REVIEW ARTICLE

Clinical profile of COVID-19 patients: A review of diagnostic aids and clinical profile of COVID-19

Neha Choudhary[1], Kumar Gaurav Chhabra[*1], Gargi Nimbulkar[1], Amit Reche[1], Punit Fulzele[2], Chaya Chhabra[3]

[1]Department of Public Health Dentistry, Sharad Pawar Dental College, Datta Meghe Institute of Medical Sciences, Sawangi (M), Wardha-442004, Maharashtra, India
[2]Department of Pedodontics and Preventive Dentistry, Sharad Pawar Dental College and Hospital, Datta Meghe Institute of Medical Sciences, Sawangi (M), Wardha-442004, Maharashtra, India
[3]Department of Pedodontics and Preventive Dentistry, Maharishi Markendeshwar College of Dental Sciences and Research, Maharishi Markendeshwar (Deemed to be University), Mullana, Ambala, Haryana, India

ABSTRACT

The SARS-CoV-2 is a novel coronavirus which originated in the province Wuhan, China, in December 2019. It is the causative agent of COVID-19, an infection mainly presenting as mild upper respiratory tract infection, with patients presenting with fever, cough, breathlessness and fatigue. The virus predominantly spreads by a person to person contact, which is why it has spread very rapidly in a short span of time, so much so, that multiple countries are affected at present. The number of casualties is ever increasing. Even though our understanding of the novel coronavirus is improving, many countries, including India, are facing a situation which is not getting better with respect to controlling the pandemic. The number of new cases and deaths are ever increasing. There is a general state of panic among all the sections of the society and almost all are affected. With the number of tests being carried out every day, also increasing, a general idea about the signs and symptoms of the disease as well as the diagnostic criterion aids will further help us control the pandemic. This narrative review focuses on the clinical symptoms, diagnostic aids, risk factors, common clinical symptoms, laboratory findings and complications of COVID-19 and also on post COVID 19 Complications.

*Corresponding Author

Name: Kumar Gaurav Chhabra
Phone: + 91 797976840339
Email: rajsushil.chhabra@gmail.com

INTRODUCTION

In December 2019, there was an unexpected rise in the cases of pneumonia in Wuhan, Hubei province, China. The symptoms varied from mild to severe, bearing similarities to those of viral pneumonia and the underlying cause seemed to be unknown. By January 7, 2020, China had isolated a "novel coronavirus" by analysis of samples from the respiratory tract and also blood and stool in a few cases. Within the next few days, China shared information about the viral genome with the rest of the world and the virus was named Severe Acute Respiratory Syndrome coronavirus 2 (SARS- CoV-2). The infection caused by this novel coronavirus was

named COVID-19 by WHO in February 2020 (Phelan et al., 2020). The infection spreads through airborne droplets and primarily involves the respiratory system (Guo et al., 2020b). The novel coronavirus is a "positive sense single stranded RNA virus, spherical in shape", with the surface showing protein aceous protruberances in the form of spikes. It can remain potentially "infectious on inanimate surfaces" up to 9 hours, thereby increasing chances of cross infection (Kampf et al., 2020). This virus is closely related to those which caused Severe Acute Respiratory Syndrome(SARS) outbreak in 2002 and Middle East Respiratory Syndrome(MERS) in 2012 (Vankadari and Wilce, 2020). On 11 March 2020, "COVID-19 was declared a pandemic" by WHO.

Diagnostic Aids

As COVID- 19 infection primarily involves the respiratory tract, it is ideal to collect samples from the "upper respiratory tract(nasopharyngeal swab, oropharyngeal swab) and the lower respiratory tract (sputum, bronchoalveolar lavage, tracheal aspirate)". The nasopharyngeal swab is collected using synthetic fibre swabs. It is the ideal specimen for testing asymptomatic patients as well. The oropharyngeal swab is collected from the posterior part of the pharynx (Iyer et al., 2020; Wang et al., 2020b) found in a study that oropharyngeal swabs were used more frequently than nasopharyngeal swabs in China, even though nasopharyngeal specimen testing is more precise. If both the nasopharyngeal and oropharyngeal specimens are kept together in the same container, the results are more accurate. Sputum is collected in cases of severe coughing. Samples can also be collected from mid- turbinates and anterior nares (Iyer et al., 2020; Wang et al., 2020c). All these samples obtained from the respiratory tract are subjected to molecular testing for confirmation of diagnosis. Real-time reverse transcriptase PCR(RT- PCR) is an effective method currently available for diagnosis of COVID-19. A big advantage of this method is that it does not cross react with other viruses of the respiratory tract (van Kasteren et al., 2020).

