SARS CoV-2: Epidemiology, Clinical Characteristics, Diagnosis, Therapeutics, Prevention and One Health Perspective with Reference to Meat Industry

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ABSTRACT

Severe Acute Respiratory Syndrome Corona Virus- 2 (SARS-CoV-2) or coronavirus disease (COVID-19) has been identified as the cause of a pandemic of respiratory illness. It has been declared as a Public Health Emergency of International Concern by the World Health Organization. The reported symptoms include fever, cough, fatigue, pneumonia, headache, diarrhea, hemoptysis, and dyspnea. The human-to-human transmission has been described via droplets, contaminated hands or surfaces. The incubation times ranges between 2-14 days. Early diagnosis, quarantine, and supportive treatments are required to cure patients. Treatments, including antiviral agents, chloroquine and hydroxychloroquine, monoclonal antibodies, and convalescent plasma transfusion have been used for successful treatment of the patients. Preventive measures such as masks, hand hygiene practices, avoidance of public contact, case detection, contact tracing, and quarantines have been discussed as ways to reduce transmission. The pandemic has impacted on the meat industry. The event demands urgent implementation of a multidisciplinary team in a One Health approach to address the present-day challenges at the human-animal-environment interface. We reviewed the literature on the epidemiology, the disease, diagnosis, therapeutics and mitigation strategies of COVID-19. Although many studies are relevant to control the current public emergency, more research is needed to provide valid and reliable ways to manage this kind of public health emergency in both the short- and long-term.

Keywords: *COVID- 19, Epidemiology, One Health, Meat Sector*

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INTRODUCTION

The coronavirus disease (COVID-19), a highly pathogenic viral infection caused by SARS-CoV-2, has caused global health concern. COVID-19 is closely related to severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome (MERS) and is a betacoronavirus. It is assumed that COVID-19 has zoonotic origin based on the large number of infected people who were exposed to the wet market in Wuhan City, China (Hamid *et al*., 2020). Bats could be the primary possible reservoir for the SARS-CoV-2 as it has shown significant sequence similarity with severe acute respiratory syndrome-like (SARS-like) bat viruses. The intermediate host and their subsequent transfer are not known yet, although human to human transfer is widely confirmed. Identifying infected individuals to curb SARS-CoV-2 transmission has been challenging as compared to SARS and other respiratory viruses as the infected individuals can be highly contagious for several days before the appearance of symptoms (Anderson *et al*., 2020; He *et al*., 2020).

There is a growing body of concern about the transmissibility of infection between humans and certain animal species. Although coronavirus infections in pets are known to be predominantly related to the gastrointestinal tract, it has been observed that there are human-to-animal transmissions of COVID 19 and some animals have similar symptoms to humans (Gonultas *et al*., 2020). There are potential for domesticated (companion) animals to serve as a reservoir of infection contributing to continued human-to-human disease, infectivity, and community spread. These may produce consequences to food security, economy, and trade issues if coronavirus gets established itself within livestock and poultry (Mcnamara *et al*. 2020). At the moment, there is no evidence to conclude that SARS-CoV-2 is transmitted through foods. However, the transmission is indeed possible if an infected individual touches food. Here, we have reviewed the general description of the virus, the disease, its epidemiology, diagnosis, and mitigation strategies.

THE VIRUS

Coronavirus (CoV) belongs to the subfamily Orthocoronavirinae of Coronaviridae family under the Order Nidovirales. HKU1, NL63, 229E, and OC43 are the four known CoVs that have been reported in humans causing mild respiratory disease (Singhal, 2020). CoV, the largest genome of known RNA viruses, is enveloped, positive-sense, single-

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stranded RNA with the size varying between 26 to 32 kb. CoVs are reported to manifest respiratory, enteric, hepatic, and neurologic diseases (De Wilde *et al.*, 2018). Based on the genotypic and serotype characteristics, subfamily Orthocoronavirinae has four genera namely, alpha-corona virus (á- CoV), beta-corona virus (a- CoV), gamma-corona virus (ã- CoV) and delta-corona virus (ä- CoV) (Li *et al.*, 2020). Mammals are frequently infected with a- and a- CoV, while birds with ã- and ä- CoV. Further, a- CoV is responsible for Severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS) viral pneumonia outbreaks (Song *et al.*, 2019; Li *et al.*, 2020). Recently, the coronavirus study group of the International Committee on Taxonomy of Viruses has designated the present CoV as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Gorbalenya *et al.*, 2020). The sequence analysis revealed that SARS-CoV-2 belongs to â-CoV (Zhou *et al.*, 2020).

The genome of SARS-CoV-2 virion is 29.90 kb with a nucleocapsid buried inside the phospholipid bilayers covered by two different types of spike proteins namely, the spike glycoprotein trimmer (S) with membrane (M) protein and envelope (E) protein present in all CoVs and the haemagglutinin-esterase (HE) shared among certain CoVs (Wu ., 2020). The phylogenetic analysis indicated that SARS-CoV-2 shared 79.50% and 50% sequence identity to SARS-CoV and MERS-CoV, respectively (Jin *et al.*, 2020; Zhou *et al.*, 2020). Nevertheless, the sequence identity between the conserved replicase domains in ORF1ab of SARS-CoV-2 and SARS-CoV (94.60%) and those of SARS-CoV-2 and other â-CoVs (less than 90%) vindicate that SARS-CoV-2 belongs to the lineage B (Sarbecovirus) of â-CoVs (Wu *et al.*, 2020).

