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Original Article

Epidemiology and population-based incidence of influenza in two communities, Bandung district, West Java, Indonesia, 2008–2011

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Abstract

Influenza surveillance is important for monitoring influenza virus circulation and disease burden to inform influenza prevention and control measures. The aim of this study was to describe the epidemiology and to estimate the incidence of influenza in two communities in West Java, Indonesia, before and after the 2009 H1N1 pandemic. A population-based surveillance study in the community health care setting was conducted to estimate the annual incidence of influenza. A real-time reverse transcription polymerase chain reaction (RT-PCR) assay was used for influenza case ascertainment. A population census was implemented to calculate the population at risk and estimate community health care utilization rate. The mean annual incidence of influenza A and B, adjusted for healthcare utilization, was 1.6 (95%CI: 1.3–2.0) and 0.7 (95%CI: 0.5–1.0) per 1000 persons, respectively, with the most affected group being young and school-age children. The annual cumulative incidence of influenza A for children under five in 2009, 2010, and 2011 was 7.0 (95%CI: 4.4–11.2), 10.6 (95%CI: 7.3–15.4), and 6.3 (95%CI: 3.8–10.2). For influenza B was 4.3 (95%CI: 2.4–7.8), 2.0 (95%CI: 0.8–4.7), and 0.4 (95%CI: 0.1–2.8), respectively. This study highlights that the incidence of influenza among young and school-age children is consistently higher compared to adults and the elderly throughout these periods. These populations are potential targets for influenza vaccination in Indonesia.

Keywords: Virus, influenza, epidemiology, incidence, pandemic

Introduction

Seasonal influenza has been reported to have a disproportionate impact on morbidity and mortality in developing countries. A study estimated that 90 million new cases of acute lower respiratory tract infections and 28,000–111,500 deaths were attributable to seasonal influenza in children younger than 5 years in 2008, with 99% of these deaths occurring in developing countries [1]. Another study estimated that 291,243–645,832 seasonal influenza-associated respiratory deaths occur annually worldwide [2]. In addition, Southeast Asia was found to have the second-highest estimated seasonal influenza-associated mortality rate (3.5–9.2 deaths per

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100,000 individuals) after sub-Saharan Africa [2]. These estimates suggest that influenza is an important public health problem in lower- and middle-income countries, including Indonesia.

Implementation of influenza prevention and control programs in Indonesia has been hindered by many factors, including the sparsity of data to guide policymakers [3]. Although influenza vaccination of priority groups has been recommended in all countries by the WHO, the Indonesian government has not added influenza vaccination to the national immunization program. Baseline disease burden data are needed to assess the potential impact of influenza vaccination programs and other preventive measures. Currently, information on the morbidity and burden of influenza in Indonesia is derived from six surveillance studies [4-9] conducted between 1999 to 2016. These studies were mainly hospital-based and/or did not utilize a population-based approach. A recent population-based study on influenza morbidity in Indonesia focused on severe hospitalized influenza cases [7]. Hospital-based studies underestimate the population incidence across the spectrum of disease and often capture patients from different areas, leading to difficulty in defining the population at risk. It is estimated that mild cases of uncomplicated influenza, of which most are not medically attended or lead to hospitalization, contribute to 98.7% of all estimated influenza-associated illness [10], potentially leading to economic losses due to absenteeism at schools and workplaces. Therefore, there is a need for population-based studies in Indonesia to estimate the influenza disease burden in the community that also take into account health care utilization.

To our knowledge, none of the previous studies in Indonesia have estimated the burden of influenza outside the hospital setting within a well-defined community area or among a population at risk. The aim of this study was to describe the epidemiology of influenza by estimating the population-based incidence of influenza in two small, well-defined communities before, during, and after the 2009 H1N1 pandemic. The study aimed to measure the total and age-specific morbidity of influenza in the community while addressing healthcare utilization.

Methods

Study location and period

This study was conducted in two peri-urban areas (Soreang and Cileunyi) of Bandung district, West Java, Indonesia (**Figure 1**). This study was a part of the Zoonotic Avian Influenza-Human Animal Interface project, where the study areas were chosen based on the previous reports of human influenza cases caused by highly pathogenic avian influenza A(H5N1) virus and with the presence of severe lower respiratory tract infections in 2008. The study areas were located in a river basin surrounded by volcanic mountains with cooler temperatures (annual average of 23.6°C) compared to other Indonesian cities, at an elevation of 768 meters above sea level. This region had a tropical humid monsoon climate with annual average rainfall ranging from 1,000–3,500 mm. In 2009, the total population in the two sub-districts was 163,024, with a total area of approximately 21 square km.

