

significant outbreak occurs due to a virus-like SARS-CoV-2.

There is a steady increase in the reports of COVID-19 in companion and wild animals around the world. Further studies are required to evaluate the potential of animals (especially companion animals) to serve as an efficient reservoir host that can further alter the dynamics of human-to-human transmission (330). To date, two pet dogs (Hong Kong) and four pet cats (one each from Belgium and Hong Kong, two from the United States) have tested positive for SARS-CoV-2 (335). The World Organization for Animal Health (OIE) has confirmed the diagnosis of COVID-19 in both dogs and cats due to human-to-animal transmission (331). The similarity observed in the gene sequence of SARS-CoV-2 from an infected pet owner and his dog further confirms the occurrence of human-to-animal transmission (333). Even though asymptomatic, feline species should be considered a potential transmission route from animals to humans (326). However, currently, there are no reports of SARS-CoV-2 transmission from felines to human beings. Based on the current evidence, we can conclude that cats are susceptible to SARS-CoV-2 and can get infected by human beings. However, evidence of cat-

out on the 1Solatca virus conlirmea tnat tnere 1S a potential risk for the reemergence of SARS-CoV infection from the viruses that are currently circulating in the bat population (105).

#### CLINICAL PATHOLOGY OF SARS-CoV-2 (COVID-19)

The disease caused by SARS-CoV-2 is also named severe specific contagious pneumonia (SSCP), Wuhan pneumonia, and, recently, COVID-19 (110). Compared to SARS-CoV, SARS-CoV-2 has less severe pathogenesis but has superior transmission capability, as evidenced by the rapidly increasing number of COVID-19 cases (111). The incubation period of SARS-CoV-2 in familial clusters was found to be 3 to 6 days (112). The mean incubation period of COVID-19 was found to be 6.4 days, ranging from 2.1 to 11.1 days (113). Among an early affected group of 425 patients, 59 years was the median age, of which more males were affected (114). Similar to SARS and MERS, the severity of this nCoV is high in age groups above 50 years (2, 115). Symptoms of COVID-19 include fever, cough, myalgia or fatigue, and, less commonly, headache, hemoptysis, and diarrhea (116, 282). Compared to the SARS-CoV-2-infected patients in Wuhan during respiratory infection (SARI) and respiratory distress, shock or hypoxaemia. Patients with SARI can be given conservative fluid therapy only when there is no evidence of shock. Empiric antimicrobial therapy must be started to manage SARI. For patients with sepsis, antimicrobials must be administered within 1 hour of initial assessments. The WHO and CDC recommend that glucocorticoids not be used in patients with COVID-19 pneumonia except where there are other indications (exacerbation of chronic obstructive pulmonary disease).”” Patients’ clinical deterioration is closely observed with SARI; however, rapidly progressive respiratory failure and sepsis require immediate supportive care interventions comprising quick use of neuromuscular blockade and sedatives, hemodynamic management, nutritional support, maintenance of blood glucose levels, prompt assessment and treatment of nosocomial pneumonia, and prophylaxis against deep venous thrombosis (DVT) and gastrointestinal (GI) bleeding.®® Generally, such patients give way to their primary illness to secondary complications like sepsis or multiorgan system failure.\*® progress from the initial focal unilateral to diffuse bilateral ground-glass opacities and will further progress to or coexist with lung consolidation changes within 1 to 3 weeks (159). The role played by radiologists in the current scenario is very important. Radiologists can help in the early diagnosis of lung abnormalities associated with COVID-19 pneumonia. They can also help in the evaluation of disease severity, identifying its progression to acute respiratory distress syndrome and the presence of secondary bacterial infections (160). Even though

chest CT is considered an essential diagnostic tool for COVID-19, the extensive use of CT for screening purposes in the suspected individuals might be associated with a disproportionate risk-benefit ratio due to increased radiation exposure as well as increased risk of cross-infection. Hence, the use of CT for early diagnosis of SARS-CoV-2 infection in high-risk groups should be done with great caution (292).

More recently, other advanced diagnostics have been designed and developed for the detection of SARS-CoV-2 (345, 347, 350-352). A reverse transcriptional loop-mediated isothermal amplification (RT-LAMP), namely, iLACO, has been developed for rapid and colorimetric detection of this

07:25 @ Q = © \ VN | was linked to a family member and 26 children had history of travel/residence to Hubei province in China. All the patients were either asymptomatic (9%) or had mild disease. No severe or critical cases were seen. The most common symptoms were fever (50%) and cough (38%). All patients recovered with symptomatic therapy and there were no deaths. One case of severe pneumonia and multiorgan dysfunction in a child has also been reported [19]. Similarly the neonatal cases that have been reported have been mild [20].