THE DISEASE

The virus utilizes human angiotensin-converting enzyme- 2 (ACE-2) functional receptor for entry into the cell, as in the case of SARS CoV (Zhou *et al.*, 2020). ACE-2 receptors, expressed in lung, heart, kidney, and intestine (Donoghue *et al.*, 2000), will bind directly to the S proteins of CoVs and undergo structural rearrangement to enable the fusion of viral membrane with the host cell membrane (De Wilde *et al.*, 2018; Jin *et al.*, 2020). Upon its entry into alveolar epithelial cells, the SARS-CoV-2 replicates rapidly which results in cytokine storm syndrome (hypercytokinaemia) and damage to the pulmonary tissue. A cytokine storm is a group of disorders characterized by uncontrolled production of pro-inflammatory cytokines that would be culminated in acute respiratory distress syndrome (ARDS) and multiple organ failure (Li *et al.*, 2020).

The major routes of transmission in humans include respiratory droplet and contact transmission. The potential ways of transmission of SARS-CoV-2 are given in Figure 1. It is recently reported that the SARS-CoV-2 could be detected in the urine and faeces of laboratory-confirmed individuals; hence implies to the faeco-oral transmission, also (NHC, 2020). Nonetheless, the transmission mediated by consumption of virus-contaminated foods, aerosols and *in utero* is not certain. Of late, COVID patients are the prime source of infection; asymptomatically infected persons, patients in the incubatory stage of infection are proven to shed infectious virion and could serve as a potential source (Hoehl *et al.*, 2020).

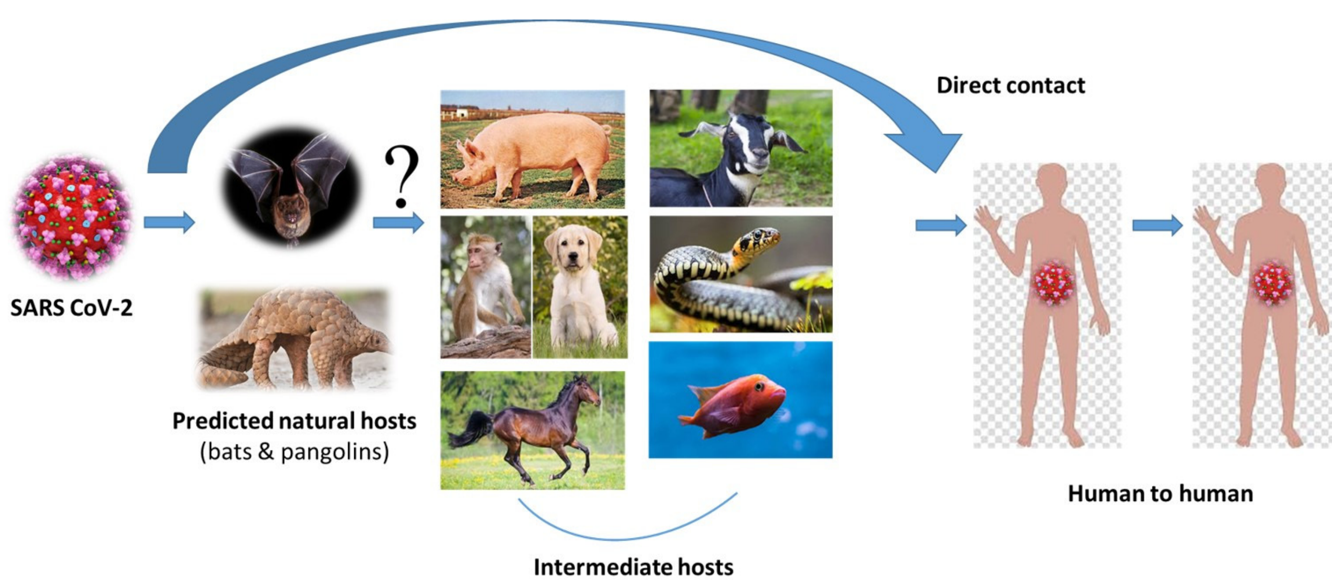

Fig. 1. Potential ways of transmission of SARS-CoV-2. Bats and pangolins are susupected as natural hosts and reservoirs of the corona viruses. Various wild and companion animals are suspected to be involved in transmission. In humans, human –human transmission is the principal way of transmission.

The transmission efficiency of any respiratory virus has significant implications in its mitigation. The basic reproductive number (R0) of SARS-CoV-2, in its initial evaluation, is estimated to be 2.20 (1.40-3.90), which implies that on average, each infected person could spread the infection to another two individuals (Li *et al*., 2020). The high viral titers, however, observed in the oropharynx during the early stage of infection, would arouse serious concern regarding the enhanced infectivity during minimal disease symptoms. The R0 of SARS-CoV and MERS-CoV in the absence of intervention was found to be 2.30-3.70, while when mitigation strategies were employed the R0 dropped to less than 1.0 (Sun *et al*., 2020), explaining why the outbreak could be controlled. It could be worth mention to note that the R0 estimates may vary upon numerous exogenous factors (biological, socio-behavioral, and environmental) and should be cautiously interpreted.

