

EPIDEMIOLOGICAL STUDY OF INFLUENZA IN JAKARTA AND SURROUNDING AREAS

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Abstrak. Telah dilakukan suatu studi epidemiologi *Influenza Like Illness* (ILI) berbasis Puskesmas di daerah Jakarta dan sekitarnya (Jabotabek). Penelitian dilaksanakan sejak bulan Agustus 2004 sampai Juli 2006. Populasi adalah penderita ILI, semua kelompok umur. Lokasi penelitian di: Puskesmas Matraman ; Jakarta Timur; Puskesmas Wana herang, Kabupaten Bogor; Puskesmas Ciputat, Kabupaten Tangerang dan Puskesmas Rawa Tembaga, Kotamadia Bekasi.

Spesimen berupa usap tenggorok atau usap nasal, ditampung dalam media transport virus (VTM) disimpan dalam termos es dingin (4°C – 8°C). Dikirim ke laboratorium Virologi Puslitbang Biomedis dan Farmasi. Pengambilan spesimen dilakukan oleh tenaga kesehatan terlatih, pengiriman dilakukan sebulan dua kali pada minggu ke 1 dan minggu ke 3. Selama penelitian telah terkumpul sebanyak 2712 spesimen usap tenggorok dan atau usap nasal, masing-masing 606 spesimen dari Jakarta; 622 dari kabupaten Bogor; 784 dari kabupaten Tangerang dan 700 spesimen dari kota Bekasi.

Isolasi virus influenza dilakukan pada biakan sel MDCK (*canine kidney*); identifikasi isolat diuji terhadap antiserum influenza: sub tipe A/H3N2; A/H1N1 dan tipe B menggunakan uji Hemaglutinasi Inhibisi.

Hasil penelitian menunjukkan bahwa: ditemukan subtipe A/H1N1 sebanyak 96 isolat dan A/H3N2 sebanyak 124 isolat, sedangkan tipe B sebanyak 12 isolat. Selain itu ditemukan 91 isolat yang belum teridentifikasi dengan antisera yang ada.

Hubungan antara umur penderita dan infeksi virus influenza menunjukkan bahwa sebanyak 8.5% anak balita telah terkena infeksi virus influenza. Data ini tidak menggambarkan keadaan influenza yang sebenarnya pada masyarakat, karena 97,0% penderita yang berobat ke Puskesmas adalah anak balita dan hanya 3,0% orang dewasa.

Hubungan antara gejala dan isolasi virus menunjukkan bahwa bila dikaitkan dengan hasil isolasi virus influenza maka gejala; batuk 97,21% (314) dan pilek 98,14% (317) serta suhu badan (37,1 – 38,4C) sebanyak 92,56% (299), merupakan gejala yang dominan ditemukan pada penderita ILI. Hubungan antara iklim dan isolasi virus menunjukkan bahwa insiden influenza terjadi serpanjang tahun dengan adanya peningkatan kasus sekitar bulan Agustus sampai April.

Key words : puskesmas, pasien ILI, infeksi virus influenza

INTRODUCTION

In Indonesia, there have not been many influenza surveillance studies published. Three surveillance studies were done soon after the Hongkong epidemic between 1968-1970. There were also a few surveillance studies completed in the 1980s and 1990s. ⁽¹⁾ measured anti-influenza hemagglutination-inhibition antibodies in sera collected from Surabaya. They found positive incidence against A/Swine/30, A0/PR/8/40, A1/FM/1/47, A2/Adachi/2/57, A2/Kumamoto/1/67 and B/Kagoshima/1/68. However, the incidence of antibodies against A2/Aichi/2/68 (Hongkong type) were very low in the 1968 sera. Therefore, it was presumed that this virus had not invaded into Surabaya before 1968. ⁽²⁾ collected pharyngeal washing from several places in Indonesia. They successfully isolated A2/Hongkong/68 as the cause of epidemic. During a four-consecutive year 1982-1986 study of ⁽³⁾ isolated influenza type A and type B viruses from throat swab of patients with respiratory disease in Jakarta and Yogyakarta. The isolates are A/H1N1/USSR and A/H1N1/England, A/H3N2/Bangkok, A/H3N2/Mississippi and B/Texas, B/Norway and B/Singapore.

