

Review Article

Indian J Med Res 153, May & June 2021, pp 577-584
DOI: 10.4103/ijmr.IJMR_2971_20



Increased human-animal interface & emerging zoonotic diseases: An enigma requiring multi-sectoral efforts to address

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Increased human–animal interfaces impose threats on human life by creating scope for the emergence and resurgence of many infectious diseases. Over the last two decades, emergence of novel viral diseases such as SARS, influenza A/H1N1(09) pdm; MERS; Nipah virus disease; Ebola haemorrhagic fever and the current COVID-19 has resulted in massive outbreaks, epidemics and pandemics thereby causing profound losses of human life, health and economy. The current COVID-19 pandemic has affected more than 200 countries, reporting a global case load of 167,878,000 with 2 per cent mortality as on May 26, 2021. This has highlighted the importance of reducing human– animal interfaces to prevent such zoonoses. Rapid deforestation, shrinking of boundaries between human and animal, crisis for natural habitation, increasing demands for wildlife products and threat of extinction compounded by biodiversity narrowing compel to increased human–animal conflict and contact. Large quantities of animal waste generated due to animal agriculture may also allow rapid selection, amplification, dissemination of zoonotic pathogens and facilitate zoonotic pathogen adaptation and hinder host evolution for resistance. Public health system faces challenges to contain such epidemics due to inadequate understanding, poor preparedness, lack of interdisciplinary approach in surveillance and control strategy and deficient political commitments. Because the management measures are beyond the purview of health system alone, policy-level adaptation in the transdisciplinary issues are required, emphasizing the engagement of multiple stakeholders towards wildlife protection, alternative land use, community empowerment for natural resource management and regulation on business of wildlife products to ensure comprehensive one health practice.

Key words Epidemic - human–animal interface - influenza - one health - SARS - zoonoses

Global increase in human–animal interfaces and mixing of different species of animals in human-dense markets, facilitated the emergence of novel viral diseases such as severe acute respiratory syndrome (SARS), avian influenza A/H7N9, H5N1, Middle East respiratory syndrome (MERS); Nipah virus disease; Ebola haemorrhagic fever, Influenza A (H1N1) 09 pandemic and the current COVID-19 disease¹⁻³. In 2002, the world was hit by SARS caused by SARS-CoV³;

a decade later, the world witnessed the emergence of another novel corona virus, MERS coronavirus and both originated from animals and then transmitted to human¹⁻³. Human Nipah virus infection, characterized primarily by fever and encephalitis, is another example of zoonotic disease causing recurrent outbreaks in some Asian countries⁴. Ebola haemorrhagic fever, another disease of zoonotic origin, is recognized worldwide as a severe, fatal disease-causing large-scale recurrent

outbreak in African countries⁵. The ongoing COVID-19 pandemic caused by SARS-CoV-2 is another addition in this list. All these diseases have caused significant mortality and morbidity and have left a huge impact on health systems, society and economy of not only the affected States/countries but also the global economy. Although the emergence and re-emergence of zoonotic diseases causing recurrent outbreaks/epidemics have increased in the last three decades, but the holistic preventive measures are still lacking in most of the countries. In this review, we tried to understand how the increased human–animal interfaces put the global health under clinical, humanitarian, ethical crisis and the possible one health approach to reduce the threats of such diseases.

Emerging and re-emerging zoonotic infections causing recurrent large outbreaks/epidemics/pandemics

Severe acute respiratory syndrome (SARS)

In 2002, SARS started in Guangdong province of China and with time, it spread over 29 countries, causing 8422 cases and 916 deaths preparing a stage for global public health partnership⁶⁻⁸. However, identification and segregation of the intermediate amplifying hosts from humans led to successful containment of this outbreak in many places and finally, the pandemic ended within seven months of its origin. Epidemiologic tracking of this pandemic was possible due to viral genome sequencing. Identifying SARS-CoV-related viruses in Himalayan palm civets and Raccoon dogs⁶⁻⁸ confirmed its zoonotic origin. Though masked palm civets were initially perceived as animal of origin, genetically diverse coronaviruses for SARS have also been identified in various species of horseshoe bats (genus *Rhinolophus*)⁹.