CLINICAL SYMPTOMS

The incubation period of COVID-19 infection is estimated to be nearly 5.2 days; however, 6 to 41 days has been recorded to be the period from disease onset to death with a median of 14 days (Li *et al*., 2020; Wang *et al*., 2020). Moreover, this period is dependent on the age of the individual and their immune system; wherein the infection is prominent among the patients of age higher than 70 years as compared to those below 70 years of age (Wang *et al*., 2020). Further, neonates, infants, and children reported milder infection than their adult counterparts (Singhal, 2020).

The unique clinical features of COVID-19 infection were targeted primarily towards the lower respiratory tract than upper respiratory tract symptoms like rhinorrhoea, sneezing, and sore throat (Rothan and Byrareddy, 2020). The most common symptoms of this infection include fever, cough, and fatigue, while other associated symptoms include headache, haemoptysis, diarrhoea, dyspnoea, sputum production, and lymphopenia (Carlos *et al*., 2020; Rothan and Byrareddy, 2020). The clinical features of COVID-19 infection evidenced by chest CT scan presented pneumonia; nonetheless, RNAemia, acute respiratory distress syndrome (ARDS), acute cardiac injury and incidence of bilateral ground- grass opacities of sub-pleural regions leading to death were the abnormal features which would result in systemic as well as localized immune response (Huang *et al*., 2020). Besides, a few cases were found to worsen the condition characterized by progressing pulmonary opacities while treated with interferon inhalation (Lei *et al*., 2020). Interestingly, patients with COVID-19 infection developed gastrointestinal symptoms such as diarrhoea which necessitates the testing of faecal as well as urine samples as a potential alternate source of transmission, particularly through the health-care personnel (Rothan and Byrareddy, 2020), which would mitigate the transmission and further to develop therapeutics to alleviate the infection.

EPIDEMIOLOGY

Near about 75 % of Coronavirus infections are zoonotic i.e., animals serve as the main source of infections. As of now, bats are considered as a reservoir of all human coronaviruses (Gorbalenya *et al*., 2020, Shen *et al*., 2020) however, the type of animal which has originated SARS-COV-2 virus is yet not clear. A study based on the genome sequence of SARS-CoV-2, reported that the virus originated from bats was almost 96% identical to bat coronavirus RaTG13 (Zhou *et al*., 2020). Also, there were speculations that SARS-CoV-2 is a laboratory-engineered CoV and leaked directly from a laboratory in Wuhan where a bat CoV (RaTG13) was recently reported, but, there is no evidence to support this allegation (Liu *et al*., 2020). Besides, researchers are trying to trace the main source of COVID-19 outbreak and also to determine the definitive and intermediate hosts. In 2003, the closely related SARS-CoV had been detected in domestic cats and dogs (WHO, 2003). However, in a recent study, two of the fifteen dogs from households with confirmed human cases of COVID-19 from Hong Kong SAR were found to be infected with SARS-CoV-2. The evidence suggests humans to the animal transmission of the SARS-CoV-2 virus. However, it is unclear, whether the infected dogs can transmit the virus to other animals or back to humans (Lun and Qu, 2004). Recently, a group of researchers found that SARS-CoV-2 replicates poorly in dogs, pigs, chickens, and ducks but efficiently in ferrets and cats (Hualan, 2020).

At the beginning of the Wuhan outbreak, the patients found positive earlier were linked to the Huanan seafood wholesale market suggesting an animal to human spread. However, after retrospective case studies, it was found that persons who never had exposure to seafood markets were also found positive suggesting a person to person spread. It is presumed that the transmission of SARS-CoV-2virus occurs mainly through respiratory droplets. For example, when an infected person sneezes or coughs, the respiratory secretion is released in the form of droplets which then can infect another person if their mucous membranes come in direct contact with the droplets. Also, the transmission of infection can occur unknowingly, if a person touches an infected surface and then proceeds to touch his own eyes, nose, or mouth. Besides, asymptomatic carriers and/or patients who have recovered from the acute form of the disease are also considered as a potential source of virus transmission to healthy persons (CDC 2020; Mosites *et al*., 2020). However, vertical transmission of the virus from mother to fetus or via breast milk has not been documented yet (Huang *et al*., 2020).

Generally, droplets generated through respiratory secretions do not travel more than six feet (approximately 2 meters) and also they do not linger in the air for a longer time (Stadnytskyi *et al*., 2020). Although, the transmission of the virus through airborne route under natural conditions is yet a controversial issue. A study in which SARS-CoV-2 virus grown in tissue culture remained viable in experimentally generated aerosols for at least three hours (van Doremalen *et al*., 2020); some have identified RNA of the virus in the ventilation systems and air samples of the hospital rooms where COVID-19 patients were hospitalized, however, virus isolation was not performed in these studies (Ong *et al*., 2020; Guo *et al*., 2020; Liu *et al*., 2020). Other studies using specialized imaging system have suggested that respiratory droplets generated while speaking, coughing, or sneezing may get aerosolized or carried in a gas cloud and can spread horizontally beyond six feet (two meters) *et al*., 2020; Bourouiba *et al*., 2020; Stadnytskyi *et al*., 2020). However, the direct relevance of these findings to the epidemiology of COVID-19 and their clinical implications are unclear. Also, long-range airborne transmission of SARS-CoV-2 has not been documented (Lu *et al*., 2020).