A virological survey of influenza virus in DKI Jakarta carried out by The Center of Disease Control for Research and Development (CDC RD) in 2002 showed that 29.9% of children under 5 years of age with acute respiratory infections were confirm infected by influenza virus. In addition, from 62 virus isolates 30 were identified as influenza virus; 27 isolates were identified as type A/H3N2/Panama and 3 isolates were A/H1N1/New Caledonia serotype.

A virological influenza surveillance conducted by NAMRU-2 in 2002 in

several big cities in Indonesia i.e.: Jakarta; Yogyakarta; Surabaya; Denpasar and Makasar showed that serotype A/H3N2/Panama and serotype A/H1N1/New Caledonia were also predominant serotypes. In addition 6 isolates were identified as type A/H3N2/Fujian and 3 isolates were identified as serotype B/Hong Kong.

Recently, there was an outbreak of A/H5N1 in some poultries in several provinces in Indonesia. A/H5N1 is originally an Avian Influenza but can infect human, causing death to 9 people in Vietnam and Thailand. Serological finding indicated that yet, there was still no transmission of A/H5N1 to human, especially to high risk population who live close to the poultry areas in Indonesia. The continuously occurrence of varieties of influenza virus subtypes transmission during the whole year in the population; the incident of A/H5N1 outbreaks in Indonesia and the character of genome instability of influenza virus itself, are strong indicators that someday an influenza pandemic or at least a multi countries epidemic of influenza may occur.

Conducting continuous influenza surveillance, of epidemiological and virological has high advantages. The burden of illness of influenza; the predominant virus transmitted in the population for influenza vaccine designation for the next year, the approximate time for influenza vaccination and an early warning outbreak recognition system will be obtained in order to control influenza in the country. However, conducting periodical surveys for influenza in Indonesia will help global influenza surveillance to monitor and study the seasonal patterns of influenza virus transmission in order to anticipate for local influenza epidemics and global influenza pandemic. The objectives of this study are to study the epidemiology of influenza in

Jakarta and surrounding areas (JABO-TABEK: Jakarta municipality, district of Bogor, Bekasi municipality and district of Tangerang).

It consist of: to estimate the influenza prevalence in the population ; to identify the age group specific of influenza cases; to further identify influenza strain transmitted in the population and to identify seasonal pattern of influenza like illness in Jakarta and surrounding areas.

The outcomes of the study are the estimation of burden of illnrss of influenza; the establishment of influenza epidemiological surveillance; the predominant virus transmitted

In the population for influenza vaccine designation in the next year, approximate time for influenza vaccination and an early warning outbreak recognition system will be obtained in order to control influenza in the country.

METHODS

Study sites:

- One (1) Public Health Center (PHC) was selected in every part of Jakarta city, Bekasi city; Bogor and Tangerang districts (Figure -1).

The reason why PHCs were used as sentinels, because in Acute Respiratory Infection Controls in Indonesia, PHCs are the centers for control activities.

- Virology Laboratory of the Center for Biomedical and Pharmaceutical Research and Development; National Institute of Health Research and Development; Ministry of Health of Indonesia.

Type of study:

PHC based study; case monitoring study. A clinical and laboratory based study.

Fig. 1. Map of Jakarta and surroundings areas for influenza surveillance.



Study population:

The study population was out-patients of all age groups from several PHC in Jakarta and surrounding areas.

Duration of study: 24 months.

Enrollment criteria:

The participants invited to the study were patients who fulfilled the following inclusion and exclusion criteria.

Inclusion criteria:

Participants included in this study were suspected influenza cases (*Influenza Like Illness*) with fever, more than 37,8°C **and** cough/sore throat **or** suffering from respiratory ailment **or** suffering from myalgia. Age 1 - 5 years and above.

Exclusion criteria:

Individuals with suspected or documented coagulopathy (such as excessive bleeding, petechiae, bruising or history of

coagulopathy); pregnant women; were excluded from the study due to potential risk of induced bleeding during sample collection and other patients who refused to participate in the study.

Estimation of Sample size:

A total of 2400 individuals were to be studied, with the expectation of approximately 50 samples from 1 PHC per month; 50 persons x 4 PHC x12 months = 2400 individuals /year of ILI patients from Jakarta and surrounding areas, i.e.: Jakarta, Bekasi; Bogor and Tangerang. All patients with influenza like illness (ILI) who attended the PHC from 1st week and 3th weeks of the month throughout the year were recruited. This was to be able to document the seasonal pattern of the influenza like illness.

