Reverse Zoonotic Disease (Zoanthroponosis)

Recently an interesting article has been published in the March issue of Ecology Letters (*Ecology Letters*202200:1-16) with grave impact of reverse zoonosis (by Frage *et al* on assessing the risk of human-to-wildlife pathogen transmission for conservation and public health). It has been pointed out that the break out of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has led to increased focus on serious concern over transmission of pathogens from humans to animals, and its potential risk involved which may threaten conservation and public health as a whole. After gathering sufficient quantum of evidences for assessing this threat, we reviewed published evidence of human-to-wildlife transmission events, with a focus on how such events could threaten animal and human health. In that endeavour, 97 mostly non-human hosts involving a wide range of pathogens, have been identified with verified examples, involving a wide range of non-human primates or large, long-lived captive animal with few documented examples resulted in morbidity and mortality, and very few led to maintenance of a human pathogen in a new reservoir or subsequent "secondary spillover" back into humans. It also been pronounced the limitations in the literature surrounding these phenomena, including strong evidence of sampling bias towards non-human primates and human-proximate mammals and the possibility of systematic bias against reporting human parasites in wildlife, both of which limit our ability to assess the risk of human-to-wildlife pathogen transmission. Multi-host pathogens are becoming a dominant feature of the zooanthroponosis driven by deforestation, land use conversion, and climate change, pathogens are increasingly being transmitted from animals into human populations,presenting a significant threat to public health. Recently, concerns have been raised about transmission of pathogens from humans into wild animals.

For a variety of reasons this process, known as "(zoo)anthroponosis," "reverse zoonosis," or more colloquially as "spillback," could pose a difficult problem for wildlife conservation and public health efforts in the near future. Concerns about human-to-wildlife pathogentransmission have grown throughout the ongoing COVID-19 pandemic. SARS-CoV-2 has been transmitted from humans to a variety of animals including household cats and dogs, big cats, gorillas, and perhaps most notably has established epizootic transmission in mink farms on multiple continents.

Only recently, SARS-CoV-2 was transmitted back into wild mink populations in Spain and white-tailed deer in North America.Further, because SARS-CoV-2 is most closely related to sarbecoviruses infecting rhinolophus bats, some fear that the virus might become established in bat populations outside Asia and form a novel reservoir, complicating efforts to prevent future resurgence in humans.

Human activities has increased the potential risks from zoonotic diseases which needs urgent all round intervention. Human and animal relationships are likely to continue to intensify worldwide over the coming several decades due to partial increasing animal husbandry practices, the growth of the companion animal market, climate change and ecosystem disruption, anthropogenic development of habitats, and global travel and business interests. As the human-animal connection or cohabitation escalates, there are possibilities of increased chances as well as the threat for pathogen spread. Interestingly, a number of factors influence the risk of disease transmission from humans to animals. For instance, human population growth, urbanisation and encroachment to forests by the name of development activities encourage different species to interact in ways and at rates previously not encountered, and to do so in novel geographical areas.

The COVID-19 has been the most widespread zoonotic pandemic to affect the human civilisation severely in early part of this century, reflecting the problem of erratic activities of human with indiscriminate activities against the mother nature, increasing the risks of pathogen spill over, such as hunting, butchering, unethical encroachment of the forest land in the name of farming, deforestation, reforestation,irrigation, mining and both intra- and intercountry travelling causing ecological feedbacks at local scales (eg, bidirectional transmission of COVID-19 between animals and humans,which could augment the COVID-19 risk in both animals and humans). Understanding of these feedbacks is crucial to mitigating zoonotic disease risks, which requires interdisciplinary and transdisciplinary collaborative research on pandemic risks among multiple fields, including epidemiology, virology, public health, geography, and ecology.

Reverse zoonosis of COVID-19 infection of animals with SARS-CoV-2 from humans has pointed out the importance of understanding of 'reverse zoonosis' (zooanthroponosis). Out of four, three possible routes of transmission for zoonotic diseases (ie, animal-human, animal-animal, human-human),which have been well studied and confirmed. Human-animal transmission lacks sufficient research due to the unusual and rare occurrence of reverse zoonosis prior to COVID-19 . Due to one such instance, when reverse zoonosis occurs it may cause the further evolution of viruses and affect the effectiveness of potential COVID-19 vaccines. Due to the growing populations of livestock and other domesticated animals,increasing proximity between animals and humans in multiple settings (eg, wet markets, home, and animal production facilities), and the relatively fewer established resources ie, diagnostic facilities assigned for animal testing during human outbreaks with zoonotic potential (particularly asymptomatic infections), new animals diseases may spread going to be undetected. Both the proactive preventive survey and encompassing early diagnosis of such reverse zoonosis enables the creation of effective management strategies. Therefore, reverse zoonosis requires more rigorous and widespread macro-ecological and microbial studies and attention.

