International Journal of Research in Medical Sciences
Verma N et al. Int J Res Med Sci. 2021 Jan;9(1):310-316
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20205862

Review Article

New challenge of asymptomatic infections from COVID-19: current scenario

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Received: 30 October 2020
Accepted: 08 December 2020

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ABSTRACT

Since the outbreak of coronavirus 2019 (COVID-19) disease in China, late December 2019, it took a substantial detriment and challenges for more than 200 countries worldwide. Recently with the upcoming insights about etiology of the virus, there is increasing evidence that many patients with COVID-19 are asymptomatic or they have only mild symptoms, but they act as carrier and are able to transmit the virus to others. There are technical difficulties in screening for these asymptomatic infections, which makes it even more challenging for any nation to control this epidemic. This article reviews entry & replication of the virus, pathogenesis, asymptomatic infections, dissemination, prevention, control & treatment in asymptomatic infections with COVID-19, expecting it would be helpful for early prevention and containment of this severe public health threat worldwide.

Keywords: COVID-19, Current scenario, Asymptomatic infections

INTRODUCTION

Coronaviruses (CoVs) are large family of viruses, several of which causes respiratory diseases in humans, from common cold to more rare and serious life-threatening diseases such as the Severe Acute Respiratory Syndrome (SARS) and the Middle East respiratory syndrome (MERS), both of which have high mortality rates and were detected for the first time in 2003 and 2012, respectively.[1] The novel coronavirus (SARC-COV-2) pneumonia originated to spread in Wuhan, China in late December 2019 where a number of patients have been admitted to the hospital with an initial diagnosis of pneumonia, which has rapidly evolved into a pandemic. On February 11, 2020, world health organization (WHO) officially named this novel virus as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The International Committee on Taxonomy of Viruses, and the associated disease was named it as coronavirus disease 2019 (COVID-19).[2] Currently this outbreak, COVID-19 has taken a substantial detriment and challenges to more than 200 countries and regions worldwide.[3,4] COVID-19 manifests with a non-specific respiratory symptom of variable severity and may require advanced respiratory support.[5] As on 23rd August 2020, more than 23,397,619 cases have been confirmed of COVID-19 worldwide with cumulative deaths have exceeded 808,942 and patients recovered are 15,918,353. While in India, more than 3,049,855 confirmed of COVID-19 cases with cumulative deaths have exceeded 56,875 & patients recovered are 2,281,982 (6- 23rd August 2020; worldometer 2020; United Nations Geoscheme). COVID-19 initially has been divided into five types: mild, moderate, severe, clinical deterioration and critical cases (WHO: use of chest imaging in COVID-19: a rapid advice guide; 11 June 2020). However, with the global outbreak of coronavirus, there is increasing evidence that many infections of COVID-19 are asymptomatic cases which act as carriers and can transmit the virus to others. Asymptomatic infections

refer to the positive detection of nucleic acid of SARS-CoV-2 in patient samples by reverse transcriptase polymerase chain reaction (RT-PCR), but have no typical clinical symptoms or signs, and no apparent abnormalities in images, including lung computed tomography (CT) (7- WHO. Laboratory diagnostics for novel coronavirus. 2020). The clinical characteristics of asymptomatic infections and other types of COVID-19 are shown in Table 1. Early detection of an infected person and tracking off the route of transmission are the key points to control COVID-19. However, most asymptomatic infections do not seek medical assistance due to no obvious clinical signs and poor prevention awareness but they act as a carrier, which contribute to the rapid spread of COVID-19 among community. Therefore, it is a great challenge for any nation to prevent and control this specific category of asymptomatic patient globally, which requires more attention worldwide.