Middle East respiratory syndrome (MERS)

In 2012, the outbreak of MERS coronavirus disease occurred in the Middle East¹⁰. Saudi Arabia was the country of origin, however, gradually it spread to Europe, Asia, Africa and North America¹¹. At the beginning, due to its similar clinical manifestations and high case fatality rate (CFR) like SARS, it was called SARS-like illness as the other human coronaviruses usually caused mild, self-limiting upper respiratory tract illness¹² (Table). Like SARS, MERS was also identified as a potential pandemic agent due to its transmissibility from person-to-person and limited effective therapeutic agents¹¹. It was hypothesized that MERS probably originated from animal reservoirs and

human infection happened as it crossed interspecies barriers¹². Though the SARS epidemic died off quickly, MERS epidemic persisted for two years within a few countries. During April 2020, laboratory-confirmed MERS cases started to appear again from Saudi Arabia and till May 31, nine MERS cases got reported¹³.

Ebola virus disease

Another deadly virus of zoonotic origin having immense focus from international public health fraternity is Ebola virus. For the last 40 yr, African countries have faced many outbreaks of Ebola virus disease with a CFR ranging from 60 per cent to as high as 90 per cent^{5,14-17}. The largest outbreak in West Africa started from Guinea¹⁴ and then spread to Sierra Leone, Liberia¹⁶⁻¹⁹ (Table). It took two years (2014-2016) to control the outbreak. The unprecedented scale of these outbreaks had potential to destabilize the fragile economy and health care systems of African countries¹⁷. Due to its transmissibility from animal-to-human and human-to-human, high CFR sparked the fear of international spread and it was identified as Category A priority pathogen²⁰.

Human Nipah virus disease

Human Nipah virus outbreaks of Southeast Asia are example of another zoonotic disease, with high CFR⁴. The first recognized large outbreak of human Nipah virus occurred in Malaysia and Singapore and continued for almost a year from September 1998 to June next year^{4,21-25}. The outbreak ceased after the infected herd of pigs of that region were slaughtered⁴. In Bangladesh, Nipah virus outbreaks have been recognized since 2001²⁵. Fruit bats of *Pteropus* species have been identified as the natural reservoir of Nipah virus²⁵⁻²⁹ (Table). It was also isolated from urine specimens collected from *Pteropus hypomelanus* in Malaysia²² and *Pteropus lylei* in Cambodia³⁰. The isolated strains of Nipah in Bangladesh showed heterogeneity in their nucleotide sequence, suggesting repeated introductions of Nipah virus from its host to people of Bangladesh^{25-28,31,32}.

Influenza A (H1N1) 09

In March, 2009, the pandemic Influenza H1N1 emerged as a lethal form of swine influenza virus infecting humans and also causing deaths in Mexico³³. Due to its high transmissibility and potential lethality, in June 2009, the pandemic alert level was raised to phase 6 by the WHO³³. Till mid-October 2009, 175 countries were affected³³. In March 2010, more than 200 countries

Table. Attributes of emerging and re-emerging infections threatening global public health