Statistical estimation of the sample size was done by the following formula:

$$n1 = n2 = \frac{Za^2 (P1Q1+P2Q2)}{d^2} = \frac{1.960^2 (0,5 \times 0,5 + 0,6 \times 0,4)}{0.01 \times 0.01} = 193$$

a = 95% (1,960)
d = 0,10
P1 = 0,70 P2 = 0,60
Q1= 0,30 Q2 = 0,40

Based on the calculation with a total sample of 193 x 4 location = 772 samples (800 samples) the study is valid.

Data Collection:

Interviews was conducted by medical doctors who examined the patients **in PHC**, using a modified WHO questionnaire.

Variables:

- **Biology** : age; sex; height and body weight , etc.
- **Symptoms:** fever (37.8C – 38.5C), cough, sore throat, runny nose; headache; myalgia, etc.
- **Climate:** rainy/wet; dry season.
- **Viral isolates:** to identify influenza viruses sub types: A/H1N1; A/H3N2 and type B.

Specimen collection:

Nasopharyngeal swabs or throat swabs were collected by trained health officials. The swabs are collected in sterile screw capped bottles containing *Hank's BSS* transport media (supplemented with antibiotics: 1000 mIU/ug/ml of penicilline and streptomycin) and stored at -70°C or in a liquid Nitrogen container. In emergency the collected samples were stored at refrigerator for 24 hours.

Specimen transportation:

The specimen collectors from the laboratory were visited the sentinel PHC participated in the study once a week. The specimens were stored in ice box containing dry ice. The collected samples were brought to the Virology Laboratory of NIHRD, immediately, and stored in -70°C before virus isolation.

Laboratory examination:**Virus isolation and identification:**

Virus isolation were done in MDCK cells. Total of 0.1 ml samples in

transport media *Hank's BSS* were inoculated into 2 tubes of monolayer MDCK cells. Cytopathic effect of virus in cells were observed up to day 7. Three times blind passages in MDCK cells were conducted to increase the virus titer. Hemabsorption test using turkey red blood cells were performed prior to virus identification. Virus identification were done by Hemagglutination Inhibition test against a batch of known influenza A and B antisera. Unknown/untypeable isolates were to be sent for further identification to WHO Collaborating Center for Reference and Research on Influenza in Melbourne, Australia.

Isolates collection:

Viral isolates were placed in cryo-tube and storage in liquid N₂ container tank

Data analysis

Data analysis and management were conducted using SPSS vs 10,0 soft ware program. The crosstabulation were performed to show the correlation between virus strains and clinical symptoms, sex and age groups. The seasonal patterns were graphed.

ETHICAL CLEARANCE AND CONSIDERATION

All participants were requested to sign a voluntary consent form for their agreement to participate in the study. They were explained about the advantages and/or disadvantages to participate in the study; prior to sign the voluntary consent. All data about the patients were filed confidentially, no drugs or medicine were injected to the participants. There was no serious risk as the consequences for nasopharyngeal and throat swab.

RESULTS AND DISCUSSIONS

Bogor district

A total of 622 samples were collected during August 2004 up to July 2006. The number of viral isolates in MDCK cells were 89 isolates of influenza viruses with HA titer > 16 HA unit.

Most of the ILI patients who came to PHC were children under 5 years of age, only few adults with 25 up to 34 years of age. There were no ILI patients at the age of 15 up to 24 years of age, and there were no ILI patients at the elderly age group.

Clinical symptoms that showed significant different between viral isolates and symptoms were fever; cough and runny nose.

Bekasi municipality

Total samples collected were 700 specimens. Isolates identification since August up to December 2005 were 89 isolates. There were 41 isolates unidentified. It was assumed that there were new strains or new subtype of viruses were circulated in the areas.

Tangerang district

A total of 784 samples were collected. Since August 2005 up to July 2006 only 30 isolates were collected. The low rate of viral isolation was possibly due to specimens transportation and specimens handling which are handled by new trained laboratory technicians.