Salivary Diagnostics- Another method being employed for testing suspected COVID-19 patients, which is easy to carry out, inexpensive and non-invasive, is a salivary sampling. This method significantly decreases the chances of healthcare workers acquiring the infection, as close contact with the patient is not required. Saliva has immense diagnostic potential as it has high "sensitivity and specificity" for respiratory tract viruses. The findings of salivary fluid are consistent with those of nasopharyngeal and oropharyngeal swabs. In this method, saliva is collected from the patient and nucleic acid extraction is carried out, followed by RT- PCR. It is particularly useful in places where there is a shortage of swabs for testing and a large number of people need to be screened (Santosh et al., 2020). However, we don't know for sure if salivary diagnostics is a definitive method in all the cases. Studies have shown that the "salivary parameters are altered in diabetics compared to non-diabetics" (Panchbhai et al., 2010). Therefore, a lot of trials need to be carried out to establish the reliability of this method in all patients (Sabino-Silva et al., 2020).

"Rapid Diagnostic Tests based on antigen and antibody detection" are not ideal as they are not very accurate. In antigen detection based tests, results hugely depend on the quality and processing of samples. On the other hand, in antibody detection based tests, the infection may progress a great deal by the time antibodies are detected as they are only produced in the second week (Carod-Artal, 2020).

In another study, Xie et al. showed that nucleic acid detection in conjunction with computed tomography may also be employed for testing patients (Xie et al., 2020).

Risk factors for COVID-19

Since the outset of the outbreak, several studies and clinical trials are being carried out for a better and more precise comprehension of the virus. Many of these reveal there are certain groups of people in which the infection has higher odds of advancing from mild to severe. Among these groups are those patients which have a history of systemic disease. Cardiovascular diseases notably contribute to the aggravation of the infection. Hypertension is the most commonly found comorbidity in severe cases of COVID-19 (Li et al., 2020a). Mortality rates vary considerably in the severe and non-severe groups, being 32.5% in the former and a meagre 1.1% in the latter. During the initial phase of the outbreak, when there was limited information available about the infection, it was found that many physicians discontinued the administration of angiotensin receptor blockers and angiotensin-converting enzyme inhibitors to their patients, as they believed these drugs to be worsening the infection. However, this is not true and there isn't much evidence to suggest that ARB and ACE- inhibitors increase a patient's chances of contacting COVID-19 (Klonoff and Umpierrez, 2020). Cardiovascular diseases severely affect the quality of life of all patients. They become even more fatal if left undiagnosed and untreated for a long time. The people in rural areas, especially fall prey to this due to their

ignorance. A study shows that majority of people in rural areas are unaware that they suffer from cardiovascular disease and haven't received any kind of treatment (Joshi *et al.*, 2013). Such people are more vulnerable to COVID-19 than healthy people.

After hypertension, diabetes is the most dangerous complicating factor. In the present situation where the world is in lockdown, many diabetic people may be finding it difficult to achieve proper glycemic control. Consequently, hyperglycemia is predisposing diabetic patients to COVID-19 by degrading the pulmonary function of the patient. The immune system also takes a major hit. Once a diabetic patient develops COVID-19, the problem intensifies. If corticosteroid therapy is being used as a treatment modality, there is a further increase in blood glucose. "Continuous monitoring of blood glucose" levels become all the more important in such cases. Proper monitoring of blood glucose may be hampered by the fact that the healthcare workers may not want to come in close contact with the patient too frequently in order to decrease their exposure to the virus. All these factors complicate the infection further and make the prognosis poor. So, it is very important that diabetics be extra cautious about their health and consults their physician regularly. Telemedicine is being promoted by several governments and hospitals for this purpose (Klonoff and Umpierrez, 2020).

