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ARTICLE

Establishing the laboratory - based Influenza surveillance network in Vietnam.

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Abstract

In 2006, national influenza surveillance was implemented in Vietnam and highlighted the importance of laboratory capacity to detect influenza viruses including novel influenza virus. Building and strengthening the influenza laboratory network by increasing trained personnel and equipped laboratories base on support from WHO and other international organizations, currently, 26 laboratories have been included in the network capable of performing polymerase chain reaction testing for influenza. This paper provides a brief overview of the laboratory-based influenza surveillance capacity for influenza virus detection and determination of their respective strengths and challenges in sustaining the network in the future.

Introduction

Influenza is one of the common infectious diseases and is a significant worldwide public health issue that can cause serious health conditions, loss of workday, human suffering and mortality. The World Health Organization (WHO) estimates that influenza infection is responsible for a mortality rate of 3.5 to 9.2 per 100.000 individuals annually, mortality being highest in infants and elderly persons ¹.

In Vietnam, influenza like illness (ILI) is one of 26 reportable communicable diseases, monthly data have been aggregated by provinces by the Ministry of Health (MOH) of Vietnam since 1979. However, the national data of the epidemiology and virology of influenza infection have not been reported during a 27 years' period (1979-2005). The MOH issued circular 54 in 2015 which updated and required 42 diseases that have to be reported based on category of

pathogen in which influenza disease should be reported monthly as well as the incidence rate and the fatal cases ².

In December 2003, Vietnam reported its first cases of Highly Pathogenic Avian Influenza (HPAI) H5N1. Within four months, the disease was detected in 57 of 64 provinces. Approximately 44 million poultry — 17% of the nation's stock—were culled to prevent further outbreaks or died from the disease. This affected not only the poultry farmers severely but also the national economy. The economic toll was about 0.5% of Vietnam's GDP at that time, or \$250 million ³.

Moreover, as 15 human deaths were recorded in 2004 and there was increasing consideration that the virus could infect human to human so that the government realized the importance of establishing and strengthening the influenza surveillance capacity.

In 2006, the Ministry of Health (MOH), supported by the World Health Organization (WHO) and the US Center of Disease Control and Prevention (CDC) launched national influenza surveillance in Vietnam with the goals: it provides information needed about epidemiological and virologic characteristics of seasonal influenza, link to health decisions, policies and actions in Vietnam ⁴.

The influenza surveillance network develops the capacity of regional laboratories to identify the causes of influenza like illness in Vietnam and strengthens the ability for early detection influenza outbreaks in sufficient time for response actions, these activities had provided good responses to the A/H1N1 pandemic in 2009. The quality laboratory testing is important for guiding public health decisions and policies, however, standardized processes to assess the quality of influenza laboratories and the fulfillment of these terms is limited in Vietnam.

This paper provides a brief overview of the laboratory-based influenza surveillance capacity for influenza virus detection and describes their respective strengths and limitations in describing the epidemiology of influenza.

Methods

To understand the development of laboratory-based surveillance, the “International Influenza Laboratory Capacity review” tool ⁵ and the annual assessment requirement of Ministry of Health issued 2017 ⁶ have been used.

Results and Discussion

1. Establishment of the influenza laboratory networks.

In the beginning (2005), the laboratory-based surveillance influenza network consisted of one National Influenza Center (NIC) and three additional regional influenza laboratories, which are located in the biggest and most densely populated cities in four different regions: North (NIC- National Institute of Hygiene and Epidemiology), South (the Influenza laboratory – Pasteur

institute Hochiminh city), High Land (the virology laboratory- Taynguyen Institute of Hygiene and Epidemiology) and Central (virology lab- Pasteur Institute Nhatrang).

The WHO recognized the first NIC for Vietnam at the National Institute of Hygiene and Epidemiology, Hanoi, which leads and is responsible for developing and implementing the standardized methodologies and training, monitoring, supervision and quality assurance of the virology aspect of National Influenza Surveillance project.

Since pandemic A(H1N1) influenza started in early June 2009, specimens of suspected cases were overloaded, the requests to be confirmed by laboratory diagnostic tests were substantially increased, thus, additional laboratories were required to provide timely, accurate diagnosis of influenza infection throughout Vietnam. The MOH approved for 11 provincial and hospital laboratories to join in the influenza laboratory network.

In 2011, an additional NIC was assigned by the WHO at Pasteur Institute Hochiminh city. Nowadays, a total of 22 laboratories are participating in seasonal influenza detection and two NICs are monitoring circulating influenza virus strains and detect new variants, potentially the combination of genetic material between human and animal influenza viruses.

