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Epizootic, Endemic and Pandemic Zoonotic Viral Infections

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Abstract

More than 60% human infectious diseases have zoonotic origin. Cross species transmission of pathogens is a continuous, dynamic process that occurs throughout the world, giving rise to epizootic (temporary, limited infection), endemic (on-going infection limited to a defined geographic region) and pandemic viral infections (infection spreading to every part of the world) like the current COVID-19 pandemic, which depends on the existing conditions on the ground. In Nov 2021, sudden mortality of numerous migrating demoiselle cranes was reported from their resting site near Jodhpur, Rajasthan. The symptomatic cranes became gradually weak and were unable to fly. They eventually fell dead which caused concern locally, given the current prevailing SARS-CoV-2 pandemic situation the world over. By the end of Dec 2021, the number of cranes with mortality and morbidity reduced, making it a temporary "epizootic infection". Molecular diagnosis carried out at a specialized laboratory identified the etiological agent to be the highly pathogenic Avian Influenza Virus H5N1 (HPAIV), which has been responsible for morbidity of avian species from different parts of the world. There was no report of spreading the H5N1 AIV infection from the infected migratory cranes to nearby chicken farms or pig farms for now. In the absence of vaccines against the highly pathogenic H5N1 AIVs, and the inherent ability of influenza viruses, both avian AIV and human IAVs to constantly mutate its envelope gene or the surface antigens, resulting from the error-prone nature of the viral RNA Polymerase enzyme are the roadblocks for development of a universal, broad-spectrum influenza vaccine. Even when such a universal vaccine against H5N1 is available, vaccinating a large number of wild migratory cranes would be difficult. However, it is possible and indeed necessary to vac-

cinate chickens in poultry farms and pigs in farms that raise pigs for human consumption.

Keywords

Zoonotic Pathogens, Natural Infection, Anthroponosis, Migratory Birds Across Countries, Aquatic Demoiselle Cranes, Viral Infectious Diseases

1. Introduction

Natural zoonotic diseases are infectious diseases that are transmitted from vertebrate animals to humans and vice versa. They are caused by different types of pathogenic agents, including bacteria, parasites, fungi, viruses and prions.

Earlier, we published a report on natural infection of "HIV-1 like" Indian SIVs from the natural habitat of wild primate species, langurs and rhesus monkeys in Rajasthan, indicating that transmission of viral pathogens occurs not only from animal to humans, but also from humans to animals, that is defined as reverse transmission or anthroponosis [1]. Although emergence of zoonotic pathogens has been recognised for many centuries, their impact on public health has been recognized and emphasized more in the last few decades. Transmission of such infectious diseases was controlled by a combination of success in antiviral therapy and vaccines. This resulted in reducing the spread of some zoonotic human infectious diseases to a large extent [2]. Influenza A Virus (IAV), that infects humans can be transmitted to wild rhesus monkeys from the natural habitat near the city of Jaipur, Rajasthan, India, as revealed by our recent report indicating human to primate transmission of IAV in nature [3]. Clearly, the cross-species transmission can happen in both directions, from animals to humans, as well from humans to animals. The emergence of novel zoonotic diseases needs to be mitigated through continuous improvement in the synthesis of logical and effective antiviral drugs and vaccines, both qualitatively and quantitatively, so as to make the antiviral arsenals available to populations who need them the most, and to improve the public health approach. A One Health approach at the human-animal-ecosystem interface is needed for effective investigation, management, prevention and control of emerging zoonotic diseases.

Reservoir wildlife hosts of novel pathogens are often identified or suspected based on serological assays, prior to the actual isolation of the pathogen itself. Serological assays might therefore be used to infer seroprevalence in reservoir wildlife host populations, until such time that specific diagnostic assays are developed [4]. Continuous surveillance of emerging infectious viral diseases is important to control epidemics and stop future pandemics caused by viral pathogens.