Chronic Obstructive pulmonary disease (COPD) and cerebrovascular disease are other risk factors for COVID-19 (Wang *et al.*, 2020a). The infection is also more severe in older age groups than younger age groups (>65). Age of the patient has a major impact on the "pulmonary function". As age progresses, people become more susceptible to respiratory diseases. As a precautionary measure, old people can practice "Sahaja yoga and meditation to enhance their respiratory system" (Yunati *et al.*, 2017).

Smoking and obesity also contribute to the infection. Males are found to be affected more than females (Jordan *et al.*, 2020; Zheng *et al.*, 2020).

Clinical Presentation

The "most common symptoms are fever (90%), cough (75%) and dyspnoea (50%)" (Jiang *et al.*, 2020). "Fatigue, sputum production, headache, diarrhea and hemoptysis" are other symptoms, although less common. In a study carried out by Zhou *et al.* (2020) where 191 patients were observed, "the median time from onset of illness to discharge was found to be 22 days", "median time from onset of illness to dyspnoea was similar in survivors and non-survivors with a mean duration of 13 days" and the "median duration for viral shedding for survivors was found to be 20 days". Proper isolation of patients is extremely important because of the constant viral shedding. The median duration of cough and fever were 19 and 12 days, respectively.

In another study carried out by Wang *et al.* (2020c) at Zhongnam Hospital of Wuhan University, 138 patients were observed. The mean age was 56 years and 75 patients were men. Fever was found to be the "most common symptom (98.6%), followed by fatigue (69.6%) and dry cough (59.5%)". Chest CT showed "bilateral patchy shadows or ground glass opacity".

The human coronaviruses are known to involve the central nervous system. Neurological symptoms include headaches, myalgia, dizziness and ansomia. Severe cases may lead to encephalopathy, stroke, epileptic seizures and encephalitis. " Guillain- Barre Syndrome associated with SARS-CoV-2 infection" may also develop. For the accurate establishment of the incidence of these neurological conditions in COVID-19 patients, clinical trials and extensive research is still required.

Just like neurological symptoms, there is limited evidence that COVID-19 infection is characterized by gastrointestinal symptoms. However, Tian *et al.* (2020) in a study, have found that the infection may involve the gastrointestinal tract in a small number of cases. Most of the symptoms include "anorexia, diarrhea, vomiting, abdominal pain and nausea".

Even if a person is asymptomatic, they may be a carrier of the virus. Hence, it is very crucial that all patients with flu like symptoms and a history of travel to an epidemic area be tested thoroughly. Prompt diagnosis and the commencement of proper management at the right time will take us a long way in controlling the outbreak.

Complications

The most commonly observed complication is sepsis. Majority of the patients develop sepsis at some point during the infection. The mean duration of development of sepsis in survivors and non-survivors is 10 and 9 days respectively. This is followed by Acute respiratory distress syndrome (ARDS) with a mean duration of 12 days. Acute cardiac and kidney injury is seen in a significant number of patients with a mean duration of 15 days. Mortality increases significantly in cases where d-dimer is greater than 1ug/ml and sequential organ failure assessment (SOFA) is high. In old patients, common cardiac complications include heart failure, myocardial infarction and arrhythmia. Cardiac arrest may occur in some cases. In CVS patients, pneumonia at the time of admission is much more severe than in those without cardiovascular dis-

ease (Zhou *et al.*, 2020). Myocardial injury is a fatal complication. Guo *et al.* (2020a) found that out of the 187 patients they monitored, the mortality rate in patients without any underlying cardiovascular disease was 7.62% whereas it was 69.44% in patients with cardiovascular disease and elevated plasma troponinT (TnT) level.

