Short Review on Vaccination and Surveillance on Avian Influenza in Bangladesh: Existing Gaps and Recent Insights

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Abstract

Avian influenza has been considered as a serious threat to veterinary public health of Bangladesh since 2007. The national and international bodies responded so quickly as to control the outbreak at that time. A full scale long time strategic plan and its implementation could protect the country from further outbreak. The dynamic antigenic nature of this virus is an extra concern. Besides, mass vaccination without proper surveillance and use of ineffectiveborder-crossed unauthorized vaccines worsened the situations silently. Recent outbreak of Highly Pathogenic Avian Influenza H5N1 is a matter of topmost national concern. It is time to navigate back to the unresolved issues prioritizing the analysis of existing avian influenza related data and metadata and fortification of surveillance system effectually. LBM (Live Bird Market) sink surveillance might serve the purpose given the feasibility of division wise surveillance system. Only by detecting existing field strain causing infections, master seed can be produced that will eventually result in efficient vaccine. Viral phylodynamics blended with computerized technology now provides prediction of variant protein and their phenotypic characteristics. Also the countries are more united than ever to share the genetic sequence of influenza virus and collaborate more actively. [Bangladesh Journal of Infectious Diseases 2017;4(2):48-51]

Keywords: Influenza in Birds; epidemiology; mutation; vaccination

Introduction

Avian influenza imparts a severe impact globally[1]. The perfidious nature of this virus has caused an exigency among scientists and has urged them to think and re-think about it. The emergence, re-emergence, epizootic spread worldwide and increasing intimidationto the economyhas rendered the whole world at a loss. In this sense, Bangladesh being an agro-based middle income country where poultry sector contributes a consequential portion of the total GDP (Gross Domestic Product) was

shattered by avian influenza several times[2]. The emergency national and international responses along with the vehement support from the human and animal health practitioners across the country succeeded in containing the H5N1 virus at that time. Even though the threat still remains as clearly evident by the H5N1 recent outbreakin January 2017 at a poultry farm in Dhaka, the capital of the country, killing 732 birds of 3000.Hence, this short review is performed to provide some insights about importance of avian influenza vaccine update by an epidemiologically relevant and regionally suited surveillance program to search for genetic variants and representative isolates of avian influenza virus.

Avian Influenza H5N1Vaccination: Local problem- Local Solution

Vaccination is the pivotal component in containing of avian influenza outbreak.The traditional influenza vaccine production relies on the stimulation of host immunity against a surface glycoprotein-hemagglutinin (HA)[3].This glycoprotein has the capacity to produce infinite number of antigenic expressions which is termed as 'antigenic drift'; the best known molecular evolution pattern described till now[4].This extreme ability of avian influenza viruses of evading immune response totally outweighs the anthropogenic factors that undermine the vaccine efficacy. So, testing vaccine efficacy in laboratory and field trials are implicated before enacting a control measure. The production of an efficacious vaccine requires matched master seed which can only be obtained from field sample isolation. Viral strains are selected either as representatives or low reactors. Then isolation of the strains is performed and antisera are produced. After hemagglutination inhibition (HI) tests of the isolated viruses against selected antisera, a thorough genetic and antigenic analysis of a representative subset of the strains is performed. Antigenic Cartography is an essential tool in this case to visualize and quantify the phenotypic differences among the viral strains. Multidimensional scaling (MDS) can be used for influenza cartographic construction[5]. These data are used to select H5N1 for vaccine development of avian species against those strains isolated earlier. This is the general protocol developed by World Health organization (WHO) for H5N1 vaccine development of avian species which is available in WHO Influenza web portal. Any outbreak requires serious thoughtregarding characterizing antigenic and genetic analysis of prevalent strains to ensure the efficacy of existing vaccine. Without doing so, mass vaccination will only create an avenue of resource wastages and genetic mutation as well as

transmission of virulence and mutant determinants among different or similar clades of viruses. Hence vaccine developed from only local matched seed straincan be expected to provide desired protection from avian influenza.