The age distribution in the two sub-districts population was comparable with Indonesia in general, with 69% of the population aged between 16–65 years. Bandung district had a reported life expectancy of 69.4 years (2010) [11], similar to the national life expectancy (70 years) [12] but slightly higher than the average for West Java (66.6 years) [11]. Stunting in children aged <5 years was 25% (2011) [11], higher than the national average of 19% [12]. There are three government-funded community public health centers (*Puskesmas*) serving the area, in addition to private clinics, with a medical doctor (general practitioner) to population ratio of approximately 1 to 25,000 [11]. *Puskesmas* provided subsidized health care services, mostly for low-income patients. During the study period, the recent Indonesian national health insurance policy had not been implemented, making most healthcare expenditures were paid out of pocket [12]. There were no published national data on influenza vaccination uptake in these communities, but it is assumed that less than 1% of the population is vaccinated for influenza each year [13].

Data collection and quality control

Surveillance for influenza was conducted among persons with influenza-like illness (ILI) from October 2008 to September 2011, at three *Puskesmas*: two in the Cileunyi sub-district and one in

the Soreang sub-district. Dedicated, trained study physicians were assigned to screen and enroll patients with signs and symptoms of ILI. ILI was defined as having a fever (measured temperature of >37.5°C) or history of fever or feverishness and antipyretic treatment, and having either cough or sore throat. Only subjects residing within the study area, as proven by an ID card, and willing to provide written informed consent were eligible for this study.

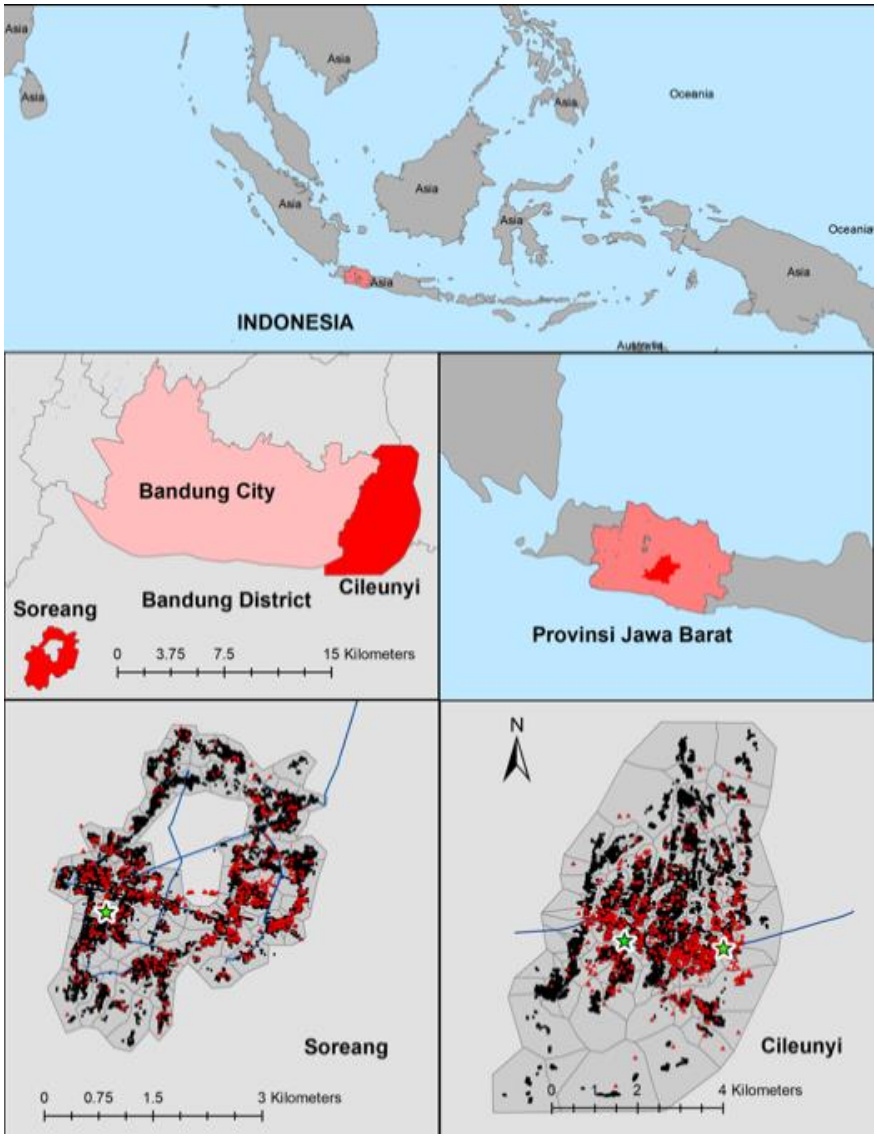

Figure 1. Location of the study. The study was conducted in two peri-urban areas (Soreang and Cileunyi) located in Bandung district, West Java, Indonesia.