Further, it has been observed that human coronaviruses can survive on steel, metal, wood, aluminum, paper, glass, plastic, ceramic, disposable gowns, and surgical gloves for almost 2–9 days. Besides this, high temperature (e”30 æ%C) has shown to reduce the persistence period of the virus in the environment, while low temperature (4 æ%C) has increased the persistence time of the virus up to 28 days (Bajema *et al*., 2020). SARS-CoV-2 (as well as other coronaviruses) has been found in the fecal samples and rectul swabs of some patients (La Rosa *et al*., 2020). However, there is no current evidence that human coronaviruses are present in surface or ground waters or are transmitted through contaminated drinking water. The available data suggest that CoV has low stability in the environment and is sensitive to oxidants, like chlorine., and seems to be inactivated significantly faster in water than non-enveloped human enteric viruses with the known waterborne transmission. The titre of infectious virus declines more rapidly at 23°C-25 °C than at 4 °C) (La Rosa *et al*., 2020). However, the virus can be efficiently inactivated within 1 minute by surface disinfection procedures with either 62–71% ethanol, 0.5% hydrogen peroxide and or 0.1% sodium hypochlorite (Kampf *et al*., 2020). There have been potential risks of transmission of SARS-CoV-2 between humans and their pets because of their close association. Detection of viral RNA has been reported in two dogs and two cats, which belonged to SARS-CoV-2 infected owners, in Hong Kong and Liège, Belgium (Leroy *et al*., 2020). A study conducted among SARS-CoV-2 positive patients (median age 49 years), found that half of them had comorbidities, including diabetes (20%), cardiovascular disease (15%), and hypertension (15%). The main symptoms were fever (98%), cough (76%), and fatigue (44%) (Bastola *et al*., 2020).

DIAGNOSIS

The differential diagnosis should always be undertaken to distinguish the SARS-CoV-2 from influenza virus, parainfluenza virus, adenovirus, respiratory syncytial virus, rhinovirus, human metapneumovirus, SARS coronavirus, and other known viral infections, as well as *Mycoplasma pneumoniae* and *Chlamydia pneumonia* and bacterial pneumonia. Also, the coinfection of SARS-CoV-2with other viruses and/or bacteria should be considered during the diagnosis of COVID-19 infection inpatient.

Based on Clinical Symptoms and History: Patients with onset of fever and/or respiratory tract symptoms such as cough, dysponea, and difficulty in breathing are suspected to be COVID-19 patient. The other symptoms such as myalgias, diarrhoea, and smell or taste aberrancies can also be exhibited by a COVID-19 patient. Although these symptoms can also occur with other viral respiratory illnesses, hence to increase the likelihood of COVID-19 it is equally important to know the history of patients such as travel history since the past 14 days to a location where there is community transmission of SARS-CoV-2 had occurred. Secondly, close contact with a confirmed or suspected case of COVID-19 in the prior 14 days, including through work in health care settings. Close contact includes being with a patient for a prolonged period without wearing personal protective equipment (PPE) or having direct contact with infectious secretions.

Nucleic acid based testing: All symptomatic patients should undergo testing. Each local health departments have specific criteria for testing. Also testing criteria have been suggested by the WHO. Normally, the diagnosis of COVID-19 is made by the detection of SARS-CoV-2 RNA employing reverse transcription-polymerase chain reaction (RT-PCR) (Patel *et al*., 2020). Various RT-PCR assays are used across the globe. These different assays amplify and detect different regions of the SARS-CoV-2 genome. Some of the common gene targets include nucleocapsid (N), envelope (E), spike (S), and RNA-dependent RNA polymerase (RdRp), as well as regions in the first open reading frame (WHO, 2020). As per the CDC and WHO, upper respiratory samples such as nasopharyngeal, oropharyngeal, and nasal swabs are the primary specimens for SARS-CoV-2 RT-PCR testing. All these samples need to be collected by trained health care professionals. In some cases, if the upper respiratory specimen turns out negative despite having clinical symptoms, then in such cases, lower respiratory tract specimens such as tracheal aspirate or bronchoalveolar lavage should be collected. Besides, additional information on testing and handling of clinical specimens can be found on the CDC and WHO websites. A positive test for SARS-CoV-2 generally confirms the diagnosis of COVID-19. In case if the test negative but the suspicion for COVID-19 remains, then in such cases testing should be repeated. Repeat testing is performed 24 to 48 hours after the initial test. Also, in such cases, WHO recommends testing a lower respiratory tract specimen if the patient has evidence of lower respiratory tract illness (WHO, 2020).

Besides, nucleic acid-based detection that has been developed for the diagnosis of SARS-CoV-2 is the reverse transcription loop-mediated isothermal amplification (RT-LAMP). The developed assay targets ORF1ab, spike (S), envelope (E) or/ and N gene of SARS-CoV-2 (Yang *et al*., 2020a; Zhang *et al*., 2020c; Yu *et al*., 2020; Lamb *et al*., 2020; Mohamed *et al*., 2020; Huang *et al*., 2020; Yan *et al*., 2020) and it can be performed under isothermal conditions and the results can be produced within 15-40 minutes. The detection limit of the assay is about 5-10 RNA copies with a 99-100 % agreement with the commercial RT-qPCR (Yang *et al*., 2020a; Zhang et. al., 2020c; Yan *et al*., 2020). Besides, some recent studies have shown that RT-LAMP targeting the N gene of SARS-CoV-2 can specifically detect viral RNAs of SARS-CoV-2 but has no cross-reactivity with related coronaviruses, as well as human infectious influenza viruses, and other respiratory disease-causing viruses (Baek *et al*., 2020).