Figure 1: The establishment of the influenza laboratory network

2. The influenza laboratory network capacity

Equipment and funding

The National Influenza Surveillance Project was supported by the WHO and US CDC to provide diagnostic equipment for all network laboratories in 2006 based on the WHO recommendation for influenza detection, i.e. PCR system, biosafety cabinet type II-A (BSC) and other essential laboratory instruments. In 2009, the pandemic A/H1N1 had occurred, the MOH collaborated with several donor agencies (WHO, US CDC, USAID) to provide more real time PCR (ABI 7500)

and additional PCR systems. The NICs, regional laboratories and five hospital/province laboratories have both real-time PCR and conventional PCR systems. The remaining provincial laboratories (17) have only the PCR system. Reagents stock was provided by international donors as well as the National Influenza Surveillance project.

After 10 years of implementation and operation under the National Influenza Surveillance project which were funded by both the US CDC and Vietnam government, from 2016, the budget for conducting National Influenza Surveillance System has been switched to Vietnam government with 8 sentinel sites connected with 2 NICs and 2 regional laboratories ⁷.

Function and management

In the beginning, the NIC-NIHE was responsible for developing and implementing the standardized operation procedures (SOPs) for specimen collection, transportation and storage; RT-PCR for influenza detection, and quality assurance system based on protocol developed by WHO. Laboratory staff at the NIC received training for RT-PCR, viral isolation, sequencing and serology test from WHO collaborating center such as US CDC, NIID Japan, VIDRL Australia. The NIC staffs then performed the training in regional and provincial, hospital laboratories in RT-PCR assays and updated primers and reagents for all laboratories networks when the novel influenza A(H1N1) pandemic occurred in 2009. To ensure accuracy of the diagnostic test, in the initial stages all RT-PCR positive samples detected at Pasteur Institutes Nha Trang and Central Highlands were sent to the NIC-NIHE or Pasteur Institute for verification and further analysis, then, they became capable of undertaking influenza diagnosis and subtyping after two years of proceedings. Nowadays, the network of the 26 laboratories are designated for seasonal influenza detection, located in 20/63 provinces in Vietnam. The GDPM receives surveillance data from 4 institutes through monthly communicable diseases report.

The MOH assigned two NIC laboratories, which have capabilities of performing avian influenza A(H5N1, H7N9) detection by using conventional/realtime RT-PCR and viral isolation, diagnostic equipment and standard procedure of biosafety and biosecurity of handling specimens and virologic assays have been developed base on WHO guideline.

3. National Influenza Centers

Establishment

The NIC-NIHE used to be the respiratory viruses laboratory, which conducted influenza and SARS diagnosis, and belongs to Department of Virology, National Institute of Hygiene and Epidemiology, Hanoi, Vietnam. The NIC-NIHE was recognized by WHO in March 2005 and is a member of the Global Influenza Surveillance Network (GISN).

The NIC-NIHE was the first laboratory, which confirmed the high pathogenic avian influenza A(H5N1) infected to human in Vietnam in 2005. It plays a key role in characterizing seasonal influenza virus, avian influenza virus in human and associated immunopathology.

The NIC-PIHCM was established in 2011 with the needs of influenza laboratory-based confirmation increased after 2009 influenza pandemic.

Quality Assurance and Quality Control

To ensure accuracy of diagnosis, the NIC-NIHE has participated in the WHO External quality assessment program (EQAP) for the detection of influenza virus by PCR since 2007 ⁸ and has good scores for seasonal influenza and avian H5/H7 influenza detection up to now.

Both NICs perform the Good Laboratory Practice (GLP) Survey every two years coordinated by WHO to enhance the technical aspect as well as the laboratory management ⁹.

Furthermore, NIC-NIHE, NIC-PIHCM and other regional/provincial/hospital laboratories also have inter-laboratory comparisons in order to strengthen the technique and update the protocols for influenza diagnosis.

The ISO 15189 Accreditation was introduced into the preventive medicine laboratory network, approved by Vietnam Bureau of Accreditation. Up to 2018, two NICs and two regional laboratories in the influenza network have been granted the ISO 15189 Accreditation.

Achievements

Through the National Influenza Surveillance project (NIS), in collaboration with the Global Influenza Surveillance networks (GISN), NICs provide up-to-date laboratory-based influenza surveillance data and other information needed to the Ministry of Health to make evidence-based decision, policies and actions. Together with epidemiological data, the virologic data from NICs shows the comprehensive national surveillance of influenza ^{4, 10, 11}.

To increase capacity for animal influenza research, the standard BSL-3 laboratory system has started operation in 2008 with support from JICA, Japan. That can be used for handling clinical specimens collected from avian influenza A(H5N1) suspected patients, virus isolation of H5N1 case, virological and serological tests. Biosafety and biosecurity training of the laboratory personnel is done by cooperation with WHO and the National Institute of Infectious Diseases (NIID) Tokyo, Japan ¹².

As leader of the influenza laboratory networks, NIC-NIHE takes responsibility for training, monitoring, supervision and quality assurance of virological aspects of all laboratories in the network. NIC trained, standardized and decentralized to provincial and hospital laboratories diagnostic protocols, which was an important step in meeting the need for clinical diagnosis when a huge number presented.

