Influenza cases from Surveillance Acute Respiratory Infection in Indonesia, 2011

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Abstrak

Latar belakang: *Infeksi Saluran Pernafasan Akut Berat (SARI) atau pneumonia memiliki kontribusi besar dalam morbiditas dan mortalitas, namun Indonesia masih belum memiliki data epidemiologi yang cukup. Tujuan dari penelitian ini adalah untuk mengetahui pola epidemiologi virus influenza sebagai etiologi kasus SARI.*

Metode: *Analisis ini didasarkan pada surveilans sentinel SARI yang dilakukan oleh Pusat Biomedis dan Teknologi Dasar Kesehatan (Pusat BTDK) pada sembilan rumah sakit di sembilan provinsi di Indonesia pada tahun 2011. Setiap pasien yang memenuhi kriteria SARI diikutsertakan dalam penelitian ini. Usap tenggorok dan hidung, serta serum diambil dan diperiksa di laboratorium Virologi Pusat BTDK untuk menentukan etiologinya. RT-PCR digunakan untuk mendeteksi jenis dan subtipe virus influenza dari usap tenggorok/hidung.*

Hasil: *Sebanyak 333 kasus SARI didapatkan dari sembilan rumah sakit sentinel. Sebanyak 6% kasus yang positif influenza melalui pemeriksaan RT-PCR. Dari seluruh kasus SARI, proporsi influenza A adalah 5% dan influenza B 1%. Influenza A subtipe H1N1pdm09 mendominasi influenza musiman yang beredar di Indonesia dari kasus SARI.*

Kesimpulan: *Virus Influenza musiman didapat dari kasus-kasus SARI namun jumlahnya tidak terlalu banyak. Oleh karena itu, penyebab lain dari kasus SARI masih perlu diteliti. (**Health Science Indones 2014;1:7-11)***

Kata kunci: *SARI, Surveilans, Influenza*

Abstract

Background: Severe Acute Respiratory Infection (SARI) or pneumonia has a major contribution in the morbidity and mortality, however, Indonesia still has lack of its epidemiology. The aim of the study is to know the epidemiological pattern of influenza virus as the etiology of SARI cases.

Methods: This analysis based on the sentinel surveillanceSARI conducted by Center for Biomedical and Basic Technology of Health (CBBTH) of Indonesia carried out at nine hospitals in nine provinces in 2011. Every patient who met the criteria of SARI was included in this study. Serum, throat and nasal swabs were taken and examined at the Virology laboratory CBBTH to determine the etiology. RT-PCR was used to detect type and subtype of influenza viruses from swabs.

Results: Total number of SARI cases were 333. We found 6% cases were influenza positive by RT-PCR. The proportion of influenza A was 5% and influenza B 1% from total SARI cases. We detected that seasonal influenza A subtype H1N1pdm09was the dominant subtypes that circulating in Indonesia.

Conclusion: We foundseasonal Influenza infection from SARI patients, however, it was only small number. Therefore, further detection of SARI cases is needed. ***(Health Science Indones 2014;1:7-11)***

Key words: SARI, surveillance, influenza

Severe Acute Respiratory Infection (SARI) or Pneumonia is a form of acute infection in the lung tissue (alveoli or interstitial tissue) with fever and coughing as its clinical manifestations along with the difficulty of breathing such as the condition of being breathless, the retraction of the chest wall and stridor during rest or results of thoracic imaging which indicates a pulmonary infiltrate.[1-3]

Pneumonia is a health issue for the world, and not only for developing countries but also for developed countries such as the US, Canada, and European countries. Pneumonia causes a high percentage of death in the world for both babies and infants under the age of 5 (14.1%).[4] According to Indonesia Basic Health Research data in 2007, pneumonia is the second leading cause of death after diarrhea among infants.