For instance, in a recent trial it was shown that alpacas shed Middle East respiratory syndrome related coronavirus (MERS Coronavirus) at challenge but are

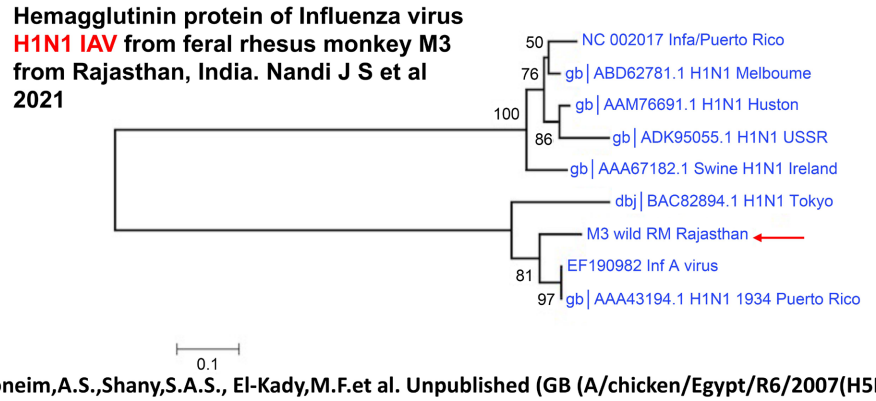
refractory to further shedding at rechallenge on day 21. The trial indicated that alpacas may be suitable models for infection and shedding dynamics of the virus. Blocking MERS-CoV zoonotic transmission from dromedary camels, the natural animal reservoir could potentially reduce the number of primary human cases. In contrast to naïve animals, in-contact vaccinated llamas did not shed infectious virus upon exposure to directly inoculated llamas, consistent with the induction of strong virus neutralizing antibody responses. The data provide further evidence that vaccination of the reservoir host may impede MERS-CoV zoonotic transmission to humans. [5] [6].

Bats, another animal species is known to harbor different viral pathogens and are considered natural reservoirs for several highly pathogenic viruses that can infect other animal species, including humans. A bat betacoronavirus has several homologies with the SARS-CoV-2, etiological pathogen of the current Covi19 pandemic but the actual animal sources is yet to be conclusively proven [7]. Achimota virus 1 (AchPV1) and Achimota virus 2 (AchPV2), members of the family Paramyxoviridae, cluster with other bat-derived zoonotic viruses. The viruses are isolated from urine collected in urban bat (*Eidolon helvum*) roosts in Ghana, West Africa. To assess the susceptibility of AchPV1 and AchPV2 in animals, experimental infection studies in small laboratory animals were conducted in ferrets, guinea pigs and mice. Seroconversion, immuno-histological evidence of infection, and viral shedding were identified in ferrets and guinea pigs, but not in mice [8].

2. Material and Methods

In November 2021, Veterinarian at the resting place of migratory demoiselle crane (*Grus virgo*) noticed sudden death of 75 cranes. The number of dead cranes increased dramatically to >300 within a short period of a month (**Figure 1**). However, there was no report of spreading of the H5N1 AIV infection from the infected migratory cranes to nearby chicken farms or pig farms according to the local villagers. Symptomatic cranes became gradually weak and were unable to fly. They eventually fell dead which caused much concern locally, especially in the prevailing SARS-CoV-2 pandemic situation the world over. By the end of Dec 2021, the number of cranes with mortality and morbidity gradually reduced, making it a temporary "epizootic infection". Necropsy and postmortem analyses were performed by Veterinary experts at Jodhpur State Government facility. Serological analyses for detection of H1N1 IAV and SARS-CoV-2 infections were performed by a Diagnostic laboratory situated in Goa in the cloacal swab samples of the cranes. The reports were negative for both H1N1 IAV and CoV-2. Molecular diagnosis of tissue samples from the crane carcasses was carried out at a specialized laboratory located in Bhopal, Madhya Pradesh. The RT-PCR results of the Haemagglutinin (HA) region of the surface region of the viral membrane identified the etiological agent to be the highly pathogenic Avian Influenza Virus H5N1 (HPAIV), akin to equivalent sequences of HPAIV reported from Egypt, that was deposited at the Genbank database: ABW37436.1 (**Figure 2**).

Figure 1. Migratory cranes at the resting site near Kaparada village, Jodhpur.