Basic demographic data and clinical information from all eligible subjects were recorded using a standardized pre-tested case report form. Nasal and oropharyngeal swabs were collected from all subjects with ILI, pooled on daily basis in a cool box with dry ice and transported on the same day to Dr. Hasan Sadikin General Hospital Laboratory, Bandung, Indonesia, for influenza virus testing. Trained nurses conducted home visits at two weeks post-enrollment, collecting information using a standardized pre-tested questionnaire on clinical outcomes, household, environmental risk factors, and house geo-coordinates, which were recorded by a handheld GPS receiver. For seasonality analysis, secondary data on weather parameters were collected during

the study period, which included rainfall, relative humidity, and maximum and minimum temperatures, from the Indonesian Geophysics, Climatology, and Meteorology Agency (BMKG), a government agency responsible for weather and climate monitoring in Indonesia.

To measure the size of the population at risk or study denominator, we conducted a census of the population within the administrative areas served by the three government *Puskesmas*. A total of 448 trained local community health workers (cadres) used standard census forms to obtain basic household demographic data such as household size and age group of all household members, classified into five categories: age <5 years old, 5–15, 16–50, 50–65, and >65 years. A field data coordinator performed quality control audits and identified errors or missing values in the survey forms. Incomplete forms were returned to the cadres for verification and corrections. After the population lists and addresses were validated, trained field surveyors conducted door-to-door visits to verify addresses and recorded all house geo-coordinates using handheld GPS receivers. All of the data-cleaned forms were entered into a secured web-based data entry system by a dedicated data entry operator.

Influenza virus detection

Combined throat and nasal swabs from each subject were transported at 4–8°C in a virus transport medium (Beckton-Dickinson, NJ, USA) to the Research Laboratory in Hasan Sadikin General Hospital in Bandung, Indonesia. A one-step multiplex real-time RT-PCR assay was used for influenza A and B viral RNA detection, using primers and probes in two separate assays following standard protocols. The first assay was comprised of specific primers and probes for matrix (*M1*) gene (influenza A) and host glyceraldehyde-3-phosphate dehydrogenase (*GADPH*) gene (influenza B). The second assay was comprised of primers and probes specifically for the H1, H3, and H5 hemagglutinin (HA) gene regions for influenza A virus subtype detection. The probes were labeled with three fluorescent dyes (FAM, HEX, and Cy5 with emission wavelengths at 518, 556, and 667 nm, respectively). Positive specimens for influenza A were further subtyped for H1N1pdm09, H3, and H5 using the protocol from CDC [14] and Suwannakarn *et al*. [15]. Positive specimens for influenza B were further characterized as Yamagata-like and Victoria-like viruses by RT-PCR using the WHO protocol [16].

Statistical analysis

The seasonality of influenza was illustrated through a time series graph, defining cases by virus type, influenza A subtype, and age-group, overlaid by weather data (humidity, rainfall, maximum and minimum temperature) throughout the study period (**Figure 2**). Age-group susceptibility was shown through a time series graph, showing the age distribution of influenza positive cases by virus type and influenza A subtype throughout the study period (**Figure 3**). Population-based cumulative incidences of symptomatic influenza A and B virus infections were estimated for 2009, 2010 and 2011 and stratified by age. Adjustments were made for age-group specific variation in community health care utilization (CHCU) and for direct standardization to census data.

CHCU was calculated as a percentage of the population with ILI seeking medical treatment at a *Puskesmas* for each age group. The denominator was the number of population for the relevant age group. This multiplier was applied to calculate the adjusted age-group specific number of cases (adjusted numerator). The age group categories used followed the age classification as defined in census data. The adjusted numerator was calculated by dividing the number of cases for each age group by CHCU percentages and standardized for 1,000 persons. For all calculations of annual incidences, the same number of populations at risk (denominator) for each age group, enumerated by the census, was used with the fixed/closed cohort population assumption during the study. The confidence intervals were calculated using the WHO method [17].

Results

Characteristics of subjects and types of influenza viruses

From October 2008 to September 2011, study physicians identified and enrolled 3,305 ILI patients (**Table 1**). Overall, 456 (14%) patients tested positive for influenza viruses, including 10.9% (359/3,305) influenza A and 2.9% (97/3,305) influenza B. Further subtyping of influenza A yielded nine (2.5%) H1N1, 157 (43.7%) H1N1pdm09, 193 (53.8%) H3N2 and none for H5N1. The majority of ILI patients were less than 15 years old with high school education or less. We found that the frequency of sneezing reported among influenza positive subjects ranged between 25–45%. Only six ILI subjects out of 3,305 were hospitalized, of which only one person had laboratory-confirmed influenza (influenza A(H3N2)) and none died.