Pneumonia may be caused by bacteria, virus or mycoplasma, including influenza virus. Seasonal influenza virus is the second cause most commonly found among children suffering from pneumonia, and it contributes significantly in cases of inpatient care and death among children under the age of 5 around the world.[6] Data from neighbouring countries showed that the influenza virus is one of the causes in SARI. In Thailand, among 28,543 patients with acute low respiratory tract infection from 2005-2010, influenza virus was detected in 8% of the patient.[7] In Bangladesh, the incidence of SARI associated with influenza in children < 5 years old was estimated around 6% per 1000 person per years in 2008-2010.[8] In 2011, Ministry of Health Indonesia data showed that severe pneumonia in children < 5 years old is around 0.9 % with CFR 0.14 %.[9]

While SARI has contributed a great amount of share in morbidity and mortality, up to this moment Indonesia still does not have any data regarding its epidemiology patternand the etiology of SARI. SARI surveillance primarily intended to detect and discover new variants or subtypes of Influenza virus, including strains that are potential of pandemics.[1] However, the other etiologies could cause SARI, such as bacteria.Therefore, SARI surveillance is highly crucial for early detection and characterization of SARI etiologies, both viruses and bacteria.[1]

METHODS

Study site

SARI surveillance is administered in ten sentinel hospitals in Indonesia. They were the HasanSadikin Hospital Bandung, Tangerang Regional General Hospital, Dr. Karyadi Hospital Semarang, Dr. Wahidin Sudiro Husodo Hospital Makassar, Mataram Regional General Hospital, and SuliantiSuroso Central Hospital for Infectious Disease Jakarta, Dr. M. Djamil Hospital Padang, Dr. Soedarso Hospital Pontianak, and DOC II Jayapura Hospital.

Enrolment and data collection

January to December 2011, laboratory-enhanced respiratory surveillance was conducted at the in-patient department of all nine sentinel hospital. During this period, trained health workers invited all patients which met definition operational of SARI to participate and enrolled to whom agreed. Next, health workers completed a questionnaire by patient interview and record review, and collected nasal and throat swabs, serum and sputum/blood to detect virus and bacteria causing the SARI. Surveillance case definitions were based on those devised by WHO both for children under five years of age and for the older ages.

Laboratory methods

Nasal and throat swabs specimens, in 1 ml viral transport medium (VTM, prepared in-house), were transported to Virology laboratory, Center of Biomedical and Basic Technology of Health, NIHRD which is located in Jakarta under specific cold chain procedures. The specimens then stored in -80 C until analysis.RT-PCR test, virus culture and Hemagglutination Inhibition (HI) test were performed based on influenza virus detection procedures in WHO guidelines.[10]

Viral RNA was extracted from the VTM-Clinical Specimens using the QiAMP Viral mini kit (Qiagen, Germany) according to manufacturer's intruction. The RNA was reverse transcribed polymerase chain reaction (RT-PCR) with the SuperScript III Reverse Transcriptase qPCR with Platinum Taq kit (Invitrogen, Carlsbad, CA - USA). RT-PCR amplification was performed by using specific primers and probes of Influenza A, B, A/H1pdm09, A/H3N2, and A/H5N1 according to CDC (Center Disease Control) Atlanta Protocol. An internal control human RNaseP PCR was included to confirm the specimen adequacy and to identify PCR inhibition. Specimens were considered positive if a virus PCR cT value was < 38 with appropriate run control results.

Viruses were grown in MDCK (Madine Darby Canine Kidney) Cell only for nasal and throat swab specimens which shown Influenza positive results by RT-PCR test. Virus titration and subtype

identification of the viruses was determined by standard haemagglutination and haemagglutination inhibition.

Data management and analysis

Clinical and laboratory data were recorded on paper-based case record forms. Those data are then entered and analyzedby an Microsoft Excell 2003.

RESULTS

A total of 333 cases were obtained from nine hospitals. The distribution of cases each month is described in table 1 below. Number of SARI cases varied in each month with the peak on December. In some month, child cases are more frequent than adult.

From all cases, 59,5% were catagorized as children (<14 years old) and 41,4% as adult, 58% were man and the rest is women.The result of rRT-PCR for influenza showed that 6 % of the SARI cases specimens contain influenza virus (table 2). From all positive influenza, flu A more dominan than Flu B. Influenza cases was only found in five hospital in five provinces; Makassar, Semarang, Mataram, Jakarta and Tangerang. One case of Avian Influenza cases was reported from Jakarta.

DISCUSSION

SARI surveillance is part of the Global Influenza Surveillance and Response Systems (GISRS). In a global level, the need of understanding influenza epidemiology is increasing significantly after the outbreak of Avian Influenza A/H5N1 influenza and A/H1N1 influenza pandemic occurred in 2009. The SARI surveillance is used to identify how many cases of influenza required inpatient care; while ILI (Influenza Like Illness) surveillance is used to obtain data of influenza cases from outpatient care.

