

Review Article

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Emergence of Zoonoses at Human-Animal Interface

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ABSTRACT

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A number of old and new pathogen has emerged or re-emerged in past 30 years. Increase in interaction at the interface of human and animals plays a crucial role in transmission of these zoonotic agents at the interface. Burgeoning human population, increased global communication, habitat destruction, bush meat consumption, intensification of animal farming. Along with emergence of antimicrobial resistance and increased incidence food borne infections are important public health implications in which human-animal interface plays a definite role. Despite initiatives taken by Indian government to consolidate inter-sectorial collaboration, still recent policies still lacks one health approach.

Introduction

Out of 1407 pathogen around 816 (58%) are zoonotic in nature. While 73% (130/177) of emerging pathogens, are zoonotic in nature (Woolhouse and Gowtage-Sequeria, 2005). In last 30 years around 30 pathogens have emerged (Woolhouse *et al.*, 2002; Smolinski *et al.*, 2003) Most of the emerged pathogens are viral in nature. While RNA virus due to increased mutation rate with low proof reading in RNA viruses as compared to DNA viruses results in increased rate of emergence of RNA viruses as compared to DNA viruses Johnson *et al.*, (2015). Emergence of disease at an interface depends on evolutionary

distance between species, plasticity of pathogen to jump species barrier, and frequency of contact of susceptible species with the reservoir species (Cleaveland *et al.*, 2007; Greger, 2007; Johnson *et al.*, 2015). The review will focus on the factors which are contributing to emergence of zoonotic pathogens at human-animal interface.

Emergence of zoonoses

In past 30 years several zoonotic diseases viz. ebola, SARS, MERS, Nipah, Hendra, HIV, Hanta viral infection, West-nile disease, Scrub typhus, Tularemia, Lyme disease, Covid-19 have emerged or re-emerged

(Woolhouse *et al.*, 2002; Smolinski *et al.*, 2003; Yee *et al.*, 2020). As defined by WHO, an emerging zoonoses is defined as 'a zoonosis that is newly recognized or newly evolved, or that has occurred previously but shows an increase in incidence or expansion in geographical, host or vector range.' While OIE defines re-emerging zoonoses as 'an already known disease that either shifts its geographical setting or expands its host range, or significantly increases its prevalence.' Increase in interaction at human-animal interface due to increased anthropogenic intervention at the interface has resulted in increase in exposure of human to novel pathogen or existing pathogen with enhanced virulence.

Emergence of zoonoses at human animal interface

Around 6 million to 11 thousand years ago transmission of zoonotic disease at the interface began with human alteration of environment with beginning of agricultural activities. Establishment of agricultural activities might have led to increase in activities of rodents around the establishments. Around 10 thousand years ago domestication of animals began. All these alteration of human activities created a scope of increased exposure of human to animal pathogens (Dobson and Carper, 1996; Wolfe and Dunavan, 2007). It has been hypothesized that recent established human diseases at some point of time originated from animal pathogen. For example human measles originated from rinderpest like virus, smallpox virus originated from camelpox/cowpox like virus having rodent borne ancestor, and similarly pertusis virus originated from ovine or porcine source (Weiss, 2001; Gubser *et al.*, 2004).

As identified by WHO/FAO/OIE, six major factors which are associated with emergence

or re-emergence of zoonoses are habitat destruction, bushmeat consumption, intensification of animal agriculture, long distance transport of animals, live animal market, and increased demand for animal protein (WHO/FAO/OIE, 2004). Role of each factor is described in detail in the context below.

Habitat destruction

As per global forest resource assessment it has been reported that more than half of global tropical forest has been destroyed till now with an average loss of 2-3% per year (Pimm and Ayres, 2001; Patz *et al.*, 2004) The principal reason behind habitat destruction is population blast. Current world population is estimated to be around 7.6 billion and it is expected to increase around 9.8 billion in 2050 and 11.2 billion in 2100 (UN, 2017). It has been estimated that availability of forest land per capita has decreased to 0.6 ha per person in 2015 as compared to 0.8 ha per person in 1990. The net global forest annual loss has decreased from 7.7 million ha during 1990-2000 to 3.3 million ha during 2010-15. Although the rate of forest loss has decreased over the years, however contribution of planted forest to net global forest as compared to natural forest is gradually increasing (FRA, 2015).