Table 1. Characteristics of subjects with influenza-like illness by laboratory test result, Bandung district, Indonesia, 2009–2011

Characteristics	Negative* n (%)	Positive n (% by column)				
		B/Yamagata	B/Victoria	A(H1N1)	A(H3N2)	A(H1N1)pdm09
	n=2849	n=39	n=58	n=9	n=193	n=157
Sex: Female	1596 (56.0)	19 (48.7)	29 (50.0)	2 (22.2)	102 (52.8)	76 (48.4)
Age group (year)						
0–5	662 (23.2)	9 (23.0)	6 (10.3)	2 (22.2)	41 (21.2)	25 (15.9)
6–15	969 (34.0)	15 (38.5)	35 (60.3)	2 (22.2)	73 (37.8)	78 (49.7)
16–50	1,136 (39.9)	14 (35.9)	17 (29.3)	5 (55.6)	74 (38.3)	49 (31.2)
51–65	113 (4.0)	1 (2.6)	0 (0.0)	0 (0.0)	5 (2.6)	5 (3.2)
>65	11 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Education						
High school or less	2,046 (71.8)	29 (74.4)	48(82.8)	5 (55.6)	140 (72.5)	124 (79.0)
Higher than high school	69 (2.4)	0 (0)	3 (5.2)	2 (22.2)	5 (2.6)	3 (1.9)
Unknown	734 (25.8)	10 (25.6)	7 (12.0)	2 (22.2)	48 (24.9)	30 (19.1)
Symptoms						
History of fever	2404 (84.4)	38 (97.4)	57 (98.3)	9 (100)	187 (95.9)	151(96.2)
Cough	2526 (88.7)	38 (97.4)	56 (96.6)	8 (88.9)	184 (94.4)	153 (97.5)
Sore throat	1984 (69.6)	32 (82.1)	42 (72.4)	5 (55.6)	125 (64.1)	109 (69.4)
Runny nose	2138 (75.0)	30 (76.9)	52 (89.7)	7 (77.8)	156 (80.0)	129 (82.2)
Headache	1750 (61.4)	31 (79.5)	45 (77.6)	5 (55.6)	134 (68.7)	110 (70.1)
Sneezing	1446 (50.8)	10 (25.6)	27 (46.6)	5 (55.6)	95 (48.7)	71 (45.2)
Fatigue	1634 (57.4)	19 (48.7)	36 (62.1)	6 (66.7)	117 (60.0)	106 (67.5

*Negative result for influenza by RT-PCR assay

Seasonality of influenza viruses infection

The pattern of seasonality and circulation of different types/subtypes of influenza viruses is presented in **Figure 2**. Five peaks of greater than 15% influenza positive occurred, with influenza activity identified every month except between December 2009 to February 2010. This window of zero detectable influenza activity occurred just after the first wave of the 2009 H1N1 pandemic. Through early 2009, seasonal influenza A(H1N1) virus was identified in our study population and later replaced in 2010 by influenza A(H1N1)pdm09 virus. Each peak of higher influenza virus activity was predominantly driven by a particular influenza A subtype or influenza B.

In **Figure 3**, influenza activity is shown by type, influenza A virus subtype, and age group, over six-month intervals. In the first six-month interval, there were relatively more A(H3N2) virus infections occurred in younger age groups, while in the second interval adults aged 51–65 years old had the highest percentage of ILI subjects with A(H3N2) virus infections. However, during the last interval, the percentage of A(H3N2) virus in the 51–65-year-old group decreased, while it increased again in the younger age groups.

In the second interval, A(H1N1)pdm09 virus infections emerged, occurring more in the school age group (5–15 years old), while during the two last intervals of study (October 2010 to March 2011 and April 2011 to September 2011), older adults were more impacted. B Yamagata-like virus had a higher infection percentage in school-age children in the first study interval, with elderly more impacted during the second interval.