Attributes	COVID-19	MERS	Influenza A (H1N1) 09	SARS	Ebola virus disease	Human Nipah virus disease
Type	Pandemic ³⁴	Epidemic ⁸⁻¹¹	Pandemic ³¹⁻³³	Epidemic ⁴⁻⁷	Large and recurrent outbreaks ¹²⁻²⁰	Outbreaks ²¹⁻³²
Yr of occurrence	2019 ³⁴	2012 ⁸⁻¹¹	2009 ³¹⁻³³	2002 ⁴⁻⁷	1976;1977; 1994; 1995; 1996; 2001; 2003; 2008; 2012; 2014; 2017; 2018 ¹²⁻²⁰	1998; 2001 (since then recurrent in Bangladesh); 2006 and 2018 (in India) ²¹⁻³²
Originated at	Wuhan, China ³⁴	Saudi Arabia ⁸	Mexico ³¹⁻³³	South China ⁴⁻⁷	2014-Started at Guinea; 2017- DRC; 2018-Equator Province, DRC ¹²⁻²⁰	1998-Malaysia, Singapore; 2001-since then recurrent outbreak in Bangladesh; 2006-Siliguri, India; 2018-Kerala, India ²¹⁻³²
Spread at	Global ³⁴	Originated at Saudi Arabia; spread to Europe, Africa, Asia, North America ⁸⁻¹¹	More than 200 countries ³¹⁻³³	Originated at South China and then spread to Asia, Canada ⁴⁻⁷	2014-Started at Guinea; 2017- DRC; 2018-Equator Province, DRC ¹²⁻²⁰	1998-Malaysia, Singapore; 2001-since then recurrent outbreak in Bangladesh; 2006-Siliguri, India; 2018-Kerala, India ²¹⁻³²
CFR (%)	Varies between <1 and 13.56% ³⁵	>35% ⁸⁻¹¹	0.4-6.7 per cent ³¹⁻³³	~0% ⁴⁻⁷	Varies between 25 and 90 per cent ¹²⁻²⁰	40-70 per cent ²¹⁻³²
Causative virus	SARS-CoV-2 ³⁴⁻³⁷	MERS-CoV ⁸⁻¹¹	Influenza A/(H1N1) pdm09 ³¹⁻³³	SARS-CoV ⁴⁻⁷	Ebola virus ¹¹⁻¹⁹	Nipah virus ²¹⁻³²
Natural reservoir	Bats (potential host) ³⁴⁻³⁷	Bats (?) (Neoromicia sp. in Africa) ⁸⁻¹¹	-	Chinese horseshoe bats (<i>Rhinolophus sinicus</i> and other <i>Rhinolophus</i> spp. in China) ⁴⁻⁷	Three species of Fruit bats (<i>Hypsignathus monstrosus</i> ; <i>Epomops franqueti</i> ; <i>Myonycteris torquata</i>) ¹²⁻²⁰	Fruit bats also known as flying fox (order Chiroptera and genus <i>Pteropus</i>) ²¹⁻³²
Intermediate host	Pangolin (potential intermediate host) ³⁶	Dromedary camels (Middle East and Africa) ⁸⁻¹¹	-	Civets and raccoon dogs in southern China ⁴	Monkey, apes, pigs ¹²⁻²⁰	Pigs ²¹⁻³²
Main transmissibility	Animal to human, person to person ³⁴⁻³⁶	Animal to human, person to person ⁸⁻¹¹	Human to human; human to animal (reverse zoonosis) ³¹⁻³³	Person to person, animal to human ⁴⁻⁷	Animal to human, person to person ¹²⁻²⁰	Animal to human, person to person ²¹⁻³²

Contd...

Attributes	COVID-19	MERS	Influenza A (H1N1) 09	SARS	Ebola virus disease	Human Nipah virus disease
Modes of transmission	Droplet, contact ³⁴⁻³⁶	Droplet, contact ⁸⁻¹¹	Droplet, aerosol ³²⁻³⁴	Droplet, contact, airborne ⁴⁻⁷	Contact with infected animals; consumption of blood, milk, or raw or undercooked meat of infected animal; Person to person through direct contact with the blood; secretions or bodily fluids of infected persons; contact with contaminated needles, equipment ¹²⁻²⁰	Transmitted to humans from animals (such as bats or pigs), or contaminated foods and can also be transmitted directly from human to human ²¹⁻³²
Incubation period (days)	4-14, up to 28 ³⁴⁻³⁶	2-15 ⁸⁻¹¹	1-7 ³²⁻³⁴	2-14, up to 21 ⁴⁻⁷	2-21 ¹²⁻²⁰	5-14 ²¹⁻³²
Basic reproduction rate (R0)	2.28 ³⁴⁻³⁶	0.3-1.3 ⁸⁻¹¹	1.4-1.6 ³²⁻³⁴	0.3-4.1 ⁴⁻⁷	1.5-1.9 ¹²⁻²⁰	0.48 ²¹⁻³²
Infection control measure	Standard contact and droplet precautions ³⁴⁻³⁶	Standard contact and droplet precautions; airborne precautions for aerosol-generating procedures ⁸⁻¹¹	Standard contact and droplet precautions; airborne precautions for aerosol-generating procedures ³²⁻³⁴	Standard contact and droplet precautions; airborne precautions for aerosol-generating procedures ⁴⁻⁷	Standard contact precautions ¹²⁻²⁰	Standard contact precaution ²¹⁻³²