Live Bird market (LBM): Sink Surveillance

Epidemiological surveillance is defined as a constant systematic accumulation, analysis, interpretation and circulation of information and data used for mapping the course of related, unrelated, and interrelated events on which epidemiological factors have arithmetic or geometric impact. The first outbreak surveillance of avian influenza H5N1 was performed in 2007[6].The traditional surveillance follows Report-Investigation-Laboratory Tests-Culling (if positive) pattern.That means only reported cases are investigated and tested for the presence of avian influenza virus (AVI). But the farmers may not report the AIV suspected death due to the fear of economic and reputation loss.So, LBM sink surveillance is a realistic approach for active surveillance program for developing countries like Bangladesh where information networking and modern diagnostics are insufficient. It follows Investigation-Lab Test-Report irrespective of disease status of a region. Considering Dhaka as the sink of live birds of the country, samples are collected from pre-specified 106 live bird markets (LBMs) of Dhaka by 14 trained personnel in daily basis. The samples collected from North part of the city are kept in Livestock Research Institute (LRI) and samples of southern part are kept in CDIL. All the samples are conveyed to Bangladesh Livestock Research Institute, National Reference Lab for Avian Influenza on daily basis. Samples are collected from accumulation area (where the live birds are first accumulated), slaughter area, and exposure area (where the dressed carcass are kept for sale). Altogether 18 samples are collected from a single market, 6 from each area. After pooling, there remain only 3 representative samples from one market. If samples are H5 positive then back test is performed to identify the exact source. Samples positive for H7 undergo either back test or forward testing for H9. But no further tests are performed for H9 positive samples. This is because H5 is highly pathogenic to poultry causing severe mortality with expression of disease symptoms whereas H7 and H9 are low pathogenic with no clinical symptoms in poultry. Sink surveillance provides overall prevalence, monitoring current trends, point of intervention and assessment of impact, new virus identification, risk factors of LBM in spreading infections to human etc. In a

nutshell, this surveillance program is proving to be efficient and suitable for Bangladesh.

Analysis of High and Low Pathogenic Avian Influenza Outbreak

Avian influenza is a complex disease, with outbreaks in poultry having a severe impact on livelihoods of people and international trade in many countries. Among all the avian influenza subtypes, H5 and H7 cause systemic spread of virus with severe clinical disease. The emergence and spread of highly pathogenic H5N1 avian influenza virus and its unusually high death rate in sporadic cases of human infection has drawn the public attention to a threat of a new influenza pandemic. Avian influenza free status cannot be achieved unless sanitary and biosecurity practices are supplemented by an organized, coordinated vaccination accompanied by disease monitoring and eradication plans.

Antigenic variability of the challenge virus greatly alters the efficiency of existing vaccines. For example- classical inactivated vaccines induce host immunity mostly; if not exclusively composed of antibodies. So, strong and specific antibody response is required which can only be achieved when the vaccine is regularly updated on account of the evolution of field strain. Theoretically, this should be possible by reverse genetics technique. New expression systems are currently being explored to produce recombinant vaccines which would be able to induce a most homologous immunity. In real life, prediction of individual mutation in circulating field isolates is very difficult to predict and even more so when and where they might occur. Currently vaccine updates can only be made after vaccination failure and the necessary new antigens have been produced e.g. by reverse genetics. Even so, this does not meet the needs of territories where field strains of various antigenic profiles are present. The use of multivalent killed vaccines or multiple vaccinations using different killed vaccines is hardly achievable.

Basic and applied research with detailed biological characterization of influenza virus and analyses of genome reassortment and mutational changes continues to be of prime importance in all affected continents. Moreover, a harmonized international activity to control and manage outbreaks in collaboration with the Tripartite Alliance- world Organization of Animal Health (OIE), Food and Agricultural Organization (FAO), and World Health Organization (WHO) is more important than ever. Worldwide collaborative efforts are necessary to share advice on surveillance, prevention and control measures.

Avian influenza novel strain: A forthcoming risk of human infection- Speculation or stipulation?