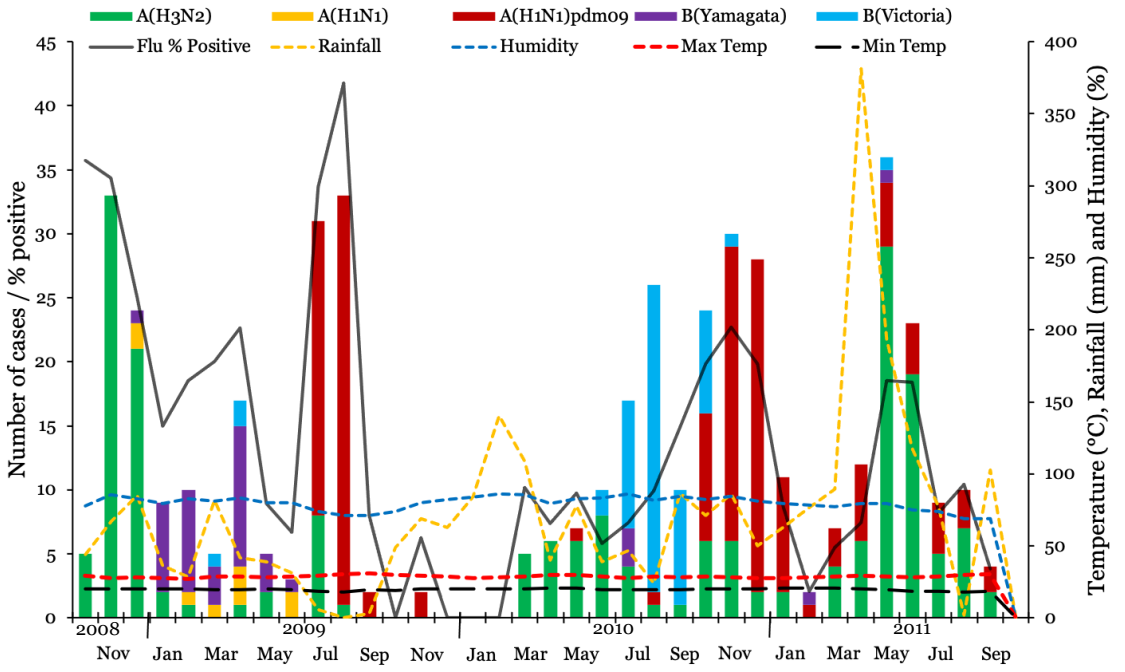

Figure 2. Seasonality of influenza viruses by types and influenza A virus subtype.

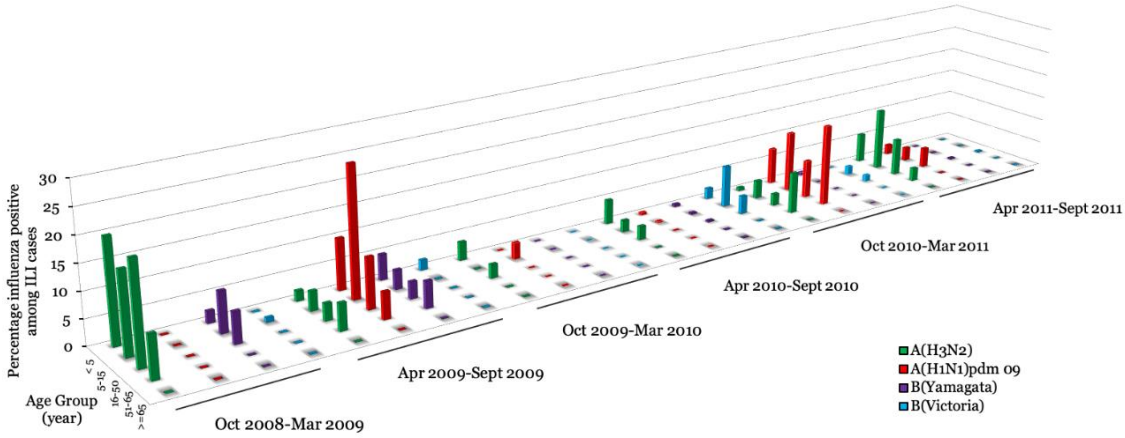

Figure 3. Percentage of influenza positive by age group, influenza type and A subtype.

Annual incidence of influenza viruses infection

During the study period, the estimated annual cumulative incidence of symptomatic influenza A virus infections varied from 1.6 to 2.3 per 1,000 persons, and the annual cumulative incidence of symptomatic influenza B virus infections ranged from 0.1 to 0.7 per 1,000 persons, after adjusting for CHCU percentages. Children aged <5 years old were most affected, with an estimated annual incidence of 6.3 to 10.6 and 0.4 to 4.3 per 1,000 persons for symptomatic influenza A and B virus infections, respectively. Persons aged >65 years old had the lowest estimated annual incidence for both influenza A and B (**Figure 4**).

The estimated number of influenza cases adjusted by CHCU for ILI and population size (adjusted numerator) is presented in **Table 2**. The estimated adjusted annual cumulative incidence of ILI, influenza A, and influenza B, by age group is presented in **Table 3**.