Another form of habitat destruction is habitat fragmentation, which arises due to establishment of human habitation or establishment of commercial venture inside natural forest. This results in expansion of ecotone zones which helps in transmission of zoonotic agents at the interface. For example emergence of lyme disease in Connecticut, USA which was due to expansion of forests around agricultural lands thereby increased exposure to vectors and natural reservoirs of the pathogen (Goldberg *et al.*, 2008; Laurance *et al.*, 2013). Similarly emergence of Nipah in

Malaysia was due to destruction of forests inhabiting bats, which subsequently fled to pig farm establishments and led to escalation of nipah outbreak in Malaysia. Migrations of bats are hypothesized to be behind emergence and re-emergence of several pathogen viz. west Nile virus, avian influenza, Hendra virus disease, SARS syndrome.

Bush meat consumption

Bushmeat refers to meat derived from wild animal intended for human purpose (Milner-Gulland and Bennett, 2003). Bushmeat consumption is popular in African countries, where in Congo and Amazon river basin the bush meat consumption activity is reported to be 4.5-5 million tonnes per year Fa et al. (2002). Hunting of wild animals poses a great risk of acquiring zoonotic pathogens as personnel involved in bush meat processing activities come in direct contact with blood and tissue of wild animals. Sick and clinically ill animals remain more susceptible to hunting. Among animal species, bats and primates pose greatest risk to human health (LeBreton et al., 2006; Subramanian, 2012; Taylor et al., 2015).

Increased bushmeat consumption is associated with increased incidence of several zoonotic diseases. Zoonotic diseases associated with consumption of bush meat species are mentioned in Table 1 Kurpiers et al., (2016). Acquired immune-deficiency syndrome, caused by HIV-1 virus was first recognised in USA around 1981. Later the emergence was associated with increased trade activity in forest cover, which along with resulted in increased bush meat trade (Weiss and Wrangham, 1999; Larkin, 2000).

Bats due to certain important characteristics play an important role as reservoir and dissemination of zoonotic pathogen. Despite, its small size bats have a life span upto 40

years. Bats can disperse over a long range and can traverse over continents, which results in dissemination of pathogens over a wide geographical area. Bats usually roost in a large density over a small area, and due high concentration of reservoirs it facilitates random spill over of zoonotic pathogens to humans during close encounters. Bats maintain a high body temperature, which facilitates co-evolution of febrile resistant virus. Bats immune system developed in such a way that it allows multiplication of virus without development of clinical symptoms (Munshi-South and Wilkinson, 2010; Streicker et al., 2010; O'shea et al., 2014). Bats acts as common reservoir for betacoronavirus family viruses such as Covid-19, SARS CoV and MERS CoV (CDC, 2020).

Long distance transport of animal

Nowadays animals are transported over a long distance due to flexibility in long distance communication. Animals are usually transported as pet animals, laboratory purpose, and food animals. Apart from that illegal smuggling of animals is one of the important reasons in dissemination of infection across continents. As per reports each year around 40,000 primates, 4 million birds, and 6,40,000 reptiles are transported for trade purpose Karesh et al., (2005). Trading of animals for food purpose has increased over five times since 1990s. Apart from these around 350 million tropical fish are traded in a year (Spellberg, 1994).

Transportation of animals over a long distance induces stress in animals which increases faecal shedding of zoonotic pathogens viz. *Salmonella*, *Campylobacter*, *E. coli*, and results in precipitation of latent infection Barham et al., (2002). Also stress induces susceptibility to infection. Transportation of animals increases contact

between herds. Following introduction of reservoir animals to a new herd which are immunologically naïve to the alien pathogens often results in precipitation of outbreaks (Crews, 2004).

Transportation has played a key role in spread of several pandemics. 1998 Nipah pandemic in which more than 105 persons died (Looi, L. M., and Chua, 2007), transportation of infected pigs across Malaysia played a key role spread of Nipah across the country Presti *et al.*, (2016). Similarly transportation of infected poultry across 8 different countries in South East Asia resulted in 2004 pandemic of H5N1 (FAO and OIE, 2007). A number of outbreaks associated transportation of animals across countries, which are mentioned in Table 2.