Table 1: Clinical characteristics of asymptomatic infections and other types of COVID-19.[2,3]

Type of disease	Clinical characteristics	Rt-PCR test for COVID-19
Asymptomatic	No clinical symptoms and chest imaging findings.	Positive
Mild	Fever, cough, fatigue, anorexia, shortness of breath, myalgias, sore throat, nasal congestion, headache, gastrointestinal symptoms, loss of smell (anosmia), loss of taste (ageusia), without evidence of viral pneumonia or hypoxia. Children are less likely than adults to present with fever and mild respiratory symptoms.	Positive
Moderate	Adolescent or adult with signs of pneumonia but no signs of severe pneumonia and with oxygen saturation (spo2) ≥90% while breathing normal room air. Child with cough or with difficulty breathing and fast breathing and chest in drawing but no need of oxygen or no signs of severe pneumonia present.	Positive
Severe	Adolescent or adult with signs of severe pneumonia: fever or suspected respiratory infection, plus one of the following: respiratory rate>30 breaths/min; severe respiratory distress; or spo2 <90% while breathing normal room air. Child with cough or with difficulty breathing and at least one of the following: central cyanosis or spo2<90% while breathing normal room air; severe respiratory distress (e.g. Grunting, very severe chest in drawing); signs of pneumonia with a general danger sign: inability to breastfeed or drink, lethargy or unconsciousness, or convulsions. Other signs of pneumonia may be present, e.g. Fast breathing for age. Chest imaging showed the lesions significantly progressed>50% within 24-48 h was a severe disease.	Positive
Clinical deterioration	Abrupt worsening of hypoxia, oedema or erythema of an extremity, unexplained shortness of breath out of proportion to oxygen saturation, increased tachycardia, or for mechanically-ventilated patients: increased dead space fraction out of proportion to change in lung compliance.	Positive
Critical	Rapid progress of disease, plus any of the following: acute respiratory distress syndrome (ards), sepsis, life-threatening organ dysfunction.	Positive

Rt-PCR, reverse transcriptase-polymerase chain reaction; RR, respiratory rate; ICU- intensive care unit.

SARS-COV-2: ENTRY AND REPLICATION IN HOST CELLS

The entry of coronaviruses into a host target cells depends on binding of spike glycoprotein to the cellular receptor and priming of S protein by host cell proteases. Like SARS-CoV, SARS-CoV-2 also uses the same angiotensin-converting enzyme 2 (ACE2) as receptor for internalization and serine proteases TMPRSS2 for S protein priming.[8,9] (Zhou et al, Hoffmann et al). Similar to SARS-CoV, the extra pulmonary spread of SARS-CoV-2 may be seen due to the widespread tissue expression of the ACE2 receptor. In addition, studies revealed that the spike protein of SARS-CoV-2 exhibits 10-20 times higher affinity as compared to that of SARS-CoV.[10] (Wrapp et al). Binding of spike protein to the ACE2 receptor results in conformational changes in spike protein that leads to the fusion of viral envelop protein with host cell membrane following entry via endosomal pathway.[11,12] (Coutard et al, Matsuyama). This event is followed by the release of viral RNA into the host cytoplasm that undergoes translation and generates replicase polyproteins pp1a and pp1b that further cleaved by virus encoded proteinases into small proteins. The replication of coronavirus involves ribosomal frame shifting during the translation process and generates both genomic and multiple copies of sub genomic RNA species by discontinuous transcription that encodes for relevant viral proteins. Assembly of virion takes place via interaction of viral RNA and protein at endoplasmic reticulum (ER) and Golgi complex. These virions are subsequently released out of the cells via exocytosis (Figure 1)[9] (Hoffmann et al).