Table 2. Estimated age-specific number of influenza cases, population size, and community health care utilization (CHCU) in Bandung district, Indonesia, 2009–2011

Year	Age category (year)	No of non-influenza	Adjusted numerator*	No of influenza A	Adjusted numerator*	No of influenza B	Adjusted numerator*	Total ILI	Adjusted numerator*	No of population	CHCU (%)#
2009	0–5	132	440	18	60	11	37	161	537	8,511	30.0
	6–15	151	338	45	101	16	36	212	475	34,217	44.6
	16–50	174	448	21	54	11	28	206	531	96,766	38.8
	51–65	24	68	2	6	1	3	27	77	16,957	35.3
	>65	4	6	0	0	0	0	4	6	6,573	66.7
	Total	485	1,459	86	258.6	39	117	610	1,835	163,024	33.3
2010	0–5	269	897	27	90	5	17	301	1,003	8,511	30.0
	6–15	437	979	50	112	36	81	523	1,172	34,217	44.6
	16–50	480	1,236	41	106	17	44	538	1,386	96,766	38.8
	51–65	33	94	4	11	0	0	37	105	16,957	35.3
	>65	3	5	0	0	0	0	3	5	6,573	66.7
	Total	1,222	3,675	122	366.9	58	174	1,402	4,216	163,024	33.3
2011	0–5	212	707	16	53	1	3	229	763	8,511	30.0
	6–15	326	730	52	116	3	7	381	853	34,217	44.6
	16–50	418	1,077	51	131	3	8	472	1,216	96,766	38.8
	51–65	49	139	4	11	0	0	53	150	16,957	35.3
	>65	2	3	1	2	0	0	3	5	6,573	66.7
	Total	1,007	3,029	124	372.9	7	21	1,138	3,422	163,024	33.3

#CHCU: community health care utilization as percentage of population who sought medical care for influenza-like illness (ILI) (unpublished data, Dwi Agustian *et al.*)
*The adjusted numerator was calculated by dividing the number of cases for each age group by CHCU percentages

Table 3. Estimated annual adjusted cumulative incidence of influenza-like illness and influenza by age group, Bandung district, Indonesia, 2009–2011

Year	Adjusted annual cumulative incidence (95% confidence interval) (per 1000 persons per year)				
	Age category (year)	Non-influenza	Influenza A	Influenza B	Total ILI
2009	0–5	51.7 (43.6–61.3)	7.0 (4.4–11.2)	4.3 (2.4–7.8)	63.1 (54–74)
	6–15	9.9 (8.4–11.6)	2.9 (2.2–3.9)	1.0 (0.6–1.7)	13.9 (12–16)
	16–50	4.6 (4.0–5.4)	0.6 (0.4–0.9)	0.3 (0.2–0.5)	5.5 (5–6.3)
	51–65	4.0 (2.7–6.0)	0.3 (0.1–1.3)	0.2 (0.0–1.2)	4.5 (3–6.6)
	>65	0.9 (0.3–2.4)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.9 (0–2.4)
	Total	8.9 (8.2–9.8)	1.6 (1.3–2.0)	0.7 (0.5–1.0)	11.3 (10–12)
2010	0–5	105.4 (93.5–118.7)	10.6 (7.3–15.4)	2.0 (0.8–4.7)	117.9 (105–132)
	6–15	28.6 (26.0–31.4)	3.3 (2.5–4.3)	2.4 (1.7–3.3)	34.2 (31–37)
	16–50	12.8 (11.7–14.0)	1.1 (0.8–1.5)	0.5 (0.3–0.7)	14.3 (13–16)
	51–65	5.5 (3.9–7.8)	0.7 (0.3–1.8)	0.0 (0.0–0.0)	6.2 (4–8.5)
	>65	0.7 (0.2–2.1)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.7 (0–2.1)
	Total	22.5 (21.3–23.8)	2.3 (1.9–2.7)	1.1 (0.8–1.4)	25.9 (25–27)
2011	0–5	83.0 (72.6–95.0)	6.3 (3.8–10.2)	0.4 (0.1–2.8)	89.7 (79–102)
	6–15	21.3 (19.1–23.8)	3.4 (2.6–4.5)	0.2 (0.1–0.6)	24.9 (23–28)
	16–50	11.1 (10.1–12.2)	1.4 (1.0–1.8)	0.1 (0.0–0.2)	12.6 (11–14)
	51–65	8.2 (6.2–10.8)	0.7 (0.3–1.8)	0.0 (0.0–0.0)	8.9 (7–12)
	>65	0.5 (0.1–1.8)	0.2 (0.0–1.6)	0.0 (0.0–0.0)	0.7 (0–2.1)
	Total	18.6 (17.5–19.8)	2.3 (1.9–2.7)	0.1 (0.1–0.3)	21.0 (20–22)