Another important addition in the nucleic acid-based detection method for SARS-CoV-2 diagnosis is the CRISPR-based nucleic acid detection platforms (SHERLOCK or DETECTR). These detection platforms can detect the virus as low as 10 copies/ìL and can be successfully used at point-of-care (Metsky *et al*., 2020; Lucia *et al*., 2020; Kostyusheva *et al*., 2020; Zhang *et al*., 2020a; Broughton *et al*., 2020). The results of these novel methods can be analyzed by fluorescent or lateral flow strip in <1 h with a setup time of less than 15 min (Kellner *et al*., 2019). Further, on comparison of the CRISPR-based assays and the RT-qPCR recommended by CDC/WHO for SARS-CoV-2 detection, it was found thatRT-qPCR was more sensitive, however, CRISPR-based assays were more convenient and timesaving than RT-qPCR (Li and Ren, 2020).

Serology based testing: The serological assays detect antibodies to SARS-CoV-2 in the blood or serum. These assays may sometime also identify some patients with current infection (particularly those who present late in the course of illness), however, these serological assays are less reactive in the first several days to weeks of infection, and therefore their utility for diagnosis in the acute setting is limited (Guo *et al*., 2020; Zhao *et al*., 2020; Qu *et al*., 2020; Zhang *et al*., 2020). Normally, detectable antibodies generally take several days to weeks to develop. In a study of 173 patients with COVID-19, the median time from symptom onset to antibody detection was 12 days for IgM and 14 days for IgG (Zhao *et al*., 2020). In the first week since symptom onset, fewer than 40 percent had detectable antibodies; but by day 15, IgM and IgG were detectable in 94 and 80 percent, respectively. FDA reckons that serologic tests should never be used as the sole test to diagnose or exclude active SARS-CoV-2 infection, because, the sensitivity and specificity of these tests are uncertain. However, large-scale serologic screening with validated tests may assist in sensing the burden of disease (identifying people who were not diagnosed by PCR or who may have had an asymptomatic or subclinical infection) and also identify individuals who may have immunity to infection.

Presently the most commonly used serological methods for detection of SARS-CoV-2 are Enzyme-linked immunosorbent assay (ELISA), colloidal gold immunochromatographic assay (GICA), and chemiluminescence-immunoassay (CLIA). Also, the results of antibody-based methods (IgG and IgM derived against recombinant N and S proteins of SARS-CoV-2) are inconsistent with the results obtained by nucleic acid-based assay (Zhong *et al*., 2020; Cai *et al*., 2020; Lin *et al*., 2020b; Jia *et al*., 2020; Xiang *et al*., 2020b; Li *et al*., 2020b). Moreover, a recent report showed that IgA level in patient serum is positively correlated with the severity of the COVID-19 (Ma *et al*., 2020), indicating that serum IgA can also be used as a biological marker for the COVID-19 identification.

Other laboratory testing: Normally blood profiles of patients suffering from SARS-CoV-2 infection reveal following, increased C-reactive protein and erythrocytes, increased myohemoglobin, liver enzymes, and muscle enzymes, with a high level of D-dimer in severe cases, and normal or decreased white blood cell counts and lymphocytes in the early stage of the disease, with advanced lymphocytopenia in severe cases (Shen *et al*., 2020). In ICU patients, high levels of plasma granulocyte colony-stimulating factor (GCSF), IP10, IL2, IL7, IL10, TNF-á, and MIP1a have been reported. Besides, Chest X-ray examination may be useful to detect COVID-19 patients, because, during the early stage of the disease, interstitial changes and multiple small plaque shadows are often observed. Also, Chest CT scans play an important role in the diagnosis of SARS-CoV-2. In the early stage of the disease, chest images show multiple small plaques and interstitial changes, which are obvious in the lung periphery, further deteriorate to bilateral multiple ground-glass opacity and/or infiltrating shadows. Lung consolidation may occur in severe cases. Pleural effusion is rarely seen (Shen *et al*., 2020).

VACCINES AND THERAPEUTICS

Until vaccines are available, non-pharmacological interventions will likely remain the primary line of defense to contain this pandemic. No clinically approved antiviral drug or vaccine against COVID-19 is reported yet. Many approaches are in progress to produce a vaccine for SARS-CoV-2 including the classical inactivated and attenuated vaccines, the protein subunit and virus-like particle vaccines (VLP), viral vector-based vaccines, as well as the newer DNA- and RNA-based vaccines (Uddin *et al*., 2020; Callaway, 2020). So far, the mRNA-1273 vaccine has entered into clinical trials. It uses part of the spike protein genetic code embedded in special lipid-based nanoparticles for injection into the body (Hodgson, 2020). Other than these, there has been an acceleration in developing other novel vaccine approaches, for example, Inovio Pharmaceuticals' INO-4800 is a DNA-based vaccine using the spike gene and Codagenix, in collaboration with Serum Institute of India, has used a reverse strategy to create a live-attenuated vaccine.

