



Perspective

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Genotype 4 reassortant Eurasian avian-like H1N1 swine flu virus: An emerging public health challenge

Rina Tilak¹✉, Sajal Bhattacharya², Shakya Sinha³

¹Department of Community Medicine, Armed Forces Medical College, Pune, Maharashtra, India

²Department of Zoology, Asutosh College (University of Calcutta), Kolkata, West Bengal, India

³Department of Zoology, Dinabandhu Andrews College (University of Calcutta), Kolkata, West Bengal, India

1. Introduction

Influenza A viruses (IAV), an orthomyxovirus, is reportedly prevalent in a large number of avian species and mammals including humans, and poses immense public health challenge as a potential pandemic originator[1]. It has been reported that IAV and Eurasian avian-like (EA) lineage influenza viruses have been co-circulating in pigs for nearly two decades in the Asian continent[2]. Pigs are known to be maintenance hosts for EA H1N1 besides acting as ‘mixing bowls’, with the potential to harbor viral strains which can cause pandemics[3]. The deadly impact of the two H1N1 pandemics in the recent past *viz.* the much famed Spanish flu of 1918 and the 2009 swine flu[1] pandemic rankles the scientific fraternity and public health experts till date. One re-assortant strain of EA H1N1 namely genotype 4 (G4) reassortant Eurasian avian-like (EA) H1N1 (G4EA H1N1) has been reported to be present in pigs of certain provinces of China since the last decade. The detection of G4 EA H1N1 amongst personnel working in slaughterhouses in the swine industry in China[4] draws attention to the likely possibility of a G4 EA H1N1 pandemic in the near future, if not addressed well in time. The G4 EA H1N1 is known to possess characteristics that are considered favorable for its adaptation amongst humans[4]. Thus, the likelihood of a potential pandemic of G4 EA H1N1 in the near future has turned into a hot, yet dreaded topic of discussion amongst the skeptic scientific fraternity. In this context, this paper is an attempt to assess and analyze the possible public health challenges from G4 EA H1N1 and the requirement of forming country-specific strategies to combat the potential human transmission and outbreaks.

2. IAV—a potent ‘pandemic originator’

IAV is one of the most dynamic viruses and a proven ‘pandemic originator’ due to its capability of extensive re-assortment resulting in novel re-assortant viruses. The 2009 swine flu undisputedly heralded the era of re-assortant viruses. Unlike the majority of human swine influenza infections, this re-assortant virus was capable of continuous human-to-human transmission, resulting in a global pandemic[5]. As per WHO, the flu reportedly impacted more

than 214 countries, making it the first global pandemic post the 1968 Hong Kong flu[6]. Similarly, another influenza virus re-assortant strain is G4 EA H1N1, commonly called the ‘G4 swine flu virus’. This ‘G4 swine flu virus’ is very similar to the 2009 ‘swine flu’-A/H1N1pdm09 which has been reported to be in circulation amongst pig populations in China with steadily increasing infectivity since 2016[4].

3. Swine flu virus ‘G4 EA H1N1’

The newly discovered G4 EA H1N1 virus is a cocktail of three lineages of influenza viruses, the H1N1 strain that caused the 2009 swine flu pandemic, the strains found in European and Asian birds and a North American H1N1 strain that has genes from human, pig and avian influenza viruses[4]. Although G4 EA H1N1 primarily affects pigs[7], yet recent evidence of its infection amongst humans has raised concerns[4]. To date, there is no evidence of human-to-human transmission, nonetheless, reports of pig populations in China being infected by G4 EA H1N1[4] raise the likely chances of virus spillover to humans. Apprehensions have been raised by some investigators that G4 EA H1N1 may likely be transmitted between humans as it possesses “all the characteristics” including the binding ability to human-like SA 2, 6Gal receptor for adapting to humans[4]. As on date, G4 EA H1N1 qualifies to be listed in the second phase of the “WHO Pandemic Phase Descriptions”[8], since evidence for only animal-to-human transmission has been confirmed with 35 people being reported to be infected with the virus[4,7]. Studies

✉To whom correspondence may be addressed. E-mail: rinatilak@hotmail.com

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have also revealed that about 4% of the 230 people from the general population had antibodies to G4 viruses[7].

4. Pigs as ‘mixing bowls’ for influenza viruses

Pigs are infamous for serving as hosts or “mixing bowls” for influenza viruses with pandemic potential by the creation of novel and potentially hazardous re-assortant viruses[3]. The presence of cellular receptors *i.e.* α -2,6-linked sialic acids (Sias) (human-like receptors) and α -2,3-linked (Sias) (avian-like receptors) in the trachea of pig supports virus replication of both the avian as well as mammalian lineages[9]. Once the pigs get infected, the viruses tend to gain the adaptations essential for either maintaining the infection in pigs, thus acting as a reservoir for human infection, or allowing mutations necessary for transmission to humans, thereby leading to its establishment in human population[10]. Results of a recent study (2011–2018) on influenza virus surveillance amongst pig populations in China revealed the presence of G4 re-assortant EA H1N1 virus since the year 2016 onwards[4]. A high sero prevalence of 10.4% amongst swine workers indicates that the G4 EA H1N1 virus has acquired increased human infectivity which enhances the chances for the virus to adapt to humans.

5. Need for country-specific ‘influenza virus surveillance cells’ (IVSC)

In the light of the fact that the future is fraught with likely pandemics of influenza viruses spilling over from animals like bats, pigs, pangolin, *etc.* to humans causing Spanish flu or swine flu-like pandemics, we need to establish country-specific IVSC for early warning of novel virus activity. The most challenging aspect is the similar clinical presentation of all influenza viruses, which further strengthens the cause for establishing these surveillance cells. These IVSC’s should continuously engage in monitoring for probable new influenza virus strains with outbreak potential. The warning from these cells will facilitate the implementation of preemptive measures to contain outbreaks at the local level and thus prevent trans-continental transmission and likely pandemics.

6. Conclusions

The era of ‘influenza virus pandemics’ has undoubtedly dawned. The influenza virus pandemics are a real threat to human health especially given the origin of new re-assortant virus strains. The report of swine flu virus ‘G4 EA H1N1’ amongst pigs is a warning sign of a novel threat of a probable pandemic in waiting. Unfortunately, there is no evidence yet of immunity amongst the human population to this new G4 strain of the avian influenza virus. The currently available flu vaccines also show minimal promise of protection against the new ‘swine flu virus’ thereby necessitating the development of a new vaccine. Although the world is relentlessly engaged in waging a war against these highly potent biological entities, yet it tends to take us for a surprise each time with an outbreak by a more potent strain than before. These re-assortant viruses possess the capability of causing fresh pandemics, hitherto

not known to humans. Any slackness of surveillance on this new emerging challenge may potentiate outbreaks of G4 EA H1N1.

Conflict of interest statement

The authors declare there is no conflict of interest.

Authors’ contributions

The conceptualization was done by R.T. The formal analysis and interpretation were done by R.T, S.B and S.S. The resource and writing-original draft preparation were carried out by R.T and S.S. The writing review and editing were performed by R.T and S.B. The supervision was done by R.T and S.B. The whole manuscript was read and approved by all authors.

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