Lots of efforts have been done to increase the HA titer, so that more isolates could be identified. However, only 30 isolates could be identified.

According to clinical symptoms,

showed that fever, cough and runny nose were the predominant symptoms found among ILI patients. The 30 isolates were yielded from 784 specimens in Tangerang district.

DKI Jakarta municipality

A total of 606 samples were collected. Virus identification since August '04 up to December 2005, yielded only 2 isolates of influenza viruses and 5 isolates were identified as noninfluenza.

Table-9 showed that cough and runny nose were the predominant symptoms of ILI patients from DKI Jakarta (PHC Matraman).

The low rate of viral isolation in Jakarta area did not describe the real situation in the areas. It was possibly due to sample selection; specimen transportation or storage.

Jakarta and surrounding areas (Jabotabek area)

Overall analysis of Jabotabek areas was an accumulation finding of all locations (PHC).

Totally, 2712 specimens were collected; consisted of throat and nasal swabs, which were collected since August 2004 up to July 2006.

The low rate of viral isolation in Jakarta area and Tangerang district did not describe the real situation of virus transmission in the areas. It might be due to specimen handling; transportation and/or specimen storage; they were handled by new technicians.

The laboratory findings in Bekasi city and Bogor district seemed to give the real appearances of both locations.

Table-1. Distribution of ILI sample by month in Jabotabek area, August 2004 – July 2006.

Months	Jakarta	Bogor	Tangerang	Bekasi	Total
August'04	61	42	104	50	257
September	17	34	55	56	162
October	28	56	50	49	183
November	29	28	51	59	167
December	65	46	49	60	220
January'05	45	33	68	60	206
February	47	42	51	55	195
March	33	34	25	23	115
April	30	27	25	38	120
May	29	29	23	35	116
June	38	37	26	32	133
July	18	38	27	32	115
August	30	13	31	25	99
September	11	25	23	15	74
October	33	17	27	23	100
November	8	16	22	15	61
December	8	18	21	16	63
January'06	10	13	23	15	61
February	8	14	16	13	51
March	2	16	10	8	36
April	0	12	16	5	33
May	11	4	16	8	39
June	47	16	13	10	86
July	0	7	10	3	20
Total	606	622	784	700	2712

Table-2. Correlation between age groups and clinical symptoms, among ILI patients, Jabotabek August, 04 - July' 06.

Age group	Fever 37-38,5C	Cough	Runy nose	Sore throat	Resp. ailment	Head ache	Pain
0 - 4	2193	2559	2547	230	155	179	541
3 - 14	0	0	0	0	0	0	0
15 - 24	0	0	0	0	0	0	0
25 - 34	63	76	75	19	14	8	42
35 - 44	0	0	0	0	0	9	0
45 - 54	0	0	0	0	0	0	0
55 - 64	0	0	0	0	0	0	0
65 - 80	0	0	0	0	0	0	0
TOTAL	2256	2653	2622	249	169	187	583

Fig. 2. Distribution of ILI samples by month in Jabotabek, August'04-July'06.

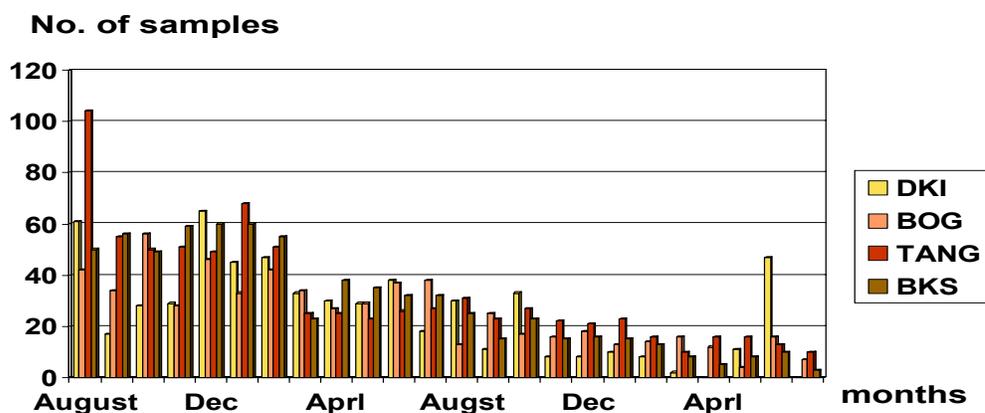


Table-3. Influenza viruses transmission by age, among ILI patients in Jabotabek, August 04 – July 06.