Expansion and intensification of animal agriculture

Since beginning of livestock revolution since, world meat, milk and egg production has increased around 4, 2.5, and 5 times respectively as compared to 1960s (FAO, 2019). Nowadays intensification of animal agriculture is gaining momentum as compared to traditional backyard rearing of animal (Thornton, 2010). In intensive farming due to presence of a large number of genotypically similar individuals at a confined place it becomes easier for a pathogen to adapt a host. In order to increase animal productivity there is selective breeding programmes are taking over a large pace. However, it results in narrowing of genetic diversity among species, which helps in easier adaptation of pathogen Drew, 2011; Behera and France, 2016; Geoghegan *et al.*, 2016). In intensive farming there is increased human-animal contact as compared to traditional farming, facilitating transmission of zoonotic diseases at the interface (Geurden and O'Handley, 2011). Due to rapid population turnover rate, new

entrants' population continuously gets admixture with existent population, which facilitates transmission of infection between herds (Brown, 2009). Due to presence of large number of animals over a small space puts the animals under stress and animals exhibit clinical signs and shed a large a large number of pathogens. Besides setting up of livestock farms in peri-urban area, acts as a focal point for transmission of zoonotic diseases in these area (Goldberg *et al.*, 2008; Rwego *et al.*, 2008).

Live animal markets and wet markets

Live animal markets along with wet markets can act as hotspot for transmission of zoonotic diseases and food borne pathogens. In animal markets, a diverse range of species are tied together resulting in interspecies transmission of zoonotic pathogens. Emergence of pandemics viz. H5N1, SARS, Covid-19 has been attributed to live animal markets (Sheahan *et al.*, 2008; Okoye *et al.*, 2013; Yee *et al.*, 2019).

In India, meat is generally sold in wet market in open without adoption of any hygienic measures. Meat obtained from the sources is subjected to potential contamination and may result in food borne outbreaks viz. salmonellosis, staphylococcosis, campylobacteriosis (Vindigni *et al.*, 2007).

Emergence of food borne infection

As per reports of WHO, globally around 600 million people fall ill due to food borne pathogens. Almost one in 10 persons in a year suffers from food-borne illness resulting loss of 33 million healthy life years. While average number of deaths associated with food-borne illness is around 4, 20,000 per year. Animal products remain the top contributors to these deaths. In children less than five years every one death of three death

accounts due to food-borne illness. Norovirus, *E. coli*, *Campylobacter* spp., No-typhoid salmonellosis alone contributes to around 550 million illnesses per year with 2, 30,000 deaths.

In South-East Asian region more than 150 million get affected with food borne illness with around 1,75,000 deaths. Children less than 5 years contribute to 60 million illness and 50,000 deaths. Novirus, non-typhoid *Salmonella*, and *E. coli* are the causative agents chiefly associated. More than half of the global deaths due to hepatitis A are from South East Asian regions (WHO, 2019).

Emerging pathogens associated with food-borne pathogens are *Listeria monocytogenes*, *E. coli* O:157 H:7, O26, O103, O111, O145, *E. coli* O157, *Toxoplasma gondii*, *Giardia* spp., *Cryptosporidium* spp., Taeniasis (Newell *et al.*, 2010).

Emergence of antimicrobial resistance

Antibiotic is used in animal chiefly for therapeutic purpose and as growth promoter. According to estimates India produces around 2/3rd of antibiotics in the world. Use of aquaculture in fish use of aquaculture in fishery industry China stands at top while India stands at 5th position. In United States 80% use of antibiotics is targeted towards animal industry. No maximum residue limits (MRIs) has been set in India for use of antibiotics in food. Although certain standards have been set in aquatic industry due to poor enforcement of regulation rampant violation of law has been observed (Van Boeckel *et al.*, 2015; Kakkar *et al.*, 2017; Venkatasubramanian, 2018).

As per reports of CSPI, most of the food-borne outbreaks associated with antibiotics resistant pathogens are from animal food products. Dairy products, ground beef, and

poultry meat are chiefly associated with these outbreaks. Most of these outbreaks are associated with *Salmonella* spp. Antibiotics against which resistant is observed most commonly are tetracycline, streptomycin, ampicillin (CSPI, 2013).

In India, common antibiotic residues secreted in milk are found to be tetracycline, oxytetracycline, gentamicin, cloxacillin, and penicillin. In a study more than 40% of poultry samples obtained are resistant to more than one antibiotics. Mastitis in animals associated with drug resistant pathogens MRSA, VRSA, pathogens with resistance against antibiotics such as carbenacillin, oxacillin, imipenem, quinolone are reported from several parts of India. Besides MDR has been reported in aquaculture with resistance has been reported against antibiotics such as sulfamethoxazole, carbenacillin, oxytetracyclin, nalidixic acid, streptomycin (Kakkar *et al.*, 2016).

These pathogens are excreted and secreted into environment and water bodies through excretions and secretions. Such antibiotic resistant pathogens enter into our food chain via consumption of meat, milk or through environmental route.