ILI: influenza-like illness

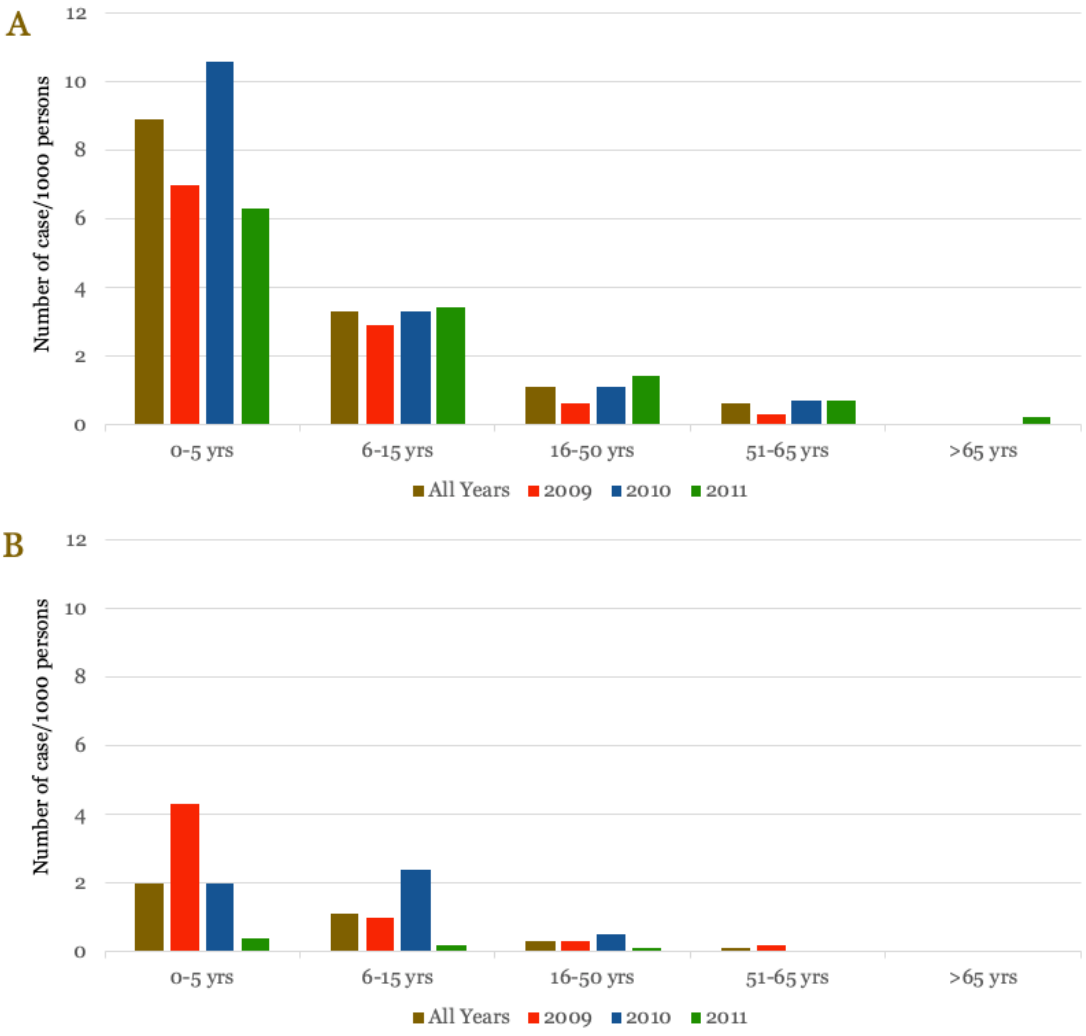

Figure 4. Age group specific annual cumulative incidence for influenza A and B. (A) Age specific annual cumulative incidences for influenza A and (B) age specific annual cumulative incidences for influenza B.

Discussion

The seasonality of influenza we documented in West Java, Indonesia, from 2008–2011 showed a typical pattern for a tropical region, with year-round influenza virus circulation, sharp short-spikes and large variations of peak timing, and is consistent with previous studies by Beckett *et al*. between 1999–2003 [5] and Kosasih *et al*. during 2003–2007 [9]. Peaks in influenza incidence coincided with higher precipitation months, which generally occurred between December and March, except from July to August 2009, when the A(H1N1)pdm09 virus emerged. Periods of high influenza activity ranged from 2 to 6 months, followed by low influenza activity for 2 to 4 months. Every year, two or three peaks of increased influenza activity were observed, with each peak typically predominated by a different virus and variability in the age group with the highest proportion of influenza positives from season to season. This variation could be due to differences in immune susceptibility by age, the introduction of bias from differential health-seeking behavior by age group or seasonal changes in healthcare-seeking behavior, or chance variation due to a smaller sample size when stratified by season and age group, However, a previous community cohort study in Vietnam also reported differences in impacted age groups by year [18].