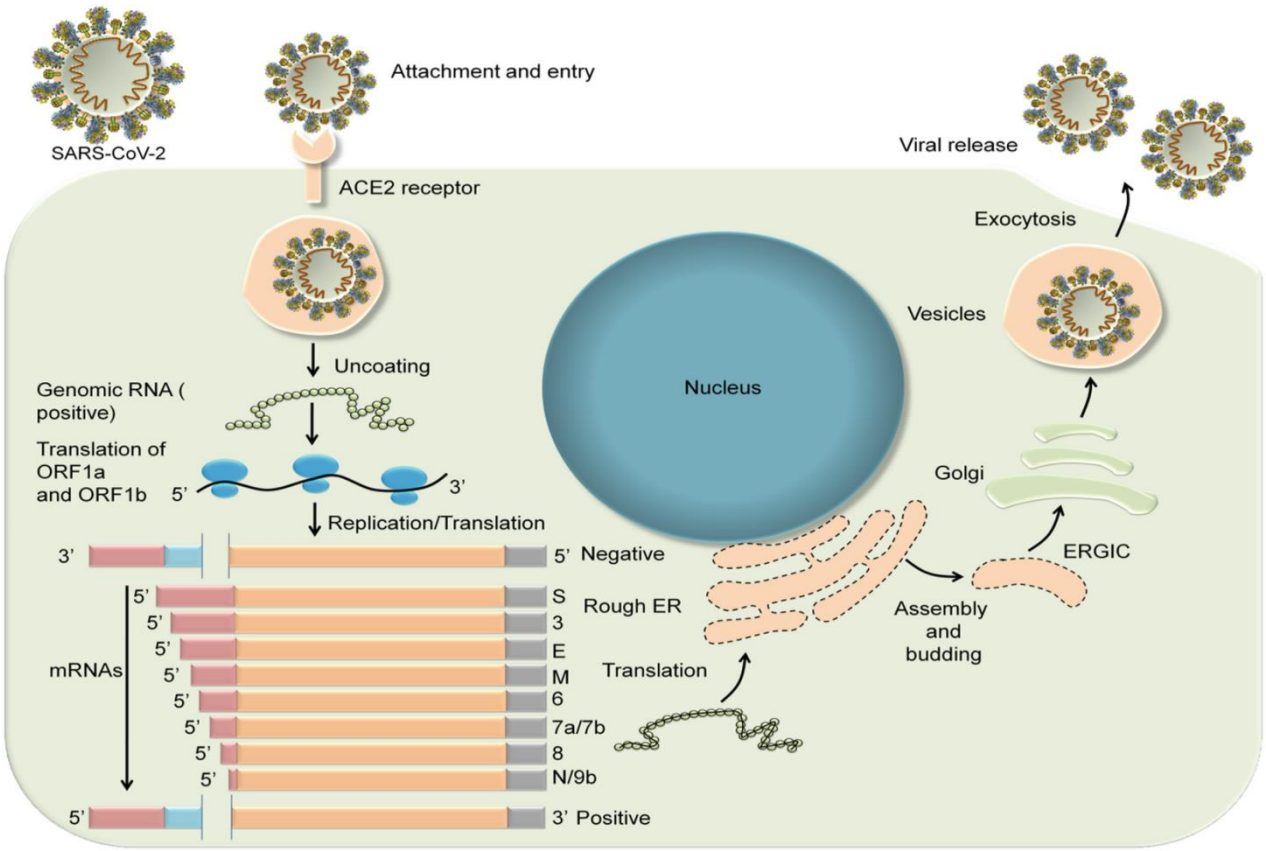

Figure 1: Entry and replication of COVID-19 in the host cell- entry of SARS-CoV-2 into host target cells depends on the binding of spike glycoprotein to the cellular receptor ACE2 for internalization.

Figure 1 describes internalization results in uncoating of viral RNA into cytoplasm that undergoes translation and generates replicase polyproteins pp1a and pp1b, which is further cleaved by virus-encoded proteinases into small proteins. The replication of SARS-CoV-2 involves ribosomal frame shifting during the translation process and generates both genomic and multiple copies of subgenomic RNA species by discontinuous transcription required for relevant viral proteins. Assembly of virion takes place via interaction of viral RNA and protein at endoplasmic reticulum (ER) and Golgi complex. These virions are subsequently released out of the cells via vesicles via exocytosis