Patients who require invasive mechanical ventilation succumb to dyspnoea more frequently. WBC count in most severe cases is less than 10.0×10^1/L (Zhou *et al.*, 2020). Other findings of severe cases include high levels of lactate dehydrogenase and cytokines (Li *et al.*, 2020b). There is also marked release in erythrocyte sedimentation rate (ESR), C- reactive protein, leucopenia, lymphopenia and leucocytosis. The lymphocytes keep decreasing with the progression of the disease. Additionally, hypoalbuminemia and high levels of alkaline aminotransferase and ferritin all contribute to poor prognosis. The immunological changes cause rapid deterioration of the patient's health and management should be aimed at controlling all the parameters (Iyer *et al.*, 2020).

Among pediatric cases, the incubation period is 8 days. Laboratory findings reveal that the number of T cells and B cells is not adversely affected, this is the reason for symptoms predominantly being mild, but the CRP levels are lower than those in adults (Chen *et al.*, 2020).

CONCLUSION

The adversities due to COVID-19 are increasing at an alarming rate with each passing day. The outbreak can be contained by testing more and more suspected people every day. RT- PCR is one of the most efficient methods of diagnosis at present. The efficacy of antigen and antibody based detection tests still need to be validated. Rapid diagnosis is the first step in curbing the infection. The presence of underlying systemic disease like hypertension, diabetes and cerebrovascular diseases increases the severity and hampers the prognosis. Most of the cases present with mild flu-like symptoms like fever, cough and fatigue. Proper isolation of patients is of utmost importance to prevent transmission to healthy individuals. Governments all around the world are adopting stringent measures to curb the infection. It is very important that we follow all the guidelines and take adequate preventative steps if we want to come out of this pandemic.

Funding Support

Conflict of Interest

REFERENCES

Carod-Artal, F. J. 2020. Neurological complications of coronavirus and COVID-19. *Revista de Neurologia*, 70(9):311–322.

Chen, J., Zhang, Z. Z., *et al.* 2020. The clinical and immunological features of pediatric COVID-19 patients in China. *Genes & Diseases*.

Guo, T., Fan, Y., Chen, M., Wu, X., Zhang, L., He, T., Wang, H., Wan, J., Wang, X., Lu, Z. 2020a. Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19). *JAMA Cardiology*, 5(7):811.

Guo, Y. R., Cao, Q. D., Hong, Z. S., Tan, Y. Y., Chen, S. D., Jin, H. J., Tan, K. S., Wang, D. Y., Yan, Y. 2020b. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak - an update on the status. *Military Medical Research*, 7(1):11.

Iyer, M., Jayaramayya, K., Subramaniam, M. D., Lee, S. B., Dayem, A. A., Cho, S.-G., Vellingiri, B. 2020. COVID-19: an update on diagnostic and therapeutic approaches. *BMB Reports*, 53(4):191–205.

Jiang, F., Deng, L., Zhang, L., Cai, Y., Cheung, C. W., Xia, Z. 2020. Review of the Clinical Characteristics of Coronavirus Disease 2019 (COVID-19). *Journal of General Internal Medicine*, 35(5):1545–1549.

Jordan, R. E., Adab, P., Cheng, K. K. 2020. Covid-19: risk factors for severe disease and death. *BMJ*, page m1198.

Joshi, R., Taksande, B., Kalantri, S. P., Jajoo, U. N., Gupta, R. 2013. Prevalence of cardiovascular risk factors among rural population of elderly in Wardha district. *Journal of Cardiovascular Disease Research*, 4(2):140–146.

Kampf, G., Todt, D., Pfaender, S., Steinmann, E. 2020. Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. *Journal of Hospital Infection*, 104(3):246–251.

Klonoff, D. C., Umpierrez, G. E. 2020. Letter to the Editor: COVID-19 in patients with diabetes: Risk factors that increase morbidity. *Metabolism*, 108:154224.

Li, B., Yang, J., Zhao, F., Zhi, L., Wang, X., Liu, L., Bi, Z., Zhao, Y. 2020a. Prevalence and impact of cardiovascular, metabolic diseases on COVID-19 in China. *Clinical Research in Cardiology*, 109(5):531–538.