The two NICs also contribute to global influenza surveillance and response efforts through the reporting of virological surveillance data to the WHO (<http://apps.who.int/flumart/Default?ReportNo=1>) through the FluNet platform and by sending the clinical specimens and/or virus isolates to WHO collaborating centers annually to detailed antigenic and genetic characterization, that may help to select and develop candidate vaccine viruses and required standard reagents.

4. Influenza laboratory network sustaining and strategic development in Vietnam.

The 2009 H1N1 pandemic provided an opportunity to gain experience, learn important lessons on influenza surveillance capacity in Vietnam and influenza laboratory networks, which are the primary resource for monitoring influenza virus activity and play a vital role in early warning outbreaks.

For future works, the trend can be seen as part of the National Influenza Surveillance in Vietnam, which is improvement on molecular diagnosis capacities for provincial and hospital laboratories, integration laboratory results between clinical, epidemiology and virology data.

However, there are many challenges to keep this influenza laboratory network sustainable recently. Firstly, the financial support for the work of NICs and other influenza laboratories by the Government was committed but may still need supports from international organizations that recently reduced the funding support for health care activities as Vietnam achieved a middle-income country status since 2011. Secondly, rotation among health personnel is high in provincial laboratories, so there is a decrease in skilled laboratory staffs. Thirdly, the need to procure new equipment, supplies and reagents and to certify, maintain, calibrate the essential equipment (BSC, PCR/realtime PCR machine) throughout laboratory network is costly and challenging for the government.

Vietnam is still facing enormous challenges related to the emergence of highly pathogenic avian influenza A(H5N1) as a significant domestic public threat. The national influenza surveillance network achieved effective functioning of surveillance laboratories, which is key roll to improve the accuracy of the surveillance system ¹².

The Institute of Vaccine and Medical Biological (IVAC) in Vietnam has been developing and licensing the pandemic influenza A/H5N1 and seasonal influenza vaccines for human (Randomized safety and immunogenicity trial of a seasonal trivalent inactivated split virion influenza vaccine (IVACFLU-S) in healthy young Vietnamese adults ¹³). Thus, virologic surveillance for circulating influenza strains is necessary to facilitate the development of annual influenza vaccines in which vaccine strains match to circulating strains in Vietnam. This may improve the effectiveness of domestic vaccine, increase the production capabilities and explore the development of influenza vaccine production capacity.

Conclusion

The laboratory - based surveillance network is an important component of the National Influenza Surveillance System, and this network make efforts for the timely response repotting of virology surveillance data to the Ministry of Health as well as Global Influenza Surveillance Network during pandemic A(H1N1) influenza 2009 and up to date. Clearly, the success and sustainability of this network depend on funding and financial supporting from international partners and government is needed for future development of these laboratory networks.

References

1. Iuliano A, Roguski K, Chang H. Estimates of global seasonal influenza-associated respiratory mortality: a modelling study. *Lancet*. 2018;391(10127):1285-1300.
2. Vietnam Ministry of Health. Circular for guiding the preparation and reporting of infectious diseases. 2015.
3. Vu T. The Political Economy of Avian Influenza Response and Control in Vietnam. *STEPS Working Paper 19, Brighton: STEPS Centre*. 2009.
4. Nguyen Y, Graitcer S, Nguyen T. National surveillance for influenza and influenza-like illness in Vietnam, 2006-2010. *Vaccine*. 2013;31(40):4368-74.
5. Association of Public Health Laboratories. International Influenza Laboratory Capacity Review 3. 2012.
6. Vietnam Ministry of Health. Criteria for assessing the quality of medical laboratories in Vietnam. 2017.
7. Vietnam Ministry of Health. National plan for surveillance of influenza-like illness syndrome, severe acute respiratory infections and hand-foot-mouth disease in Vietnam for the period 2017-2020. 2017.
8. World Health Organization. External Quality Assessment Programme for the Detection of Influenza Viruses by RT-PCR. 2018.
9. World Health Organization. Good Laboratory Practice Survey Report. 2016.
10. Le Q, Wertheim , Tran. A community cluster of oseltamivir-resistant cases of 2009 H1N1 influenza. *N Engl J Med*. 2010;362(1):86-7.
11. Vuong CD, Hoang PV, Nguyen HK. The genetic match between vaccine strains and circulating seasonal influenza A viruses in Vietnam, 2001–2009. *Influenza and Other Respiratory Viruses*. 2012:DOI:10.1111/irv.12038.
12. Creanga A, Nguyen HK. Highly Pathogenic Avian Influenza A(H5N1) Viruses at the Animal–Human Interface in Vietnam, 2003–2010. *The Journal of Infectious Diseases*. 2017;216 (Suppl 4):S529–38.
13. PATH. Supporting influenza vaccine production in Vietnam - Increasing vaccine supplies against a seasonal and pandemic threat. 2016.