#### Diagnosis [21]

A suspect case is defined as one with fever, sore throat and cough who has history of travel to China or other areas of persistent local transmission or contact with patients with similar travel history or those with confirmed

help us to control the spread of this virus. However, this is both challenging as well as time-consuming due to the present extent of infection (226). The current scenario demands effective implementation of vigorous prevention and control strategies owing to the prospect of COVID-19 for nosocomial infections (68). Follow-ups of infected patients by telephone on day 7 and day 14 are advised to avoid any further unintentional spread or nosocomial transmission (312). The availability of public data sets provided by independent analytical teams will act as robust evidence that would guide us in designing interventions against the COVID-19 outbreak. Newspaper reports and social media can be used to analyze and reconstruct the progression of an outbreak. They can help us to obtain detailed patient-level data in the early stages of an outbreak (227). Immediate travel restrictions imposed by several countries might have contributed significantly to preventing the spread of SARS-CoV-2 globally (89, 228). Following the outbreak, a temporary ban was imposed on the wildlife trade, keeping in mind the possible role played by wild animal species in the origin of SARS-CoV-2/COVID-19 (147). Making a permanent and bold decision on the trade of wild animal species is necessary to prevent the possibility between the genome sequence of the new coronavirus (SARS-CoV-2) and SARS-like CoVs, the comparative analysis recognized a furin-like cleavage site in the SARS-CoV-2 S protein that is missing from other SARS-like CoVs (99). The furin-like cleavage site is expected to play a role in the life cycle of the virus and disease pathogenicity and might even act as a therapeutic target for furin inhibitors. The highly contagious nature of SARS-CoV-2 compared to that of its predecessors might be the result of a stabilizing mutation that occurred in the endosome-associated-protein-like domain of nsp2 protein.

Similarly, the destabilizing mutation near the phosphatase domain of nsp3 proteins in SARS-CoV-2 could indicate a potential mechanism that differentiates it from other CoVs (100). Even though the CFR reported for COVID-19 is meager compared to those of the previous SARS and MERS outbreaks, it has caused more deaths than SARS and MERS combined (101). Possibly related to the viral pathogenesis is the recent finding of an 832-nucleotide (nt) deletion in ORF8, which appears to reduce the replicative fitness of the virus and leads to attenuated phenotypes of SARS-CoV-2 (256).

Coronavirus is the most prominent example of a treated symptomatically along with oxygen therapy. In such cases where the patients progress toward respiratory failure and become refractory to oxygen therapy, mechanical ventilation is necessitated. The COVID-19-induced septic shock can be managed by providing adequate hemodynamic support (299). Several classes of drugs are currently being evaluated for their potential therapeutic action against SARS-CoV-2. Therapeutic agents that have anti-SARS-CoV-2 activity can be broadly classified into three categories: drugs that block virus entry into the host cell, drugs that block viral replication as well as its survival within the host cell, and drugs that attenuate the exaggerated host immune response (300). An inflammatory cytokine storm is commonly seen in critically ill COVID-19 patients. Hence, they may benefit from the use of timely anti-inflammation treatment. Anti-inflammatory therapy using drugs like glucocorticoids, cytokine inhibitors, JAK inhibitors, and chloroquine/hydroxychloroquine should be done only after analyzing the risk/benefit ratio in COVID-19 patients (301). There have not been any studies concerning the application of nonsteroidal anti-inflammatory drugs (NSAID) to COVID-19-infected patients. However, reasonable pieces of evidence are available that link NSAID Splits Tree phylogeny analysis.

In the unrooted phylogenetic tree of different betacoronaviruses based on the S protein, virus sequences from different subgenera grouped into separate clusters. SARS-CoV-2 sequences from Wuhan and other countries exhibited a close relationship and appeared in a single cluster (Fig. 1). The CoVs from the subgenus Sarbecovirus appeared jointly in SplitsTree and divided into three subclusters, namely, SARS-CoV-2, bat-SARS-like- CoV (bat-SL-CoV), and SARS-CoV (Fig. 1). In the case of other subgenera, like Merbecovirus, all of the sequences grouped in a single cluster, whereas in Embecovirus, different species, comprised of canine respiratory CoVs, bovine CoVs, equine CoVs, and human CoV strain (OC43), grouped in a common cluster. Isolates in the subgenera Nobecovirus and Hibecovirus were found to be placed separately away from other reported SARS-CoVs but shared a bat origin.