Abdel-Moneim,A.S.,Shany,S.A.S., El-Kady,M.F.et al. Unpublished (GB (A/chicken/Egypt/R6/2007(H5N1)Sequence ID: ABW37436.1, Haemagglutinin protein, H5N! HPAIV Infecting demoiselle cranes near Jodhpur, Rajasthan, India 2021

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MEKIVLLLAIVSVVKSDQICIGYHANYSTEQVDTIMEKDVIVTH
AQDILEKTHNGKLCNLEGMKPLILRDCSVAGWLLGNPMCDEFHNVPEWSYIVEKINPA
NDLCYPGNFDDYEELQHLFSRINHFEKIQIIPKNCWSDHEASGVSSACPYQGRSSFFR
NVVWLTKKDNAYPTIKRSYNNTNQEDLLVLWGIHHPNDAAEQTRLYQNPTTYISVGTS
TLNQRLVPKIATRSKVNGQSGRMEFFWTILKSNDAINFESNGNFIAPENAYKIVKKGD
STIMKSELEYGNCNTKCQTPIGAINSSMPFHNIHPLTIGECPKYVKSNRLVLATGLRN
SPQGKRRRKKRGLFGAIAGFIEGGWQGMVDGWYGYHHSNEQGSGYAADKESTQKAIDG
VTNKVNSIIDKMNTQFEAVGREFNNLERRIENLNKKMEDGFLDVWTYNAELLVLMENE
RTLDFHDSNVKNLYDKVRLQLRDNAKEFGNGCFEFYHRCDNECMESVRNGTYDYPQYS
EEARLKREEISGVKLESIGTYQILSIYSTVASSLALAIMVAGLFLWMCSNGSLQCRIC
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Figure 2. Phylogenetic tree based on neighbour-joining algorithm of the viral hemagglutinin (HA) sequences (GB Accession Number: MZ298601, Nandi *et al.*, 2021). Equivalent HA protein sequence of HA protein of HPAIV from Egypt infected chickens from a local poultry farm (A/chicken/Egypt/R6/2007(H5N1) Sequence ID: ABW37436.1).

3. Discussion

The ecological and epidemiological relationship of zoonotic viruses with its common natural hosts: wild birds, pigs and humans is complex and keeps evolving. Cross-species transmission of HPAIV H5N1 of wild demoiselle migratory birds has not been reported before. Demoiselle cranes are found in extremely cold parts of Euro-Siberia, Mongolia, and north-eastern China. In winter the cranes migrate to distant, warmer countries like India to avoid the harsh weather.

Waterfowl and aquatic birds are the natural reservoir for influenza viruses [9] [10] [11]. Pigs and humans are also known hosts for influenza viruses. AIVs are the progenitors of human Influenza A Virus (IAVs), that causes human respiratory infections and mortality in severe cases. In October 2010, H5N1 viruses

were isolated from fecal samples of ducks at Lake Ohnuma, Wakkanai, Hokkaido, on their way south from their nesting lakes in Siberia. Since then, nationwide H5N1 HPAIV infections in wild birds and chickens have occurred in Japan, and 63 and 24 isolates were identified from wild birds and chickens, respectively.

These viruses were maintained in wild migratory bird reservoir and were brought to Japan in the 2010-2011 winter season. To clarify whether H5N1 HPAIV has been perpetuated dominantly at their nesting lakes in Siberia intensive surveillance of avian influenza in migratory birds should be strengthened. AIVs, especially the zoonotic H5Nx viruses are recognized as public health threats [12]. In 1996, a highly pathogenic H5N1 avian influenza virus was detected in Chinese geese [13].

South Asia has experienced regular outbreaks of H5N1 avian influenza virus since its first detection in India and Pakistan in February 2006. Till 2009, the outbreaks in this region were due to clade 2.2 H5N1 virus. In 2010, Nepal reported the first outbreak of clade 2.3.2 virus in South Asia. Sequencing of all the eight gene-segments of seven H5N1 viruses isolated in these outbreaks was carried out. The predicted amino acid sequence analysis revealed high pathogenicity to chickens. Phylogenetic analyses indicated that these viruses belong to clade 2.3.2.1 and were distinct to the clade 2.3.2.1 viruses isolated in Nepal. Identification of new clade 2.3.2 H5N1 viruses in South Asia is reminiscent of the introduction of clade 2.2 viruses in this region in 2006-2007. It is important to monitor whether the clade 2.3.2.1 is replacing clade 2.2 in this region or co-circulating with it [14] [15].