SARS-CoV, severe acute respiratory syndrome-coronavirus; MERS-CoV, Middle East respiratory syndrome-coronavirus; CFR, case fatality rate

reported confirmed cases of Influenza A (H1N1) 09 and the global death count in that pandemic rose to 16,931³³. However, in August 2010, the WHO declared that the virus has moved to the post-pandemic period³³. The protein homology and phylogenetic analysis of the new Influenza A (H1N1) 09 demonstrated evolutionary trait to influenza A virus commonly in circulation in American countries for the last two decades and being evolved from swine viruses, emphasizing the role of pigs for this evolution to take place³¹⁻³³.

COVID-19 pandemic

The ongoing pandemic caused by SARS-CoV-2 is another addition to the list of zoonotic diseases, putting humankind under immense threat (Table). It first broke in Wuhan, China, in December 2019 and was possibly related to a local seafood market, however, this has not been proved so far³⁴⁻³⁹. Bats have been mentioned as its natural reservoir as it is known to harbour a variety of CoVs, including SARS-CoV- and MERS-CoV-like viruses³⁷⁻³⁹. The non-availability of bats for sale in that sea market, sparked the debate on the existence of alternative intermediate hosts as genome sequencing of COVID-19 showed 96.2 per cent similarity to the Bat CoV RaTG13³⁹. However, the coronavirus identified from Malayan Pangolins had a similarity of 91.02 per cent to SARS-CoV-2, indicating the probability of Pangolins being the intermediate host of SARS-CoV-2⁴⁰. According to The initial reported studies from China, 31.3 per cent of the patients had a history of travel to the place of origin, whereas 72.3 per cent of the patients had a contact history of people visiting from Wuhan³⁹. Though it originated from animal source, the transmissibility of this virus is mainly human-to-human³⁹. During SARS-CoV and MERS-CoV epidemics, nosocomial route was identified to be a major route of spreading infection⁵. In the case of SARS-CoV-2, the possible routes of transmission are still under research.

As of August 31, 2020 globally 24,413,598 COVID-19 cases with a CFR of 3.3 per cent have been reported⁴¹. The USA has so far reported a case burden of 18,637 per million population with a CFR of three per cent⁴¹ followed by Brazil, having an incidence of 18,149/million population with a CFR of 3.1 per cent. More than 200 countries across the globe have been affected by the COVID-19 pandemic. European countries being the worst hit, Spain has reported an incidence of 9744 cases/million population with a CFR of 6.4 per cent⁴¹. Italy, France, Germany and

the UK have reported an incidence of 4437/million, 4257/million, 2902/million and 4923/million, respectively⁴¹. Though originated from China, the reported incidence till date was 58/million Chinese population, whereas, Qatar, Singapore, Israel, Iran and Turkey reported an incidence of 42,230/million, 9698/million, 12,509/million, 4458/million and 3179/million, respectively⁴¹. Among the mentioned Asian countries, Iran reported the highest CFR of 5.7 per cent⁴¹. Asian countries altogether shared 27.6 per cent (7,010,590/25,413,598) of the total global COVID-19 cases and contributed 16.6 per cent of the (141,479/851,078) global COVID-19 deaths⁴¹. Till the month of April 2020, European countries shared 43.3 per cent of the global COVID-19 cases (1,325,314/2,828,826), in August, it reduced to 14.02 per cent with 24.4 per cent share to the global COVID-19 deaths (207,565/851,078)⁴¹.

Increasing human–animal interfaces & potential impact

Increased human–animal interfaces impose repeated threats on human life by creating scope for the emergence of various new infectious diseases. Rapid deforestation leading to shrinking of boundaries between the human and the animals and further approach of human to wildlife for livelihood leave the animals threatened due to destruction of their habitat. Increased demands for wildlife products lead to poaching and trafficking. Decreasing biodiversity also compels animals to search for food in neighbouring human dwelling, and all these lead to an increase in human–animal conflict and contact as well.