Classic adaptive immunotherapy that has been applied to many infectious diseases for more than a century for prevention and treatment is convalescent plasma (CP) Therapy. CP has been tried successfully against SARS, MERS, and H1N1 infection (Cheng *et al*., 2005; Ko *et al*., 2018). In this therapy, plasma (with neutralizing antibodies) extracted from a donor recovered from the infection is administered to infected patients. Tocilizumab is a humanized monoclonal antibody against the interleukin-6 receptor (IL-6R) that is approved to treat patients with rheumatoid arthritis, systemic juvenile idiopathic arthritis, and giant cell arteritis (Zhang *et al*., 2020) is a key mediator of cytokine release storm (CRS) observed in critically ill COVID-19 (Zhang *et al*., 2020). Obstructing the interaction of SARS-CoV-2 with the viral spike protein to gain entry into human cells could potentially be used as an effective treatment in COVID-19 patients (Zhang *et al*., 2020).

The approach of repurposing old drugs with antiviral properties and agents approved or under investigation for other viral infections has been adopted to find an effective treatment for symptomatic patients. In the absence of a vaccine, the SOLIDARITY trial has been recently launched by WHO to address this challenge. The drugs included in this trial are lopinavir and ritonavir, lopinavir, and ritonavir plus interferon beta as well as chloroquine, and redeliver (Uddin *et al*., 2020). Lopinavir-Ritonavir has been used either on its own or in combination with either alpha interferon or chloroquine/hydroxychloroquine for COVID-19 treatment with some success (Lim *et al*., 2020; Yan *et al*., 2020). Favipiravir (FPV), an RNA-dependent RNA polymerase inhibitor, is useful against SARS-CoV-2 in initial clinical trials (Cai *et al*., 2020).

Chloroquine is thought to inhibit virus replication by increasing endosomal pH as many viruses such as Ebola and Marburg that require the acidic environment of the endosome for successful replication (Akpovwa, 2016; Li *et al*., 2017). Hydroxychloroquine, an analog of chloroquine, is more stable with better clinical safety profile and has anti-SARS-CoV-2 activity (Uddin *et al*, 2020) and has been shown to quicken recovery and clearance of the virus in COVID-19 patients and used successfully in combination with the macrolide antibiotic azithromycin (Gautret *et al*., 2020). However, disappointing results have shown with the combination of azithromycin with hydroxychloroquine in critically-ill COVID-19 patients in a recent clinical trial (Molina *et al*., 2020).

Remdesivir, a nucleotide analog prodrug with broad-spectrum antiviral activity against many RNA viruses (Sheahan *et al*., 2017), has shown to inhibit replication of MERS-CoV, SARS-CoV, and SARS-CoV-2 in animal models (Sheahan *et al*., 2017; 2020; Wang *et al*., 2020; de Wit *et al*., 2020). Results on multiple clinical trials of remdesivir in several countries for more conclusive guidelines on its use in COVID-19 patients are awaited. It has been hypothesized national vaccination policies such as universal Bacillus Calmette-

Guérin (BCG) childhood vaccine may impact the severity of the pandemic and the transmission patterns of SARS-CoV-2 including morbidity and mortality (Gursel and Gursel, 2020; Ozdemir *et al*., 2020).

ONE HEALTH APPROACH

The world itself has transformed into a global village by the advent of a technological revolution. It is well evident that COVID-19 is an epitome of the complex threats of emerging infections in humans and animals. Along with such infections, are allied public health threats comprising of antimicrobial resistance, food safety, and environmental issues related to escalating population growth. Such complex public health threats demand solutions based exclusively on interdisciplinary 'One Health' approach which could engage professionals from various disciplines (human, veterinary, environmental, and social sciences) (Zowalaty and Järhult, 2020). This approach would identify and emphasise interrelationship between experts from various domains and encourages collaborative efforts to improve public health through animal as well as ecosystem health. Besides, the expert team could effectively recognise source of emerging pathogens and find suitable ways to reduce its outbreak (Lebov*et al*.,

In recent times, it has been proven that SARS CoV-2 is most likely to be a bat-origin virus that has been occurred through a spillover mechanism from bats or any completely undetermined animal host (avian, bovine, canine, swine, phocine or wild animals). The animals sold from the wet markets of Wuhan province ranged from poultry, wild birds, and exotic animals (frogs, civets, snails, crocodiles, snakes, cicades) to reptiles and hedgehogs (Wu *et al*., 2020). However, scientific data concerning the detection of SARS CoV-2 from any of the associated environmental samples are sparsely available (Zowalaty and Järhult, 2020). For expediting host-pathogen interaction of this pandemic requires exploring the intermediate host(s) of SARS CoV-2, its disease dynamics (including, biosurveillance and biosecurity) and the possibility of reverse zoonosis that warrants interaction between different disciplines working cohesively with an ultimate aim to reduce the transmission and further spread of infection. This demands urgent implementation of a multidisciplinary team in a One Health approach to address the present-day challenges at the human-animal-environment interface.

IMPACT ON THE MEAT SECTOR

COVID-19 had a tremendous effect on the Indian meat industry. The sector is passing through a difficult phase. Among various sectors, the poultry industry got affected the most due to misinformation and rumors linking Coronavirus with poultry products. Buffalo meat export was also affected badly mainly due to the stoppage of the functioning of export abattoirs and problems in transportation of livestock carrying vehicles especially at interstate borders consequent to restriction on movement of labour working in the abattoirs.