SARI surveillance in Indonesia has been administered since 2008, long before the A/H1N1 influenza pandemic occurred in 2009. While in other countries, especially Europe, SARI surveillance is conducted after the pandemic took place, in Indonesia the surveillance was performed due to the human cases of Avian Influenza A/H5N1 which first reported in 2005. Besides the expectation that SARI surveillance can determine the distribution of cases and types of seasonal influenza circulating in Indonesia, the surveillance is also expected to detect any human cases of Avian Influenza A/H5N1. In 2011, through the SARI surveillance, one case of A/H5N1 influenza was found in Tangerang Regional Hospital.

Table 1. Number of SARI cases per month in selected city/town in Indonesia in 2011

	Adult	Children	Total
January	6	6	12
February	5	23	28
March	4	36	40
April	0	37	37
May	6	16	22
June	13	11	24
July	28	6	34
August	13	5	18
September	11	6	17
October	10	12	22
November	11	20	31
December	31	17	48
Total	138	195	333

Table 2. Distribution of Influenza cases per sentinel

Sentinels	Flu B	Flu A			Neg Inf	Total
		H3	Hpdm09	H5		
Dr. Hasan Sadikin Hospital, Bandung	0	0	0	0	77	77
Dr. Wahidin Sudirohusodo Hospital, Makassar	4	1	5	0	77	87
Mataram Hospital,	0	1	1	0	49	51
Dr. Kariadi Hospital, Semarang	0	2	1	0	24	27
Dr. Sulianti Saroso Hospital, Jakarta	0	0	0	1	3	4
Tangerang Hospital,	0	2	2	0	22	26
Dr. M. Djamil Hospital,Padang	0	0	0	0	37	37
RS Doc II Jayapura	0	0	0	0	17	17
Dr. Soedarso Hospital, Pontianak	0	0	0	0	7	7
Total	4	6	9	1	313	333

The sentinel system applied in the SARI surveillance are determined based on several considerations which include limited resources, both human, financial and laboratory capacity, and also disease characteristics of influenza which are usually mild. According to the manual established by WHO for European regional, the sentinel system adopted by Indonesia is a simple system which include epidemiology and virology data collecting from several sites.[11]

SARI cases obtained from sentinel hospitals varied by month and age group, but there is no significant different between month. This may be influenced by many factors including.the variation of etiology SARI. For example, study in UK reported that SARI cases caused by Respiratory Syncytial Virus were found earlier than SARI cases caused by influenza during winter.[12]

As previously stated, SARI surveillance is aimed to detect influenza epidemiology. The examination used in detecting the presence of influenza virus is by utilizing RT-PCR and virus culture. RT-PCR influenza test results on the SARI specimens showed that only 6% of the specimens which contain influenza virus. This is similar to the results found through SARI surveillance conducted in 2008-2009, where influenza virus was only found in 6 % of the cases.[1] If further compared to the surveillance results in 2008-2009, there is also a difference in subtype Influenza A which was dominant; where in 2008-2009 subtype A/H3N2 was dominant, while in 2011, subtype A/H1N1pdm09.[13] In 2008-2009, 2 cases of A/H5N1 were found, while in 2011 only one case was found through the SARI surveillance.In other study conducted in Bangladesh, influenza contributed in about 4 to 6% of acute lower respiratory infection in children > 5 years, and only 1% in adult.[8]Study in Thailand showed that influenza was found in 8% children younger than 5 years hospitalized with acute lower respiratory tract infection.

However, SARI surveillance can be used as a tool in detecting novel influenza virus in Indonesia, which potential of causing pandemic. It is crucial in considering the SARI surveillance sentinel system in a condition where human resources are limited such as in Indonesia. In the coming future, the improvement of surveillance system is required to detect novel influenza virus strains as the early warning of pandemic. In a global scale, WHO is continuing developSARI surveillance manual after the influenza pandemic occurred in 2009.

In conclusion, influenza contributed only in small percentages of SARI cases. Therefore the finding of other bacteria and viruses is needed to be developed in the future.

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