PATHOGENESIS

The pathological findings of SARS-CoV-2 infected patient highly resemble that of SARS-CoV and MERS-CoV infected patients. Flow cytometric analysis of peripheral blood samples showed significant reduction of CD4 and CD8 T-cell counts, and their status was found to be hyper activated as higher proportion of dual positive (HLA-DR and CD38) was seen. Rapid progression of pneumonia was seen in chest X-ray images with some differences between the right and left lung. Histopathological investigation of lung biopsy showed cellular fibromyxoid exudates with bilateral diffuse alveolar damage.[13] (Xu et al). In addition, both lungs were found to exhibit interstitial mononuclear patchy inflammatory infiltrates dominated specifically by lymphocytes.[14] (Tian et al). The intra-alveolar spaces were characterized by multinucleated syncytial cells with atypical enlarged pneumocytes showing virus-induced cytopathic effect. Liver biopsy of patients infected with SARS-CoV-2 showed moderate micro vesicular steatosis and mild portal and lobular activity, suggesting that injury might have been caused by the virus or drug induced. A few interstitial mononuclear inflammatory infiltrates were observed in the heart tissue. These pathological changes may provide new insights into the pathogenesis of pneumonia induced by SARS-CoV-2 that may help clinicians to effectively deal with COVID-19 patients. However, more clinical samples should be collected, and a relative examination of ACE2 should be performed and compared for different types of COVID19 cases, as this would be helpful to explain its pathogenesis.

ASYMPTOMATIC INFECTIONS

In the early months of the coronavirus disease 2019 (COVID-19) pandemic, an iconic image has been the "proned" patient in intensive care, gasping for breath, in imminent need of artificial ventilation. This is the deadly face of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which as of 26 May 2020 had claimed

more than 348 000 lives worldwide.[15] (COVID-19 Case Tracker; 26th May 2020). But it is not the only face, because SARS-CoV-2 now seems to have a dual nature: tragically lethal in some persons and surprisingly benign in others. Asymptomatic infections have the same infectivity as symptomatic infections.[16] (Chen Y et al). Globally the likelihood that approximately 5% to 82% (14,37,38,39) (S. Tian et al, Day M, Kenji M et al, Moran Ki) Indian council of medical research (ICMR), press conference, April 20, 2020) of those infected with SARS-CoV-2 will remain asymptomatic which suggests that the virus might have greater potential than previously estimated to spread silently and deeply through human populations. Asymptomatic persons can transmit SARS-CoV-2 to others for an extended period, perhaps longer than 14 days. The absence of COVID-19 symptoms in persons infected with SARS-CoV-2 might not necessarily imply an absence of harm. The focus of testing programs for SARS-CoV-2 should be substantially broadened to include persons who do not have symptoms of COVID-19. More research with larger sample number is needed to determine the significance of subclinical lung changes visible on computed tomography scans.

Since February 2020. (Nishiura et al, Bai et al), there have been reports of persons who were infected with SARS-CoV-2 but did not develop symptoms of COVID-19.[17,18] In some cases (Zou et al, Kimball et al), the viral load of such asymptomatic persons has been equal to that of symptomatic persons, suggesting similar potential for viral transmission.[19] The prevalence of asymptomatic SARS-CoV-2 infection, however, has remained uncertain. We sought to review and synthesize the available evidence on testing for SARS-CoV-2 infection, carried out by real-time reverse transcriptase polymerase chain reaction using nasopharyngeal swabs in all studies that specified the method of testing.

The difficulty of distinguishing asymptomatic persons from those who are merely pre symptomatic is a stumbling block. To be clear, the asymptomatic individual is infected with SARS-CoV-2 but will never develop symptoms of COVID-19. In contrast, the pre symptomatic individual is similarly infected but eventually will develop symptoms. The simple solution to this conundrum is longitudinal testing—that is, repeated observations of the individual over time. We must therefore acknowledge the possibility that some of the proportions of asymptomatic persons are lower than reported.

These asymptomatic cases may play a role in the transmission and therefore pose a significant challenge to infection control. Estimates of the incidence of asymptomatic infections will clarify the epidemiological potential of COVID-19 transmission and understanding of the true universality of the disease. The ability of asymptomatic infections to spread the virus is not low, and these patients are likely to cause a new round of outbreaks. Therefore, finding asymptomatic infections is the key point for early prevention and control of COVID-19 worldwide.