Restrictions on the movement of livestock and persons due to lockdown and an interstate ban on travel, closing down of restaurants, unjustified rumours and decreasing disposable income among consumers are among the major reasons affecting meat consumption and demand in India. Learning the lessons from the current pandemic, the meat industry needs to look forward and work on alternatives to overcome such situations. There is a need to encourage the online trade. The cold storage capacity to store meat and meat products during the period of slump needs to be enhanced. Promotion of marketing of hygienically produced packaged and chilled/frozen meat needs to be encouraged. Shelf-stable meat products may be produced in case of surplus meat is available. The unscientific, generally unhygienic practices of selling meat roadside need to be given away.

Congregate work and residential locations are at increased risk for infectious disease transmission including respiratory illness outbreaks. Nationwide the meat and poultry processing industry employ a huge number of persons, many of whom work in proximity to other workers. In the US, aggregate data on COVID-19 cases among 115 meat or poultry processing facilities in 19 states revealed COVID-19 in 4,913 (approximately 3%) workers, and 20 COVID-19-related deaths (Dyal *et al*., 2020). Academic researchers and food sector experts will have to ensure food safety and food security, introduce tools to reduce losses and waste of food, as well as identify alternative and safe protein sources that meet the nutritional expectations of consumers (Galanakis, 2019; 2020). There is undoubtedly a need to think out of the box and accelerate efforts to develop sustainable and modern food systems, e.g., to reduce the cost of aseptic lab-grown meat, reduce the cost of food waste recovery and reutilization in the food chain, and develop new and large food supply chains.

PREVENTION AND CONTROL

Globally robust steps have been taken to monitor the current outbreak and to reduce the transmission of COVID-19 infection particularly banning international and domestic flights, inducting lockdowns in vulnerable areas, social distancing, etc. Dietary supplementation with the vitamins D and E, bioactive lipids, flavonoids, and herbs may be a tool to support the human immune system against COVID19 (Galanakis, 2020; Wang *et al*., 2020). The oral or intravenous administration of bioactive lipids (such as arachidonic acid and other unsaturated fatty acids) may aid in enhancing resistance and recovery from SARS-CoV-2, SARS, and MERS infections (Das 2020).

In the meat industry, the methods to decrease transmission include a screening of workers for symptoms, social distancing, and policies to discourage working while experiencing symptoms compatible with COVID-19. Source control measures (e.g., use of mask), as well as increased disinfection of high-touch surfaces, are also important means of preventing SARS-CoV-2 exposure. Implementation of these public health strategies will help protect workers from COVID-19 in this industry and assist in preserving the critical meat and poultry production infrastructure. Extensive hand washing or sanitizing should be followed while the handling of packages to minimize any risk from touching food potentially exposed to coronavirus (FSHN, 2020). Suggested ways of prevention of spread of SARS-CoV-2 in food industries are given in Figure 2.