## CURRENT WORLDWIDE SCENARIO OF SARS-CoV-2

This novel virus, SARS-CoV-2, comes under the subgenus Sarbecovirus of the Orthocoronavirinae subfamily and is entirely different from the viruses stalk (45). Recently, structural analyses of the S proteins of COVID-19 have revealed 27 amino acid substitutions within a 1,273-amino-acid stretch (16). Six substitutions are located in the RBD (amino acids 357 to 528), while four substitutions are in the RBM at the CTD of the S1 domain (16). Of note, no amino acid change is seen in the RBM, which binds directly to the angiotensin-converting enzyme-2 (ACE2) receptor in SARS-CoV (16, 46). At present, the main emphasis is knowing how many differences would be required to change the host tropism. Sequence comparison revealed 17 nonsynonymous changes between the early sequence of SARS-CoV-2 and the later isolates of SARS-CoV. The changes were found scattered over the genome of the virus, with nine substitutions in ORF1ab, ORF8 (4 substitutions), the spike gene (3 substitutions), and ORF7a (single substitution) (4). Notably, the same nonsynonymous changes were found in a familial cluster, indicating that the viral evolution happened during person-to-person transmission (4, 47). Such adaptive evolution events are frequent and constitute a constantly ongoing process once the virus spreads among new hosts (47). Even though no functional changes occur in the virus associated with this adaptive evolution, close monitoring of the viral

wearing a facemask and practising hand hygiene before feeding the baby. In addition, it is advisable that breast pumps are cleaned properly after each use and, if possible, a healthy individual is available to feed the expressed breast milk to the infant.

## 7.2 Children and elderly population

On the basis of the available reports, COVID-19 among children accounted for 1-5% of the confirmed cases, and this population does not seem to be at higher risk for the disease than adults. There is no difference in the COVID-19 symptoms between adults and children. However, the available evidence indicated that children diagnosed with COVID-19 have milder symptoms than the adults, with a low mortality rate.\*<sup>4</sup> On the contrary, older people who are above the age of 65 years are at higher risk for a severe course of disease. In the United States, approximately 31-59% of those with confirmed COVID-19 between the ages of 65 and 84 years old required hospitalisation, 11-31% of them required admission to the intensive care unit, and 4-11% died.”<sup>o</sup>

residues for receptor binding” (FIG. 3b). In comparison with the Guangdong strains, pangolin coronaviruses reported from Guangxi are less similar to SARS-CoV-2, with 85.5% genome sequence identity”. The repeated occurrence of SARS-CoV-2-related coronavirus infections in pangolins from different smuggling events suggests that these animals are possible hosts of the viruses. However, unlike bats, which carry coronaviruses healthily, the infected pangolins showed clinical signs and histopathological changes, including interstitial pneumonia and inflammatory cell infiltration in diverse organs”. These abnormalities suggest that pangolins are unlikely to be the reservoir of these coronaviruses but more likely acquired the viruses after spillover from the natural hosts.

An intermediate host usually plays an important role in the outbreak of bat-derived emerging coronaviruses; for example, palm civets for SARS-CoV and dromedary camels for MERS-CoV. The virus strains carried by these two intermediate hosts were almost genetically identical to the corresponding viruses in humans (more than 99% genome sequence identity). Despite an RBD that is virtually identical to that of SARS-CoV-2, the pangolin coronaviruses known to date have no more than 92% genome identity with SARS-CoV-2 (REF.\*). The available data are insufficient to interpret pangolins as the intermediate host of SARS-CoV-2. So far, no evidence has shown that pangolins were directly involved in the emergence of SARS-CoV-2.

07:25 @ Q = © \ VN | Interestingly, disease in patients outside Hubei province has been reported to be milder than those from Wuhan [17]. Similarly, the severity and case fatality rate in patients outside China has been reported to be milder [6]. This may either be due to selection bias wherein the cases reporting from Wuhan included only the severe cases or due to predisposition of the Asian population to the virus due to higher expression of ACE<sub>2</sub> receptors on the respiratory mucosa [11].

Disease in neonates, infants and children has been also reported to be significantly milder than their adult counterparts. In a series of 34 children admitted to a hospital in Shenzhen, China between January 19th and February 7th, there were 14 males and 20 females. The median age was 8 y 11 mo and in 28 children the infection was linked to a family member and 26

07:23 @ @ + © o4i and Middle East respiratory syndrome coronavirus (MERS-CoV), but has lower fatality. The global impact of this new epidemic is yet uncertain.

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The 2019 novel coronavirus (2019- nCoV) or the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as it is now called, is rapidly spreading from its origin in Wuhan City of Hubei Province of China to the rest of the world [1]. Till 05/03/2020 around 96,000 cases of coronavirus disease 2019 (COVID-19) and 3300 deaths have been reported [2]. India has

reported 29 cases till date. Fortunately so far, children have been infrequently affected with no deaths. But the future course of this virus is unknown. This article gives a bird's eye view about

0728 MQ \* ¢ \ VN | (entertainment parks etc). China is also considering introducing legislation to prohibit selling and trading of wild animals [32].

The international response has been dramatic. Initially, there were massive travel restrictions to China and people returning from China/ evacuated from China are being evaluated for clinical symptoms, isolated and tested for COVID-19 for 2 wks even if asymptomatic. However, now with rapid world wide spread of the virus these travel restrictions have extended to other countries. Whether these efforts will lead to slowing of viral spread is not known.

A candidate vaccine is under development.

Practice Points from an Indian Perspective