The incubation period is the approximate time from the first exposure to the virus until the clinical symptoms or signs onset, and patients can also transmit the virus in this period.[20] (Gao et al). Asymptomatic infections have no special incubation due to no clinical signs. Since the viral nucleic acid positivity refers to that the virus load in samples reaches a certain limit, but the infectivity mainly depends on when the virus is in a reproductive state.[21] (Shen M et al., 2020). That is, sometimes, despite ongoing high viral loads, no live virus can be isolated, which means that viral nucleic acid positivity does not indicate infectivity.[22] (Wolfel et al). Due to the limited data from current studies, we think that it is necessary for us to be highly vigilant to asymptomatic infections.

Moreover, viral nucleic acid positivity has been reported not to be always considered, and more clinical studies are still needed to verify that. A previous study found that the median period of asymptomatic patients from viral nucleic acid positive to negative was 9.5 days, the longest was up to 21 days among the 24 asymptomatic cases.[23,24] (An et al, Hu et al). Then in another study found that the median period from contact to diagnosis and the last positive nucleic acid test was 19 days (8- 24 days) and 21.5 days (10-36 days), respectively.[25] (Pan et al). The median period from diagnosis to negative nucleic acid test was 7.5 days (2- 20 days) with normal or atypical chest CT infections and 12.5 days (8- 22 days) with typical CT findings.[25] (Pan et al) However, an asymptomatic infection should be quarantined for 14 days until now.[26] (Gao et al) more studies are still needed to assess the infectivity duration of asymptomatic cases. And if necessary, more attention should be paid to some special infectious individuals who need longer segregation due to the result of nucleic acid test.

DISSEMINATION

The most likely source of asymptomatic infections is close contacts of patients who have been diagnosed or suspected, and family clusters have been presented before. Also, colleagues, friends, and people who coincide with the trajectories of diagnosed or suspected patients are all regarded as high-risk populations.

Familial cluster has made the epidemic challenging to prevent and control. Some family members do not have any clinical manifestations, but the nucleic acid test result is positive, and this has become a major difficulty in the prevention and treatment of COVID-19. In one case report, all three of the family members were diagnosed with COVID-19, and only one family member had clinical symptoms.[27] (Chan JF et al). Another family cluster report showed that the first patient was in good health without clinical manifestations, including fever and cough, and went to the local hospital for treatment of urticaria. The patient stated that he had lived in the local

area for a long time and had not been to the epidemic area. However, the investigation of the disease control experts found that the patient had close contact with his relatives in Hubei Province one week before the onset of symptoms. Finally, by investigating the family members and close contacts of the patient, three pulmonary CT scans were normal, but the nucleic acid test results were positive.[28] (Lu S et al). As far as the Indian scenario from different states is concerned, the asymptomatic cases were reported as: Punjab-75%, Karnataka-50%, Maharastra-65%, Uttar Pradesh-75% & Assam-82% (Hindustan times; 19 April, 2020). Family members of COVID-19 patients, even without any symptoms, should be closely monitored and examined to rule out infection. These cases also highlight the need for a close epidemiological investigation to prevent the omission of possible sources of contamination. Different individuals may have different clinical signs. Studies have shown that asymptomatic infections are more common in populations of young and middle-aged individuals with functional performance status without underlying diseases. It was reported that asymptomatic cases were more common in middle-aged people in Shenzhen (median age: 49 years, 30.9% between 30 and 49 years).[29] (Wang et al) and a few younger people in Nanjing (median age: 32.5 years).[24] (Hu et al). Above all, age, immunity & any co-morbid condition may play an important role in the severity of COVID-19, and this is related to different immune responses and other potential pathogenesis.