Currently researches focussed on zoonotic diseases often highlighting on diseases of animals have been transmitted to humans.However, an increasing number of reports indicate that humans are also transmitting pathogens to animals, such as methicillin-resistant *Staphylococcus aureus* (MRSA), influenza A virus, *Cryptosporidium parvum*, and *Ascarisl umbricoides*, etc. Here attempts have been undertaken to provide an overview of available information regarding reverse zoonosis and highlight the need for future multidisciplinary strategies to be worked out in this area.

With today's rapid improved system of transportation as well as development of speedy travelling from place to place globally especially air travelling systems covering intra- and intercountry, became apriority addressable issues of modern public health systems which are growing with increased complexity. A pathogen that emerges today in one country can easily be transported unnoticed in people, animals, plants, or food products to distant parts of the world in less than 24 hours . This high level of mobility makes tracking and designing interventions against emerging pathogens exceedingly difficult, requiring close international and interdisciplinary collaborations. Fundamental to these efforts is an understanding of the ecology of emerging diseases. Published works often cite the large proportion of human emerging pathogens that originate in animals.However, scientific reports seldom mention human contributions to the variety of emerging diseases that impact animals.

Bacterial pathogens are reported mostly from centring North America and Europe. Viral studies were well-distributed globally. Parasitic disease reports were conducted chiefly in Africa. Fungal studies were conducted almost exclusively in India. It has been calculated animals with reported infection or inoculation with human diseases included wildlife (50%), livestock (43%), companion animals (23%), and other animals or animals not explicitly mentioned (4%).

The majority of companion and livestock animals were studied in North America and Europe,while wildlife studies were most prevalent in Africa. Typically, diagnostic specimens were collected at veterinary hospitals (27%), national parks (14%) and livestock farms (14%). Direct contact was suggested as transmission route in about 71%. Other routes of transmission, included fomite, oral contact and aerosols and inoculation as early as 1988, zoonosis research focusing on fungal pathogens was being conducted. Initial studies implied human transmission of microsporum and trichophyton to various animal species, later on article cantred on *Candida albicans*. These publications were set in India and the United States. Since 1988, research with implications of reverse zoonosis has been largely focused on infections of bacterial origin beginning in 1995 the majority of the studies in this scenario focused on MRSA and *Mycobacterium tuberculosis*. Reports regarding these bacteria were primarily conducted in the United States among livestock or companion animals. Viruses were the second most common pathogen associated with human-to-animal transmission. Reverse zoonosis reports regarding viral pathogens began in 1998 and have since been focused primarily on influenza with great interest surrounding the 2009 H1N1 pandemic. These studies were conducted largely in the United States in livestock and wildlife. Studies suggestive of transmission of human parasites to animals were first published in 2000. The most commonly reported parasitic agents to be transmitted from humans to animals were *Giardia duodenalis* and *Cryptosporidium parvum*. Parasitic research has been carried out most frequently in Uganda and Canada. Moreover other investigators have reported, human parasitic infections chiefly in wildlife and livestock. Human-to-animal transmission is plausible for a large number of diseases because the pathogens concerned are known to infect multiple species. For instance, 77.3% of the pathogens infecting livestock are considered "multiple species pathogens". So underscoring of reverse zoonosis being a potential impending threat to livestock, which needs for further research in this area.

Similarly, situation of reverse zoonosis on companion animals has been culminated or implied as a possible cause of infection, despite the fact that 90% of known pathogens for domestic carnivores are recognised as "multiple species pathogens". The majority of publications in reverse zoonosis, involved studies documenting human-to-wildlife transmission. Unfortunately, they too were severely lacking as per research demands.

A newly coined term "pathogen pollution" refers to the process of bringing a foreign disease into a new locality due to human involvement and carelessness by the human society. For examples the endangered African painted dog, wild dogs (Dhole) have been infected with human strains of *Giardia duodenalis*, had established that "pathogen pollution" occurred through open defaecation in and around national parks by tourists and local residents. Anthropogenic changes in the ecosystem increase the amount of shared habitats between humans and animals thus exposing both to new pathogens. Emergence of human pandemic025:H4-ST131 CTX-M-15,due to extended spectrum-beta-lactamase producing *Escherichia coli* in many different companion species of animals indicating interspecies transmission from humans to pets and livestock particularly in Europe as well as additionally, change of habitat, growth, and/or destruction, there are the ever-increasing global movement of products and travellers that extends to both humans and animals. During the pandemic of 2009 H1N1 influenza, the novel virus was able to travel across the globe and from humans to swine in less than two months which due to the transport of animals and animal products, by the worldwide shipment of meat.

While food and animal safety guidelines attempt to keep up with the speed of global trade, international efforts appear to be ignored due to increased product demand. It has been recorded as well as documented that five tons of illegal bushmeat pass through Paris' main Roissy-Charles deGaulle airport each week in personal luggage. Again, transmission of retail market systems of animals and animal products can also contribute to the danger of propagation of zoonosis and reverse zoonosis. Many animals are sold in markets which allow humans and a myriad of animal species to interact in conditions that are known to trigger emergence of diseases. Specifically, this is true for live animal markets and warehouses for exotic pets.The pet industry is an enormous global business that now expands from domestic to exotic animals. A 2011-2012 national pet owners survey found that in the United States alone, 72.9 million homes or 62% of the population have a pet. Of these pets, the majority of animals are dogs (78.2 million) or cats (86.4 million), but a large number of pets are birds (16.2 million), reptiles (13 million), or small animals (16 million). As pet ownership seems to be increasing worldwide and more exotic pets are being introduced to private homes, the potential for disease transmission between humans and animals will continue to increase. Veterinarians must more fervently protect animals under their care from human disease threats. Adopting a One Health strategy for emerging disease surveillance and reporting will benefit both humans and animals and produce a more collaborative response plan.