India: a hotspot for zoonoses

As per ILRI, India is one of the global hotspot for zoonotic diseases. Poverty is one of the major causes for emergence of zoonotic diseases. India remains at top in number of poor livestock keepers and global zoonoses burden. While India remains at 5th position in endemic zoonoses prevalence. Livestock owner with literally no awareness regarding zoonotic diseases and with poor financial bearings barely adopts any biosecurity measures to prevent acquiring of zoonotic pathogens. Besides there are around 19 million stray dogs population are there in the

country. Besides, in India meat animals are generally slaughtered in unregistered slaughter houses in an unhygienic manner and sold in wet markets (Grace *et al.*, 2012; DAHDF, 2010). As per reports farming systems in India are chiefly based on mixed crop based livestock raising system (Fig. 1).

Governmental activities in India for surveillance and control of zoonotic diseases

A standing committee on zoonoses has been formed in 2007 ministry of health to facilitate intersectorial collaboration between veterinary and medical sector. Recently a MOU has been signed between ICMR and ICAR, for joint research on zoonotic disease, antibiotic resistance and pesticide residues (ICAR, 2016). Along with joint working group on zoonoses and food safety has also been formed to facilitate collaborative research (DHR, 2012; ICAR, 2013). Recent outbreak of avian influenza has led to establishment of Joint monitoring group on avian influenza (Ghatak and Singh, 2015). Integrated disease surveillance programme stresses upon intersectorial collaboration for better surveillance of zoonotic diseases and has recruited epidemiologists, veterinarian, microbiologists, and entomologists (NCDC, 2019).

However gaps are still observed in regard to cooperation between veterinary and medical sector at field level. Research activities targeting epidemiological factors that influence distribution of the zoonotic pathogens are scarce. No separate unit for veterinary public health has been formed at centre or state government level except Goa and Manipur (Ghatak and Singh, 2015). National health policy- 2017 does not mention role of public health veterinarian in surveillance and control of zoonotic diseases (NHP, 2017). As per national strategic plan

2017-25, India aims to eliminate tuberculosis by 2025. However it fails to mention control of tuberculosis in domestic and wild animals, birds which acts as important reservoir for MTC (*Mycobacterium tuberculosis* complex) and MAC (*Mycobacterium avium* complex) respectively (NSP 2017-25).

Prevention of emergence of zoonoses

Strengthening of human-ecosystem integrity by building national parks, protected areas with strict enforcement of rules will prevent spill over of zoonotic pathogen to domestic animals and human (Ryan and Walsh, 2011). Inclusion of molecular epidemiology in research can help to identify range of reservoirs of pathogen, its genetic variability and source of infection in an outbreak associated with zoonotic or food borne pathogen (Sonyaolu *et al.*, 2016). Along with researches should be conducted for identification risk factors associated with presence and distribution of pathogen. Studies of these kinds will help in control of active outbreaks and prevention of future outbreaks (Liverani *et al.*, 2013). One of the most important factors in imbalance of natural ecosystem is blast of population size. Hence controlling population growth rate can help to prevent habitat loss and can help to maintain natural integrity of ecosystem (National Research Council, 2010). An intersectorial collaboration between different sectors is crucial and strategies should be formulated with an one health approach for prevention of emergence of zoonoses (WHO, 2019).

Pasture based rearing of animals instead of intensive form of animal farming is more close to natural raising of animals. Pasture raising of animals will help to reduce stress on animals and will decrease precipitation of diseases and shedding of pathogens. Along with adoption of biosecurity practices at farms such as quarantine and isolation

practices in farm, safe disposal of farm effluents etc should be incorporated in daily activities, which in-turn will reduce exposure of farm animals and humans to zoonotic pathogens (Sahu *et al.*, 2018). Along with promotion of native breeds which are comparatively resistant to pathogens to that of exotic breeds, should be adopted. This will help reduce size of susceptible population (FAO, 2019). Consumption of bush meat

which is on increasing trend must be discouraged to prevent transmission of pathogen associated with the activities.

For control of antibiotic resistant pathogens over use of antibiotics in animal industry must be prohibited. MRL must be set by FSSAI regarding use of antibiotics in animal food products. Strict amendment of rules must be made to ensure these standards as been met.