PREVENTION AND CONTROL

The main mode of transmission of COVID-19 is through droplet and contact transmission and high-concentration aerosols. Droplet transmission occurs when nearby people ingest or inhale respiratory droplets (produced when an infected person coughs or sneezes). The successful isolation of live virus from throat swabs is a significant difference from SARS, suggesting that viral replication in upper respiratory tract is active and that SARS-CoV-2 is more effective than SARS-CoV in spreading through active shedding of pharyngeal viruses.[22] (Wolfel et al). A German team found that some people with COVID-19 had high levels of virus in their throat swabs when their initial symptoms were mild, meaning that the pathogen was quickly released and transmitted to others by coughing or sneezing (droplet transmission).[30] (Rothe). This means that protective measures, including hand hygiene, wearing protective masks and maintaining a safe social distance of six feet, can prevent infection with new coronavirus to a certain extent.

Most people with an asymptomatic infection do not seek medical assistance due to no obvious clinical signs and poor prevention awareness. More epidemiological methods, including close contact screening, cluster epidemic surveys specifically of the containment zone and follow-up surveys of the source of infection, were used to identify people with asymptomatic infections. The significance of asymptomatic infections as a source of infection depends on the distribution in the population and the amount and duration of virus elimination. However, clinical symptoms are hidden, and we can only rely on immunology or nucleic acid detection technology to obtain information about the infection; therefore, this kind of infectious source cannot be effectively identified, making it very difficult to prevent and control. Nucleic acid testing should be performed in persons who have contacted diagnosed or suspected COVID-19 patients. A person with an asymptomatic infection should be quarantined for 14 days.[26] (Gao et al). After the quarantine period expires, in principle, those who have negative test results for two consecutive samples of nucleic acid (sampling interval of at least 24 h) can be released from quarantine. If symptoms occurred during quarantine, the person should be home quarantined as per the regulations & norms or admitted immediately to the hospital depending upon the clinical manifestation. However, due to the limitations of specimen collection and detection methods, the influence of the high false-negative rate of the RT-PCR should be paid attention to, which may lead to missed diagnosis or delay in effective diagnosis.[31] (Lan et al). For this purpose, the combination of repeated nucleic acid detection and chest CT imaging examination should be effectively carried out for those highly suspected of SARS-CoV-2 infections.[32] (Ai et al).

TREATMENT AND OUTCOME

There is no specific treatment available for SARS-CoV-2 and the current treatment relies on supportive care of the infected patients (centre for disease control and prevention 2020b). There is currently controversy regarding the treatment of asymptomatic infections. Some researchers supported that antiviral therapy could fasten viral clearance on asymptomatic infections.[24,28] (Hu et al, Lu et al) while, it has been reported that isolation and close contact observation are enough for asymptomatic infections. In one report, lopinavir/ritonavir and abidol were not reported to be effective in improving symptoms or accelerating viral clearance.[33,36] (Chen et al) It was also reported that despite the treatment of aerosolized interferon (IFN) a2b, and two tablets of lopinavir/ritonavir (200 mg/50 mg) were used twice a day for 10 days, viral nucleic acid results were still positive, which showed that these antiviral drugs did not seem to be effective. In addition, side effects were observed after antiviral therapy, such as liver impairment.[34] (Luo et al). It is recommended to continue the isolation management, and health examinations should be continued for 14 days after being discharged, and regular follow-up visits should be conducted in the 2nd and 4th weeks after being discharged.[35] (national health commission., 2020). Therefore, antiviral treatments are not suggested for asymptomatic infections now, maybe more clinical studies are needed with larger patient sample to further confirm its effectiveness. Until now, isolation and close

contact observation are regarded as a better option for these asymptomatic infections.