Mainly H5N1 is highly prevalent in Bangladeshas compared to any other zoonotic avian influenza virus (H7 & H9). But only sporadic infections by H5N1 are observed in Bangladesh. The exact reason is vague. There are several hypotheses that people get immunized to influenza virus due to the frequent exposure in early life as seasonal human influenza is extremely prevalent in Bangladesh.Besides, the absence of hygienic abattoir practice and traditional indoor poultry farming renders the workers and farmers immune to the influenza viruses. But H5 and H7N9 accounts for much higher case fatality than seasonal influenza.So, any human case should be promptly reported and investigated thoroughly to prevent avian influenza outbreak in human.Besides risk assessment of human infection with novel avian influenza strain should be prioritized.

LBM Sink Surveillance: Serving the purpose?

It is known that H5N1 is endemic in Bangladesh. As LBM Sink Surveillance only provides the status of disease in a single area of the country, itcannot be used in containment of the disease. However such an approach is praiseworthy as a pilot project eventually to be followed up on a larger scale.This program is helping to get the real picture of Dhaka city. In Chittagong, the next program is going to be instigated soon. At first, it might seem that resources are being wasted barely to identify the virus and calculate the prevalence. But an overall picture will help to take necessary measures effectively so that suitability of efficient prevention and control measures can be ensured in future. On top of that, this wider coverage surveillance will help to identify the matched seed strain for vaccine preparation.

Discussion and Recommendation

'Bangladesh has a real chance to get the virus under control, if it commits itself to a full-scale comprehensive national control campaign. FAO is ready to continue its assistance and further international aid will be essential to support the country in this huge challenge.' still the sound of Joseph Domenech, FAO's Chief Veterinary Officer at that time, hangs in the air- while 10 years have passed since the country faced avian influenza crisis in 2007[7]. No matter how cautious and concerned the international community is- how stronger their

unity and policy becomes; eventually the principal duties and responsibilities put pressure on the individual nation's burden. Avian influenza is a noxiously designed biological entity that possesses magical power of evolution. But timely sharing of Gene Sequence Data (GSD) of avian influenza by the scientists of the member countries of '*A global initiative on sharing avian flu data*' (GISAID) turned out to be fruit bearing for the scientists of WHO's Global Influenza Surveillance and Response System (GISRS)[8]. Besides, sophisticated biomedical technologies are mapping the antigenic variations producing matched seed strain that provides desired protection from specific strains. Even analysis of comprehensive avian influenza related bioinformatics are performed by the scientists in order to assist in effective vaccine development, diagnostics, therapeutics and predictions of variant antigens and their phenotypic effect- these are freely accessible without any restrictions from the IRD (Influenza Research Database). So, this virus is not indomitable today. Albeit Bangladesh lacks any in depth analysis of avian influenza transmission in human-animal interface, LBM sink surveillance is likely to serve the purpose. But it should also be taken into consideration that nomadic ducks are constantly substantiated as the potential reservoir and possible reassortment vessel of H9 with HPAI H5N1[9]. As duck is less popular in Dhaka where currently LBM sink surveillance is in operation, division wise sink surveillance might be a good chance of getting the big picture. Without a proper strengthened national surveillance, mass vaccination would be a detrimental decision. Egypt suffered from a devilish avian influenza outbreak causing more than 100 human infections in 2010 due to commercial vaccine failure[10]. In no time Bangladesh should tie more collaboratively with the international community implementing effective policy in the containment of avian influenza. So, there is no alternative to the unanimity of animal and human health professionals.

Conclusion

The constantly evolving nature of influenza virus requires continuous global monitoring and frequent reformulation of existing vaccine. It is imperative that monitoring and surveillance system of avian influenza virus should be precise and fruit bearing. Policies should be originative, not rhetoric.

Secondly, matched master seed must be considered for reformulated vaccines otherwise the country might fall into abject abyss. And finally an all-out firm collaboration, particularly among human and animal health professionals, is a must to overcome the present situation as well as confront the upcoming threat. Given appropriateness of these steps, we might be optimistic for better future.

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