Veterinarians, animal health workers, and public health professionals are not the only ones who should recognise the threat of reverse zoonosis. Increased awareness must also be communicated to the general public. Worldwide, there are 1,300 zoos and aquaria that sustain more than 700 million visitors each year. The potential for pathogen spread to animals can come from a visitor with an illness, contamination of a shared environment or food, and the spread of disease through relocation of animals for captivity or educational purposes. In Tanzania, a fatal outbreak of human meta-pneumovirus in wild chimpanzees is believed to be the result of researchers and visitors viewing the animals in a national park that was once the great apes' territory. Public education and awareness should be augmented to include the potential health threats inflicted on a susceptible animal by an unhealthy human. This report has limitations. As demonstrated in this review paper, the trend for reporting pathogen spread of human-to-animal is increasing. However the route of human transmission to animal disease manifestation is often unknown in these reports and not well documented in this review. Also the report did not examine articles that did not document human-to-animal transmission.We acknowledge that many additional works that have recorded the existence of human pathogens in animals were not evaluated. However, this review was designed to summarise only the publications that document reverse zoonotic transmission. Many common and dangerous pathogens have not, to the authors' knowledge, been researched as reverse zoonosis threats to animals representing a significant gap in the scientific literature.Future investigations of reverse zoonosis should take into account both transmission routes and disease prevalence. Prospective research should also include a wider variety of aetiological agents and animal species. Scientific literature must document the presence and transmission of human diseases in animals such that the wealth of literature on this subject will become defined and accessible across multiple disciplines. A wider knowledge and understanding of reverse zoonosis should be sought for a successful One Health response. We recommend that future research be conducted on how human disease can, and does, affect the animals around us.

In conclusion, some conceivable evidences has been gathered, indicating reverse zoonosis may cause reduction and even partial or total extinction of the wild animal populations susceptible to viruses, which could destroy local biodiversity and ecological balance. The risk factors for and transmission routes of reverse zoonosis vary by animal type (eg, pet, livestock, wildlife), which may not be fully identified and prevented by traditional methods. It is vital as well as demanding to take advantage of upmost advance and effective methods to improve the control, management, and prevention of reverse zoonosis. These technologies developed enable the chronology of infection to be determined, which, together with serosurveillance, may help to reveal the direction of transmission between human and animal. Also, global positioning system and wearable sensors embedded in collars for farm livestock can monitor their daily activities and enable disease detection and monitoring of their health status. Prevention of reverse zoonosis also requires understanding of pathogen feedback loops at the wildlife-livestock/pet-human interface. This will require greater capacities and commitments for pathogen discovery, mutation rate detection, and surveillance, in order to improve the prediction of pandemic potential, leading to management actions that interrupt possible pathways of spill over and transmission, understanding these key evolutionary processes and ecological interactions calls for integrated virus-animal-human-environment surveillance systems. Spatial life course epidemiology also provides a uniform analytical framework to link ecological surveillance to the national disease reporting system. In the real world, the governance of all the key components (ie, host, agent vector, environment) can be substantially strengthened by the participation of the United Nations Environment Program in the tripartite collaboration among theWHO, the World Organisation for Animal Health, and the Food and Agriculture Organisation of the United Nations, which would help countries implement the One Health approach.

There are several implications when considering and studying reverse zoonoses.At the individual level, awareness of reverse zoonoses should be raised for better self-protection, as it has extended our definition of population groups vulnerable to COVID-19, from those with closer and/or more frequent contact with people/ patients (eg, healthcare workers, safety guards, delivery service people) to those with closer and/or more frequent contact with animals (eg, pet owners, farmers, zoo keepers), although the risk of pet-human transmission is currently considered to be low. More regulations should be prepared to raise awareness of COVID-19 risks among these vulnerable populations. At regional and national levels, due to limited resources for SARS-CoV-2 detection and containment measures for animals,especially for home pets, there could be a high likelihood of transmission, a lower recovery rate, and hence a large number of infections among animals, which would pose a severe threat to humans. Therefore, resources for SARS-CoV-2 detection should be reserved for testing animals that may be most at risk (eg, pets of confirmed COVID-19 patients) and regulations should be made to manage infected and at-risk animals, especially at the farm. Attention should also be paid to animals on duty during the COVID-19, such as dogs that are used at airports in some countries to detect passengers infected with COVID-19. In addition, human-animal transmission would expand the total population in COVID-19 forecasting models to both humans and animals, the increased risk of which, together with animal-animal and animal-human transmission, should be considered in future COVID-19 forecasting models.

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