Age groups (years)	H3N2	H1N1	B	NID
0-4	120	92	12	90
5-14	0	0	0	0
15-24	0	0	0	0
25-34	4	4	0	1
35-44	0	0	0	0
45-54	0	0	0	0
55-64	0	0	0	0
65-74	0	0	0	0
Total	124	96	12	91

Table-4. Correlation between symptoms and virus identification among ILI patients, Jabotabek, August 2004 - July 2006.

Symptoms	H3N2	H1N1	B	NID
Fever: 37-38,5	107	96	12	84
Cough	119	95	7	30
Runny nose	99	69	12	88
Sore throat	14	6	0	8
Respiratory ailment	8	9	1	8
Headache	5	1	0	2
Pain	30	17	3	15

Fig. 3. Distribution of ILI clinical symptoms by age groups among ILI patients, Jabotabek, August'04 – July'05.

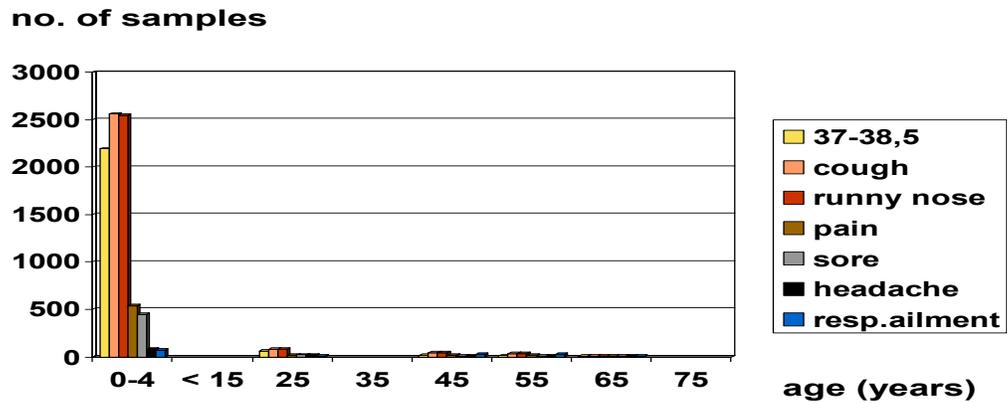


Table-5. Influenza virus transmission in Jabotabek area, August 2004 – July 06.

Months	H3N2	H1N1	B	NID
August	19	2	0	7
Sep	15	2	0	2
Oct	7	2	0	9
Nov	14	10	0	6
Dec	9	8	0	3
Jan	23	5	3	11
Feb	6	3	3	10
Mar	8	4	0	9
Apr	4	3	0	0
May	7	4	2	0
Jun	4	3	3	0
Jul	7	3	0	0
Agst	0	0	0	4
Sep	0	2	0	13
Oct	1	8	0	13
Nov	0	17	1	2
Dec	0	9	0	1
Jan	0	1	0	0
Feb	0	2	0	0
Mar	0	1	0	0
April	0	2	0	1
May	0	2	0	0
Juni	0	3	0	0
Juyi	0	0	0	0
Total	124	96	12	91

Fig. 4. Influenza virus distribution by ILI clinical symptoms, Jabotabek, August'04 – July'06.