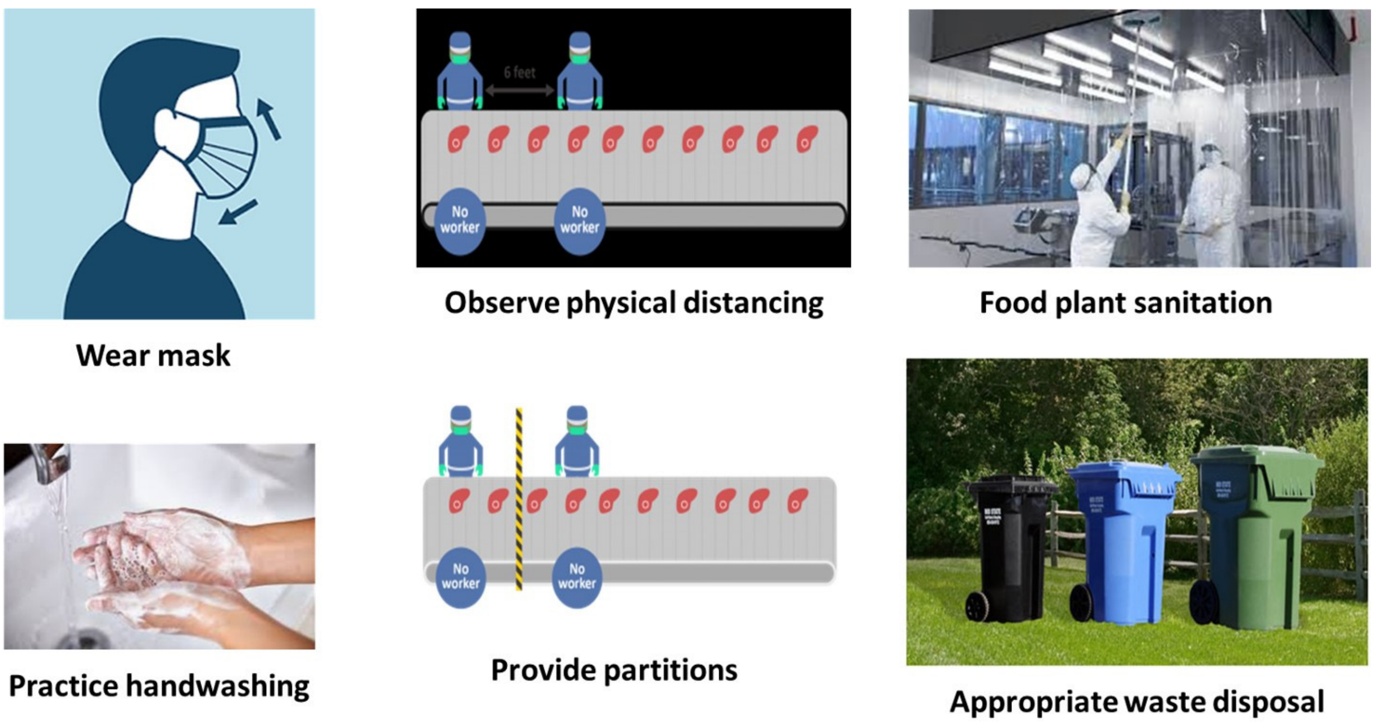

Fig. 2 Suggested ways of prevention of spread of SARS-CoV-2 in food industries.

Recently, it has been shown that SARS-CoV-2 may be transmitted through aerosols in addition to droplets. A study in China found SARS-CoV-2 in aerosols further than 6 ft from patients with higher concentrations detected in more crowded areas (*Liu et al*., 2020). It has been indicated that 1 min of loud-speaking could generate >1000 virion-containing aerosols as estimated using an average sputum viral load for SARS-CoV-2 (Stadnytskyi *et al*., 2020).

The recommendations for the social distancing of 6 ft and hand washing to reduce the spread of SARS-CoV-2 by WHO is based on studies of respiratory droplets carried out in the 1930s (Prather *et al*., 2020). It has been suggested that the 6 ft distancing is likely not enough under many indoor conditions where aerosols can remain airborne for hours, accumulate over time, and follow air flows over distances further than 6 ft (Mittal *et al*., 2020; Buonanno *et al*., 2020).

Meat industry personnel are required to work in their usual workplaces and therefore Food Safety Management Systems (FSMS) based on the Hazard Analysis and Critical Control Point (HACCP) principles should be in place. There is now an urgent requirement for the meat industry to ensure compliance with measures to protect workers from contracting COVID-19 or similar infections, to prevent exposure to or transmission of the virus, and to strengthen food hygiene and sanitation practices.

Staff working in the food/meat sector needs to be aware of the symptoms of COVID-19 because they can recognise symptoms early and accordingly can seek appropriate medical care and testing, which in turn can minimise the risk of infecting their fellow workers. The most common symptoms of COVID-19 include fever (high temperature – 37.5^{o}C or above), cough - this can be any kind of cough, not just dry, shortness of breath, breathing difficulties, and fatigue. The food/meat industry should ensure that all personnel working in the food industry, regardless of their apparent health status, should practice personal hygiene and appropriately use PPE.

Food safety practices in food premises should continue to be delivered to the highest hygiene standards such as proper hand hygiene, frequent use of alcohol-based hand sanitizers; good respiratory hygiene, frequent cleaning/disinfection of work surfaces and touchpoints such as door handles; staggering workstations on either side of processing, providing PPE such as face masks, hair nets, disposable gloves, clean overalls, and slip reduction work shoes for staff. At retail food/meat premises maintaining physical distancing is critical. Also regulating the numbers of customers who enter the retail shop, using floor markings inside the retail store to facilitate compliance, encouraging the use of contactless payments; and advising the consumers to bring their shopping bags are necessary.

In India, Food Safety and Standards (Licensing and Registration of Food Businesses) Regulations 2011, in Part IV of Schedule 4 outlines specific Hygienic and Sanitary Practices to be followed by Food Business Operators engaged in the manufacture, processing, storing and selling of Meat and Meat Products. This covers the requirements to be followed by slaughterhouses, meat processing units, and retail meat shops which include location, equipment and machinery, sanitary facilities, ante-mortem, and post-mortem inspection, animal welfare, personal hygiene, and health requirements and others. Community-wide mask-wearing may contribute to the control of COVID-19 in a community can be hampered by wearing community-wide masks that reduce the amount of emission of infected saliva and respiratory droplets from individuals with subclinical or mild COVID-19.

CONCLUSIONS AND PERSPECTIVE

Coronavirus disease 2019 (COVID-19), a global pandemic caused by the zoonotic SARS-CoV-2, represents a critical pivot point in modern times and is a world-changing event. The pandemic nature of the COVID-19 insists rigorous surveillance and on-going monitoring to accurately track and potentially predict its future host adaptation, evolution, transmissibility, and pathogenicity. These factors also influence mortality rates and prognosis in human patients. The unique features of this episode are its assumed origin at the human–environment–animal interface and its rapid explosion as a result of unprecedented levels of human interconnectivity, mobility, and global trade. The involvement of companion animals in the transmission of the infection may complicate the food web. The event exemplifies One Health, the fundamental interconnectedness of humans, animals, and their shared environment, is key to ensuring the healthy and sustainable future of the planet. Identification of the possible zoonotic emergence and the exact mechanism responsible for its initial transmission would pave the way to design and implement appropriate preventive barriers against the further transmission of SARS-CoV-2. Application of modern tools like artificial intelligence need to be evaluated to predict and track infections to better prepare for future episodes.

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