------|
| China  | Research article (hospitalized patients) | 26 | 29.5 years | 16 males, 10 females | RT-PCR positive for SARS-CoV-2. C-reactive protein and lymphocytes count were normal in all patients. Three patients had reduced albumin and two patients with slightly elevated creatinine levels | Nine patients with normal CT scans, 10 patients with typical manifestations (patch-like, ground-glass opacities distributed in the extrapulmonary zone), seven patients with changes in a unilateral lung, and three patients with changes in bilateral lungs. | [44] |
| China  | Familial cluster study | 8 | 3 (37.5%) | Female | RT-PCR positive for SARS-CoV-2. No clinical symptoms | Ground-glass opacities except in the infant | [45] |
| China  | Research letter | 6 | 1 (16.6%) | Female | RT-PCR positive for SARS-CoV-2. No elevated temperature measured or self-reported fever and no gastrointestinal or respiratory symptoms, including cough and sore throat, reported or observed by the physicians. | Normal chest CT image | [46] |
| Country (Region) | Document Type | Participants | Age Range | Gender | SARS-CoV-2 Diagnosis | Findings/Notes |
|-----------------|---------------|--------------|-----------|--------|----------------------|---------------|
| Japan (Cruise Ship) | Rapid communication | 634 | 328 (51.7%) | Female: age ranged 0–59 years. Males: not determined | SARS-CoV-2 positive by PCR | - | [14] |
| Japan | Research article | 112 | 38 (33.9%) | Age ranged (61.5–73.75) years | RT-PCR positive for SARS-CoV-2. IgM was detected in 27.8%, of the specimens collected and IgG was detected in 3.3%, Chest CT showed abnormal lung findings consistent with the radiographic features of COVID-19 in 22 (57.9%). | [47] |
| USA (Texas) | Case report | - | 1 | 63-year-old | Female | SARS-CoV2 nasopharyngeal swab RT-PCR resulted positive. CT-simulation scan revealed interval development of new multifocal ground-glass opacities of the lungs | [48] |
| USA (Washington) | Research article | 48 | 27 (56%) | Age mean 75.9 | 14 females 13 males | real-time reverse-transcriptase polymerase chain reaction (rRT-PCR) to test all samples. 15 reported no symptoms and 12 reported only stable chronic symptoms. Fifteen (56%) residents who were asymptomatic | - | [49] |
| Location         | Type                  | Count | Percentage | Details                                                                                     |
|------------------|-----------------------|-------|------------|--------------------------------------------------------------------------------------------|
| USA (Washington) | Synopsis              | 23    | 13 (57%)   | Age mean 80.7; documented cognitive impairment; The reverse transcription–polymerase chain reaction (RT-PCR) testing cycle threshold (Ct) values indicated large quantities of viral RNA. | [50] |
| USA (Washington) | Editorial             | 48    | 27 (56%)   | RT-PCR positive for SARS-CoV-2                                                             | [51] |
| USA (New York)   | News journal article  | 33    | 29 (87.9%) | Pregnant Females; RT-PCR positive for SARS-CoV-2                                           | [52] |
| USA (New York)   | Case series           | 43    | 14 (32.6%) | Maternal age ranged from 20 to 39 years with a mean age of 26.9 years old; PCR-confirmed SARS-CoV-2; 8 patients developed fever ranging from 37.9°C to 39.2°C during admission in the hospital. | [8]  |
| Italy (Brescia)  | Report (Incidental Findings) | 7    | Median age 64.6 years old (Range: 55-79) years; 2 males, 5 females; RT-PCR positive for SARS-CoV-2; Patient 3: chest CT showed a suspicious retrosternal lymph node but no lung pathology. | [53] |
Patient 5: Thoracic CT displayed several ground-glass opacities in the right lung.

Patient 7: CT showed diffuse interstitial pneumonia with peripheral ground-glass opacities.

| Italy Case report | - | 1 | 1 month | Male | Real-time PCR confirmed infection | - | [54] |
|-------------------|----|---|---------|------|-----------------------------------|---|----|
| Italy News journal article | 3300 | 90 (2.7%) | - | - | RT-PCR positive for SARS-CoV-2 | - | [55] |
| Germany Correspondence | - | 4 | Patient 1: 33-year-old | Patient 1: male | RT-PCR positive for SARS-CoV-2 | - | [56] |
| Iran (Tehran) Case report | - | 1 | 44-year-old | Male | RT-PCR positive for SARS-CoV-2 | Patchy ground-glass opacity in the upper lobe of the right lung | [57] |
| Iran | Case report | multiple trauma patients admitted to hospital | 8 | $49.71 \pm 13.13$ (range: 34–67) years | 62.5% male | None of the patients had COVID-19 symptoms at the time of admission to the hospital. RT-PCR positive for SARS-CoV-2. Laboratory results showed 4 (50%) patients with slight increase in C-reactive protein | Pneumonia in chest CT scan | [58] |