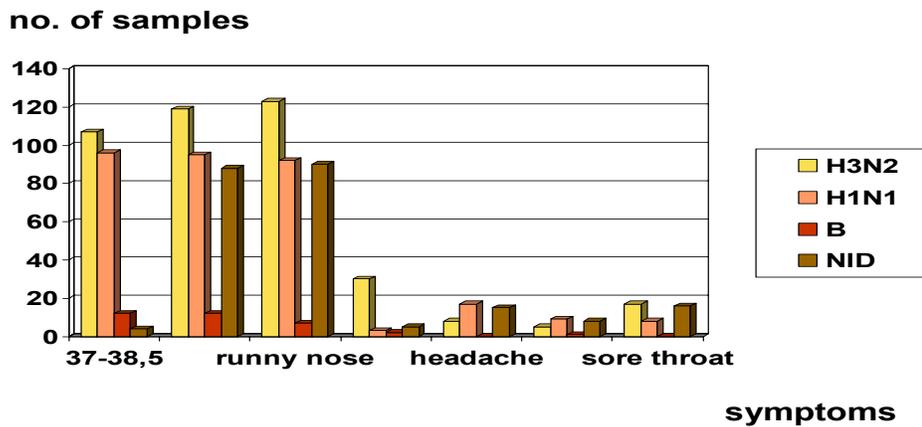
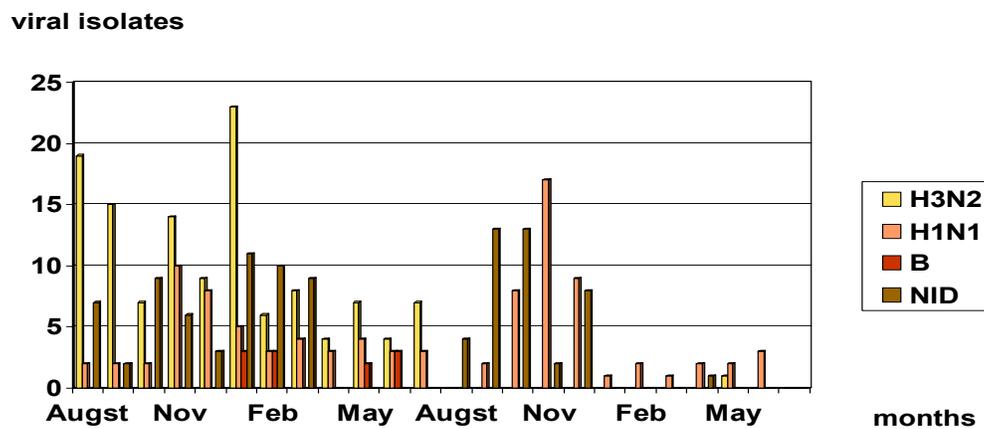


Fig. 5. Transmission of influenza viruses by month, Jabotabek, August'04 – July'06.



CONCLUSIONS

From the study some conclusions were drawn, i.e.:

1. It has been showed that ILI is a common respiratory ailment occurred among population in Jakarta and

surrounding areas. According to this PHCbased study, were almost 8.5% children below five years of age were positive infected by influenza viruses. However, it seems that the data only represent all ILI patient in PHC, but do not describe the whole population

in general. Most of the ILI patients (97.0%) who came to PHC were children below five years of age; the rest, or 3.0% of the ILI patients were consisted of adults (group 25 to 34 years of age).

2. Clinical symptoms such as fever; 37°C – 38,5 °C (22.28%), cough (22.30%) and runny nose (21.67%) were the main symptoms found among ILI patients.
3. Influenza viruses subtype A/H3N2 and A/H1N1 were predominant , and they were isolated throughtout the year. In additiaon, influenza viruses type B are isolated sporadically in several months. But in Bekasi city and Bogor district we found 26 (8.12%) and 5 (1.56%) isolates respectively, which can not be identified, so, it was possible that new strains of influenza viruses were actually circulating.
4. Eventhough influenza viruses were found throughout the year, it seemed that the peak season for influenza transmission occured during October to March.

IMPLICATION TO THE NATIONAL INFLUENZA PROGRAM

The strategy to control influenza is implemented by providing influenza immunization to the community. Moreover, with the genetic mutation of influenza viruses, the vaccine composition for global use has have to be determined annually. The global influenza virological surveillance program organized by WHO in a global program will be very useful to determine the influenza vaccine composition for the coming year. Unfortunately the economic situation make the situation slightly different in developing countries like Indonesia. Our study provides the

evidence in community that at least 8.5% influenza were found among children below five years of age with ILI. The non-identified influenza isolates were still found in the study. It indicated that there is still a possibly that new strains of influenza viruses were circulating, especially in Bekasi municipality during 2006. More over, the occurrence of Avian Influenza epidemics in Indonesia since July 2005 support the idea of using the seasonal influenza vaccine for high risk population. The effectiveness of seasonal influenza vaccine to protect against seasonal influenza virus infection, as well as against highly pandemic avian influenza, is an interesting aspect for further study.

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