Li, X., Xu, S., Yu, M., Wang, K., Tao, Y., Zhou, Y., Shi,

J., Zhou, M., Wu, B., Yang, Z., Zhang, C., Yue, J., Zhang, Z., Renz, H., Liu, X., Xie, J., Xie, M., Zhao, J. 2020b. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. *Journal of Allergy and Clinical Immunology*, 146(1):110–118.

Panchbhai, A. S., Degwekar, S. S., Bhowte, R. R. 2010. Estimation of salivary glucose, salivary amylase, salivary total protein and salivary flow rate in diabetics in India. *Journal of Oral Science*, 52(3):359–368.

Phelan, A. L., Katz, R., Gostin, L. O. 2020. The Novel Coronavirus Originating in Wuhan, China. *JAMA*, 323(8):709.

Sabino-Silva, R., Jardim, A. C. G., Siqueira, W. L. 2020. Coronavirus COVID-19 impacts to dentistry and potential salivary diagnosis. *Clinical Oral Investigations*, 24(4):1619–1621.

Santosh, T. S., Parmar, R., Anand, H., Srikanth, K., Saritha, M. 2020. A Review of Salivary Diagnostics and Its Potential Implication in Detection of Covid-19. *Cureus*, 12(4).

Tian, Y., Rong, L., Nian, W., He, Y. 2020. Review article: gastrointestinal features in COVID-19 and the possibility of faecal transmission. *Alimentary Pharmacology & Therapeutics*, 51(9):843–851.

van Kasteren, P. B., van der Veer, B., van den Brink, S., Wijsman, L., de Jonge, J., van den Brandt, A., Molenkamp, R., Reusken, C. B., Meijer, A. 2020. Comparison of seven commercial RT-PCR diagnostic kits for COVID-19. *Journal of Clinical Virology*, 128:104412.

Vankadari, N., Wilce, J. A. 2020. Emerging COVID-19 coronavirus: glycan shield and structure prediction of spike glycoprotein and its interaction with human CD26. *Emerging Microbes & Infections*, 9(1):601–604.

Wang, B., Li, R., Lu, Z., Huang, Y. 2020a. Does comorbidity increase the risk of patients with COVID-19: evidence from a meta-analysis. *Aging*, 12(7):6049–6057.

Wang, D., Hu, B., Hu, C., Zhu, F., Liu, X., Zhang, J., Wang, B., Xiang, H., Cheng, Z., Xiong, Y., Zhao, Y., Li, Y., Wang, X., Peng, Z. 2020b. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. *JAMA*, 323(11):1061.

Wang, W., Xu, Y., Gao, R., Lu, R., Han, K., Wu, G., Tan, W. 2020c. Detection of SARS-CoV-2 in Different Types of Clinical Specimens. *JAMA*, 323(18):1843–1844.

Xie, C., Jiang, L., Huang, G., Pu, H., Gong, B., Lin, H., Ma, S., Chen, X., Long, B., Si, G., Yu, H., Jiang, L., Yang, X., Shi, Y., Yang, Z. 2020. Comparison of different samples for 2019 novel coronavirus detection by nucleic acid amplification tests. *International Journal of Infectious Diseases*, 93:264–267.

Yunati, M., Deshpande, V., Yuwanate, A., Sorte, S., Sirsam, S. 2017. Sahaja yoga meditation as a tool to enhance aging pulmonary functions. *National Journal of Physiology, Pharmacy and Pharmacology*, 7(3):1.

Zheng, Z., Peng, F., Xu, B., Zhao, J., Liu, H., Peng, J., Li, Q., Jiang, C., Zhou, Y., Liu, S., Ye, C., Zhang, P., Xing, Y., Guo, H., Tang, W. 2020. Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. *Journal of Infection*, 81(2):16–25.

Zhou, F., Yu, T., Du, R., Fan, G., Liu, Y., Liu, Z., Xiang, J., Wang, Y., Song, B., Gu, X., Guan, L., Wei, Y., Li, H., Wu, X., Xu, J., Tu, S., Zhang, Y., Chen, H., Cao, B. 2020. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The Lancet*, 395:30566–30569.