Table.1

Species	Associated zoonotic pathogens
Primate	Zaire ebola virus, Tai-Forest Ebola Virus, HIV-1, HTLV, Simian foamy virus, Marburg virus, <i>Strongyloides fulleborni</i> , <i>Entamoeba histolytica</i> , <i>Balantidium coli</i> , <i>Giardia intestinalis</i>
Rodents	Monkey pox, Leptospira, Rabies, Mokola virus, Lassa fever, Salmonella
Ungulates	Anthrax, Leptospirosis, Rabies, Zaire Ebola Virus, Hepatitis E
Bats	Lagos Virus, Zaire Ebola Virus, Duvengahe virus, SARS, Nipah virus disease, Hendra virus disease

Table.2

Outbreak	Associated species	Exporting country	Reference
Monkey pox, Texas, US	Gambian giant rat	Ghana	Chomel <i>et al.</i> , 2007
Tularemia, West Virginia	Hare	Central & Eastern Europe	Godfroid <i>et al.</i> , 2005
Avian Influenza, United Kingdom	Finch	China and Taiwan	DEFRA, 2005
Psittacosis, West Nile virus, United States	Pet birds	Middle East	Lanciotti <i>et al.</i> , 1999
Herpes-B virus, United States	Primates	United States	Holmes <i>et al.</i> , 1995
Salmonellosis, Ireland	Terrapins	United	Lynch <i>et al.</i> , 1999

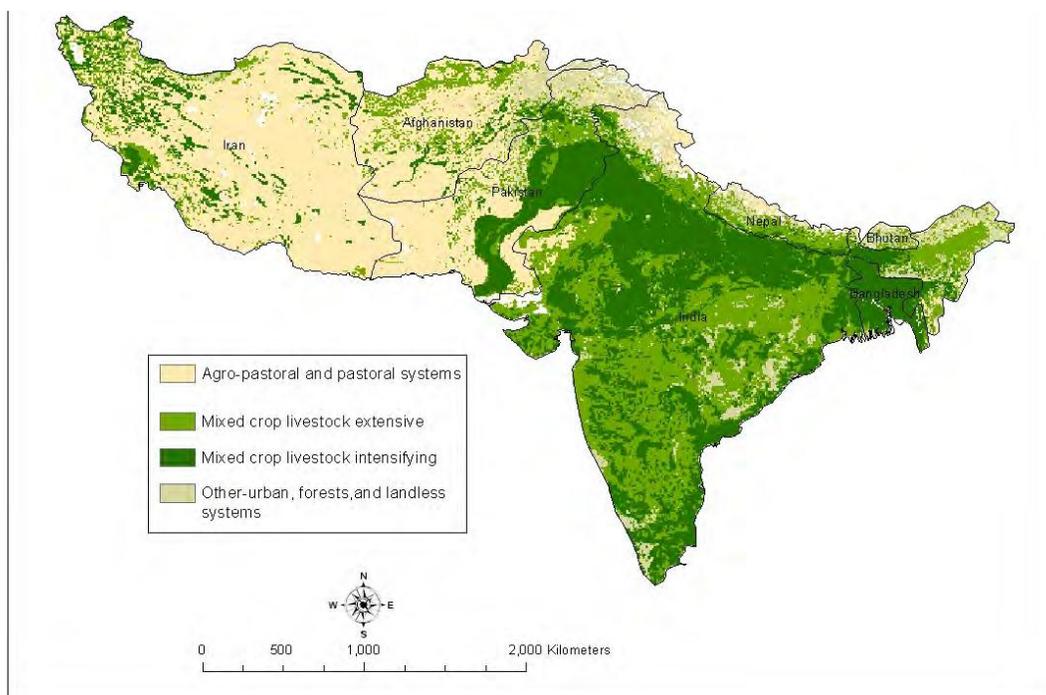


Fig.1 Livestock raising system in India *Herrero et al., 2009*

To control outbreaks associated with animal food steps should be taken for establishment of hygienic slaughter houses. Although prevention of Cruelty to Animals (Slaughter House) Rules, 2000 prohibits slaughter of animals anywhere except slaughter houses, this is grossly overlooked. Accreditation of slaughter house by competent organisation should be made mandatory to allow operation. Similarly, selling of meat in open wet markets should be prohibited. Sufficient measures should be adopted to prevent external contamination with chilling facility should be made available at the selling point.

Amidst increasing risk of emerging zoonotic diseases in the present situation, it is essential to adopt implement suitable strategies. Suitable policies must be formulated by government to enhance collaboration between veterinary and medical sector. Awareness should be created among farmers, regarding protection of themselves from zoonotic pathogens. Apart from that strict laws should be enforced ensure hygienic slaughter and

selling of meat in local markets. Similarly emergence of AMR must be prevented by strict enforcement of law preventing indiscriminate use of antibiotic in animal sector.

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