Continued co-circulation of various subclades of the H5N1 virus which are more adapted to land based poultry in a highly populated region such as India increases the risk of evolution of pandemic zoonotic H5N1 viruses [16]. However, in the present investigation, transmission of HPAIV to poultry farms and pig farms situated close to the resting site of the migratory cranes was not reported, and the observed fatal infection of the migratory crane was of limited and temporary duration. All subtypes can infect avian species except H17N10 and H18N11 subtypes, which infect bats. Influenza disease outbreak in a poultry farm in Hong Kong was caused by a reassorted H5N1 virus [17].

Interaction between receptors present on host respiratory epithelial cells and viral surface protein determines the susceptibility of a given species to influenza viruses. Wild bird AIVs were found to recognize avian-like receptors, while some viruses exhibit human-like receptor binding, indicating the potential risk of cross-species transmission of AIVs from wild aquatic birds to humans. Sialic acid linked to galactose via an α2-3 linkage (SAα2,3Gal) or via α2-6 linkage (SAα2,6Gal) are preferential receptors for AIVs and IAVs respectively [18].

Reassortment between human IAVs, and zoonotic AIVs leads to the emergence of pandemic influenza strains.

4. Summary

The capacity of wild bird viruses to infect mammals needs to be assessed vigo-

rously. Investigation of pathogenic mechanism of AIV infection is helpful to develop anti-influenza virus strategies and to decipher molecular steps responsible for virulence of highly pathogenic influenza viruses. Routine surveillance and monitoring of IAV infection in wild birds, pigs and humans are essential to aid in the design and manufacture of broad-acting influenza vaccines.

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Authors' Contribution

SSR, HSG, and GP took part in the field work. SSR performed post-mortem of the cranes and necropsy taking full precautions. JSN conceptualized and guided the investigation and wrote the manuscript which was approved by all authors.

Conflicts of Interest

Authors declare no conflict of interest.

References

[1] Nandi Jayashree, S., Chhangani, A.K., Rathore, S.S. and Mathur, B.R.J. (2019) Diversity of Primate Lentiviruses Rebooted. *Journal of Biosciences and Medicines*, **7**, 126-138. https://doi.org/10.4236/jbm.2019.712011

[2] Wang, L.F. and Crameri, G. (2014) Emerging Zoonotic Viral Diseases. *Revue Scientifique et Technique*, **33**, 569-581. https://doi.org/10.20506/rst.33.2.2311

[3] Nandi Jayashree, S., Rathore, S.S. and Mathur, B.R. (2021) Transmission of Infectious Viruses in the Natural Setting at Human-Animal Interface. *Current Research in Virological Sciences*, **2**, Article ID: 100008. https://doi.org/10.1016/j.crviro.2021.100008

[4] Peel, A.J., McKinley, T.J., Baker, K.S., Barr, J.A., Crameri, G., Hayman, D.T., Feng, Y.R., Broder, C.C., Wang, L.F., Cunningham, A.A. and Wood, J.L. (2013) Use of Cross-Reactive Serological Assays for Detecting Novel Pathogens in Wildlife: Assessing an Appropriate Cutoff for Henipavirus Assays in African Bats. *Journal of Virological Methods*, **193**, 295-303. https://doi.org/10.1016/j.jviromet.2013.06.030

[5] Rodon, J., Okba, N.M.A., Te, N., van Dieren, B., Bosch, B.J., Bensaid, A., Segalés, J., Haagmans, B.L. and Vergara-Alert, J. (2019) Blocking Transmission of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in Llamas by Vaccination with a Recombinant Spike Protein. *Emerging Microbes & Infections*, **8**, 1593-1603. https://doi.org/10.1080/22221751.2019.1685912

[6] Crameri, G., Durr, P.A., Klein, R., Foord, A., Yu, M., Riddell, S., Haining, J., Johnson, D., Hemida, M.G., Barr, J., Peiris, M., Middleton, D. and Wang, L.F. (2016) Experimental Infection and Response to Rechallenge of Alpacas with Middle East Respiratory Syndrome Coronavirus. *Emerging Infectious Diseases*, **22**, 1071-1074. https://doi.org/10.3201/eid2206.160007

[7] Boni, M.F., Lemey, P., Jiang, X., Lam, T.T., Perry, B.W., Castoe, T.A., *et al.* (2020)