As in the industrialized countries, developing countries also have started doing intensive animal agriculture mainly of chickens and turkeys to meet the demand of meat supply and usually 15,000-50,000 birds are reared together under a long shade^{42,43}. This unnatural indoor confinement of a large number of animals in a limited air space and production of large quantities of waste probably allow rapid selection, amplification and dissemination of zoonotic pathogens⁴⁴. In 2005, Woolhouse and Gowtage-Sequeria⁴⁵ reviewed 177 emerging or re-emerging human pathogens. Changes in land use and agriculture were identified to be the major causes of their appearance⁴⁶. Another concern is extinction or risk of extinction of many breeds of animals, and this leads to the loss of genetic diversity in modern livestock production⁴⁷. The narrowly focused breeding schemes are actually creating a genetic

bottleneck which may finally increase the probability of disease susceptibility by facilitating adaptation of zoonotic pathogen and hindering host evolution for resistance against the pathogens⁴⁸.

Identified major gaps in outbreak/epidemic/pandemic preparedness & response strategy

The definitions of outbreaks/epidemics/pandemics are primarily driven by their geographic spread⁴⁹⁻⁵⁰. Each of these events has its own frequency, severity and disease characteristics requiring optimal preparedness and response strategy. However, from the past and the current experience, it is evident that each time the discussed diseases have put major challenge to the public health fraternity due to⁴⁹⁻⁵¹: (i) lack of understanding and knowledge among the communities regarding outbreaks/epidemics/pandemics; (ii) poor preparedness of health system to deal with catastrophic health events; (iii) resource constraints particularly in low- and middle-income group countries; (iv) poor surveillance and monitoring; (v) lack of interdisciplinary one-health approach to reduce the threats of emerging infectious diseases; and (vi) fundamental bureaucratic and public management capacities.

With the repeated occurrence of these events, it is important to understand that the direct health impact is catastrophic. The indirect health impacts can increase the mortality and morbidity further due to diversion or depletion of resources for routine care and less access to routine care due to travel restrictions/fear⁴⁹. Increased probability of infection, deaths and fear leads to decreased availability of healthcare workers during the epidemics/pandemics, making the situation further worse. The impacts of large outbreaks/epidemics/pandemics are also noticed at the societal and political levels, leaving the affected ones to deal with social stigma, whereas it may reduce state capacity to manage instability⁵⁰.

Allied issues requiring urgent policy adaptation to reduce the effect of increasing human–animal interfaces

Certain changes in pathogens which allow them to pass from animals to humans may be increased by modification or destruction of the natural ecosystems. Deforestation and species collection and trafficking, open animal markets followed by increased risk of zoonosis have been identified as the pathways leading to epidemic or pandemic^{50,51}. There are transdisciplinary issues requiring urgent policy-level

adaptation to mitigate this complex issue⁵⁰⁻⁵²: policies to engage international bodies, local governments, non-governmental organizations, communities and consumers for effective prevention of human–wildlife conflict; policies for protected key areas, creating buffer zones for wildlife and investing in alternative land uses; policies related to empowering communities to manage their relationship with wild animals as a part of community-based natural resource management plan; policies related to compensation or insurance for animal-induced damage; policies related to payment for environmental services and policies regarding selling and buying of wildlife-unfriendly products.

Currently, the world is experiencing the complexities of a threatening novel infectious disease COVID-19. The animal origin of SARS-CoV-2, then its human transmission and even presence of it in environmental samples⁵³ reflects the importance of having a linkage between veterinary services, local farming community, sellers and consumers which needs to be continuously monitored. However, establishment of such mechanism requires a thorough assessment⁵³. These linkages are essential for rapid communication and response mechanisms to control disease⁵³. These emphasize the need to develop and nurture an efficient epidemiology surveillance network and exhaustive national territorial meshing to capture the animal diseases inclusive of zoonotic and emerging diseases⁵³. In conclusion, this is the right time globally to undertake interdisciplinary one-health approach to understand the interrelationship between environment, humans and animals for improving the health outcomes of all.

Financial support and sponsorship: None.

Conflicts of Interest: None.

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