CONCLUSION

SARS-CoV-2 has been declared as a pandemic that causes COVID-19. This manuscript reviewed the epidemiological characteristics and prevention measures of people with an asymptomatic infection of COVID-19. However, for better prevention & control from the risk of COVID-19, the research evidence is very limited, and the specific characteristics of asymptomatic infections need to be further clarified with larger patient sample size. In summary, rigorous epidemiological investigations specifically in the containment zones or people who are in direct contact with the diagnosed or suspected infected patients and laboratory testing are helpful in tracking people with asymptomatic infection for early control of this global epidemic effectively. Personal protective measures should be strictly followed to prevent SARS-CoV-2 infection.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Novel coronavirus (2019-nCov) – Situation Report 22. Geneva: World Health Organization; 11 February 2020. Available at: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200211-sitrep-22 ncov.pdf?sfvrsn=fb6d49b1_2. Accessed on 22 May 2020.
2. WHO/2019-nCoV/FAQ/Virusorigin/2020.1https://www.who.int/covid-19/information.
3. WHO. Coronavirus disease 2019 (COVID-19). 2020. Situation Report-100. Available at: https://www.who.int/ emergencies/ diseases/ novel-coronavirus-2019/ situation-reports. Accessed on 20 May 2020.
4. WHO. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected. 2020. Available at: https://www.who.int/publications-detail/clinical management- of-severe-acute-respiratory- infection-when novel- coronavirus-(ncov)-infection-is-suspected. Accessed on 20 May 2020.
5. WHO: use of chest imaging in covid-19: a rapid advice guide; 11 JUNE 2020. Accessed on 20 May 2020.
6. 10th July 2020, Worldo meter 2020; United Nations Geoscheme. www.worldometers.info › coronavirus.
7. WHO. Laboratory diagnostics for novel coronavirus. 2020. Available at: https://www.who.int/emergencies/diseases/novelcoronavirus-2019/technical guidance/ laboratory. Accessed on 20 May 2020.
8. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020;579(7798):270-3.
9. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell. 181:1-10.
10. Corbett KS, Goldsmith JA, Hsieh CL, Abiona O, Graham BS, McLellan JS. Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. Science. 367(6483):1260-3.
11. Coutard B, Valle C, de Lamballerie X, Canard B, Seidah NG, Decroly E. The spike glycoprotein of the new coronavirus 2019-nCoV contains a furin-like cleavage site absent in CoV of the same clade. Antivir Res 2020;176:104742.
12. Matsuyama S, Taguchi F. Two-step conformational changes in a coronavirus envelope glycoprotein mediated by receptor binding and proteolysis. J Virol. 2009;83(21):11133-41.
13. Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med. 2020;8(4):420-2.
14. Tian S, Hu W, Niu L, Liu H, Xu H, Xiao SY. Pulmonary pathology of early-phase 2019 novel coronavirus (COVID-19) pneumonia in two patients with lung cancer. J Thorac Oncol. 2020;S1556-0864(20):30132-5.
15. COVID-19 Case Tracker. Johns Hopkins Coronavirus Resource Center. 2020. Accessed at https://coronavirus.jhu.edu. Accessed on 26May 2020.
16. Chen Y, Wang AH, Yi B, Ding KQ, Wang HB, Wang JM, et al. The epidemiological characteristics of infection in close contacts of COVID-19 in Ningbo city. Chin J Epidemiol. 2020:41.
17. Nishiura H, Kobayashi T, Suzuki A, Jung SM, Hayashi K, Kinoshita R, et al. Estimation of the asymptomatic ratio of novel coronavirus infections (COVID-19). Int J Infect Dis. 2020;94:154-5.
18. Bai Y, Yao L, Wei T, Tian F, Jin DY, Chen L, et al. Presumed asymptomatic carrier transmission of COVID-19. J Am Med Assoc. 2020;323(14):1406-7.
19. Kimball A, Hatfield KM, Arons M, James A, Taylor J, Spicer K, et al. Asymptomatic and presymptomatic SARS-CoV-2 infections in residents of a long-term care skilled nursing facility-king county, Washington, march 2020. Morb Mortal Wkly Rep. 2020;69(13):377e81.
20. Gao WJ, Li LM. Advances on presymptomatic or asymptomatic carrier transmission of COVID-19. Chin J Epidemiol. 2020;41(4):485-8.
21. Shen M, Zhou Y, Ye J, Abdullah Al-Maskri AA, Kang Y, Zeng S, et al. Recent advances and perspectives of nucleic acid detection for coronavirus. J Pharm Anal. 2020;10(2):97-101.

22. Wolfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Muller MA, et al. Virological assessment of hospitalized patients with COVID-2019. Nature 2020. Available at: https://doi.org/10.1038/s41586-020-2196-x. Accessec on 20 May 2020.
23. An JH, Liao XJ, Xiao TY, Qian S, Yuan J, Ye HC, et al. Clinical characteristics of the recovered COVID-19 patients with redetectable positive RNA test. medRxiv 2020.
24. Hu Z, Song C, Xu C, Jin G, Chen Y, Xu X, et al. Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China. Sci China Life Sci. 2020;63(5):706-11.
25. Pan Y, Yu X, Du X, Li Q, Li X, Qin T, et al. Epidemiological and clinical characteristics of 26 asymptomatic SARS-CoV-2 carriers. J Infect Dis. 2020.
26. Gao WJ, Zheng K, Ke J, Li LM. Advances on the asymptomatic infection of COVID-19. Chin J Epidemiol. 2020:41.
27. Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet. 2020; 395(10223):514-23.
28. Lu S, Lin J, Zhang Z, Xiao L, Jiang Z, Chen J, et al. Alert for nonrespiratory symptoms of Coronavirus Disease 2019 (COVID-19) patients in epidemic period: a case report of familial cluster with three asymptomatic COVID-19 patients. Med Virol. 2020.
29. Wang Y, Liu Y, Liu L, Wang X, Luo N, Ling L. Clinical outcome of 55 asymptomatic cases at the time of hospital admission infected with SARS-Coronavirus-2 in Shenzhen, China. J Infect Dis. 2020;221(11):1770-4.
30. Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C, et al. Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. N Engl J Med. 2020;382(10):970-1.
31. Lan L, Xu D, Ye G, Xia C, Wang S, Li Y, et al. Positive RT-PCR test results in patients recovered from COVID-19. J Am Med Assoc. 2020; 323(15):1502-3.
32. Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W, et al. Correlation of chest CT and RT-PCR testing in coronavirus disease 2019(COVID-19) in China: a report of 1014 cases. Radiology. 2020:200642.
33. Chen J, Ling Y, Xi XH, Liu P, Li F, Li T, et al. Efficacies of lopinavir/ritonavir and abidol in the treatment of novel coronavirus pneumonia (in Chinese). Chin J Infect Dis. 2020;38(2):86-9.
34. Luo SH, Liu W, Liu ZJ, Zheng XY, Hong CX, Liu ZR, et al. A confirmed asymptomatic carrier of 2019 novel coronavirus (SARS-CoV-2). Chin Med J. 2020;133(9):1123-5.
35. National Health Commission of People's Republic of China. Diagnostic and treatment plan of Coronavirus disease 2019. 7th ed. 2020. Tentative. Available at: http://www.nhc.gov.cn/yzygj/s7653p/202003/46c9294. Accessed on 20 May 2020.
36. Sutiningsih D, Rahatina VE, Prabowo Y, Haryanto A, Wibowo MA. Epidemiologic and Clinical Characteristics of Patients with Covid-19 in Central Java, Indonesia. InE3S Web of Conferences. 2020;202:12014).
37. Day M. Covid-19: four fifths of cases are asymptomatic, China figures indicate. Bio Med J. 2020;369:m1375
38. Mizumoto K, Kagaya K, Zarebski A, Chowell G. 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):2000180.
39. Ki M. Epidemiologic characteristics of early cases with 2019 novel coronavirus (2019-nCoV) disease in Korea. Epidemiology and health. 2020;42.

Cite this article as: Verma N, Verma V, Sagar HK, Singh N, Karuna V, Gupta P, et al. New challenge of asymptomatic infections from COVID-19: current scenario. Int J Res Med Sci 2021;9:310-6.