Evolutionary Origins of the SARS-CoV-2 Sarbecovirus Lineage Responsible for the COVID-19 Pandemic. *Nature Microbiology*, **5**, 1408-1417. https://doi.org/10.1038/s41564-020-0771-4

[8] Barr, J., Todd, S., Crameri, G., Foord, A., Marsh, G., Frazer, L., Payne, J., Harper, J., Baker, K.S., Cunningham, A.A., Wood, J.L.N., Middleton, D. and Wang, L.F. (2018) Animal Infection Studies of Two Recently Discovered African Bat Paramyxoviruses, Achimota 1 and Achimota 2. *Scientific Reports*, **8**, Article No. 12744. https://doi.org/10.1038/s41598-018-31193-z

[9] Sakoda, Y., Ito, H., Uchida, Y., Okamatsu, M., Yamamoto, N., Kosuke, S., *et al.* (2012) Reintroduction of H5N1 Highly Pathogenic Avian Influenza Virus by Migratory Water Birds, Causing Poultry Outbreaks in the 2010-2011 Winter Season in Japan. *Journal of General Virology*, **93**, 541-550. https://doi.org/10.1099/vir.0.037572-0

[10] Kajihara, M., Matsuno, K., Simulundu, E., Muramatsu, M., Noyori, O., Manzoor, R., Nakayama, E., Igarashi, M., Tomabechi, D., *et al.* (2011) An H5N1 Highly Pathogenic Avian Influenza Virus That Invaded Japan through Waterfowl Migration. *Japanese Journal of Veterinary Research*, **59**, 89-100.

[11] Chai, H., Li, X., Li, M., Lyu, X., Yu, W., Li, Y., Sun, J., *et al.* (2021) Emergence, Evolution, and Pathogenicity of Influenza A(H7N4) Virus in Shorebirds, China. *Journal of Virology*, **96**, Article ID: e0171721. https://doi.org/10.1128/JVI.01717-21

[12] Lee, D.H., Bertran, K., Kwon, J.H. and Swayne, D.E. (2017) Evolution, Global Spread, and Pathogenicity of Highly Pathogenic Avian Influenza H5Nx Clade 2.3.4.4. *Journal of Veterinary Science*, **18**, 269-280. https://doi.org/10.4142/jvs.2017.18.S1.269

[13] Donatelli, I., Castrucci, M.R., De Marco, M.A., Delogu, M. and Webster, R.G. (2017) Human-Animal Interface: The Case for Influenza Interspecies Transmission. In: Rezza, G. and Ippolito, G., Eds., *Emerging and Re-Emerging Viral Infections*, Vol. 972, Springer, Cham, 17-33. https://doi.org/10.1007/5584_2016_136

[14] Sonnberg, S., Webby, R.J. and Webster, R.G. (2013) Natural History of Highly Pathogenic Avian Influenza H5N1. *Virus Research*, **178**, 63-77. https://doi.org/10.1016/j.virusres.2013.05.009

[15] Nagarajan, S., Tosh, C., Smith, D.K., Peiris, J.S., Murugkar, H.V., Sridevi, R., Kumar, M., Katare, M., Jain, R., Syed, Z., Behera, P., Cheung, C.L., Khandia, R., Tripathi, S., Guan, Y. and Dubey, S.C. (2012) Avian Influenza (H5N1) Virus of Clade 2.3.2 in Domestic Poultry in India. *PLoS ONE*, **7**, Article ID: e31844. https://doi.org/10.1371/journal.pone.0031844

[16] Wu, Y., Tefsen, B., Shi, Y. and Gao, G.F. (2014) Bat-Derived Influenza-Like Viruses H17N10 and H18N11. *Trends in Microbiology*, **22**, 183-191. https://doi.org/10.1016/j.tim.2014.01.010

[17] Kilbourne, E.D. (2006) Influenza Pandemics of the 20th Century. *Emerging Infectious Diseases*, **12**, 9-14. https://doi.org/10.3201/eid1201.051254

[18] Du, W., de Vries, E., van Kuppeveld, F.J.M., Matrosovich, M. and de Haan, C.A.M. (2021) Second Sialic Acid-Binding Site of Influenza A Virus Neuraminidase: Binding Receptors for Efficient Release. *The FEBS Journal*, **288**, 5598-5612. https://doi.org/10.1111/febs.15668