This continuous and dynamic year-round circulation of influenza viruses in West Java suggests that the best timing of influenza vaccination is not easily defined; therefore, if a national influenza vaccination program is implemented in Indonesia, one strategy is for influenza vaccination to begin as soon as influenza vaccine is available each year. One study suggested that influenza vaccination should be given before the Hajj [19], since thousands of people travel from Indonesia to the Hajj annually, and influenza vaccination is required for Hajj pilgrims upon entry to Saudi Arabia. However, the dates of the Hajj pilgrimage vary from year to year, adding practical challenges to this implementation. Alternatively, since increases in influenza activity coincide with high precipitation months, influenza vaccination could be implemented before the start of the rainy season, usually around October or November.

We observed that following the introduction of the 2009 H1N1 pandemic virus in Indonesia, overall influenza virus activity in the population dropped significantly and was not detectable in our study during January 2010. This was despite the relatively higher precipitation levels during that interval (**Figure 2**). Other studies conducted during the same time period, including a study in East Java, Indonesia [4], in rural Thailand [20], in an urban Kenya [21] and in Ha Nam district, Vietnam [18], also showed a similar pattern of low seasonal influenza A and B virus activity after the first 2009 H1N1 pandemic wave. This suggests that the first wave of the pandemic might have led to a disruption of influenza virus activity afterward, not only in Indonesia but also in other tropical climate countries. We also observed the displacement of seasonal influenza A(H1N1) virus by the emergence of influenza A(H1N1)pdm09 virus in mid-2009.

To our knowledge, there are no existing data on the population-based incidence of uncomplicated influenza in Indonesia. The estimated annual incidence of influenza A in the community varied from 1.6 to 2.3 per 1,000 persons during the three years of our study. The CHCU rates we used to adjust the incidence were comparable to the estimated medically-attended rate among cases of influenza from a study in South Africa [10]. The incidence of influenza in our Indonesian study was low compared to the influenza incidence among ambulatory patients in sub-tropical China (4.1 to 19.2 per 1,000 population in 2008 and 2009) [22], Kenya (13.6 to 23/1,000py in 2007 to 2010) [21], and Bangladesh (130 to 170/1000py in 2009 and 2010) [23]. The lower influenza incidence in our study may reflect differences in the study populations (health-seeking behavior, demographics, nutrition, and medical risk factors) and health system factors (healthcare accessibility) [3], or study design and methodology (inclusion criteria, case definition, laboratory testing and estimation approach).

We found children younger than 5 years old to be the most affected age group for both influenza A and B-associated illnesses, with an estimated incidence of 7 to 10.6 /1,000 person-year and 0.4 to 4.3 /1,000 person-year, respectively. The exception was in 2010 when school-age children (6–15 years old) had the highest estimated annual incidence of influenza B. Other studies in Indonesia and Kenya reported that the highest incidence of hospitalized influenza-associated severe acute respiratory infection was in children under five years old [7,24]. Our finding based upon virologic testing that young children were most affected by influenza is consistent with a

community cohort study that utilized serological testing for influenza virus detection [25]. School-age children had the second highest influenza incidence, similar to what was reported in a community cohort study in Vietnam [18]. One study indicated that children aged 5–17 years are a driver of influenza A virus epidemics and that influenza vaccination of this group may contribute to reducing the overall impact on the community [26].

This study showed a trend of decreasing annual cumulative incidence with increasing age for both influenza A and B cases (**Figure 4**). The age-specific influenza incidence trends did not change when we performed stratified analyses by influenza A virus subtype, influenza B, or study sites. Individuals older than 65 years had very low estimated influenza incidence compared to younger age groups (**Table 3**), which aligns with the findings of an influenza surveillance study conducted during a similar period in East Java, Indonesia [4]. The small number of older adult subjects enrolled in this study, which appeared to be proportional to the Indonesian population age structure, implied a higher uncertainty or random error margin. It is possible that the small number of infections we detected in older adults was that elderly persons may not always seek medical care or may not manifest fever with influenza when presenting for primary care and would have been missed by our ILI case definition, and we would have underestimated influenza disease burden in the elderly population. To perform sensitivity analysis, we also calculated the annual incidence among the elderly by using a lower CHCU percentage among the elderly (21.7%) as reported in another Indonesian study [27], but the incidence of influenza among the elderly was still the lowest among all age groups (see **Table 4**).

There were several limitations of this study. It is known that most persons with influenza do not seek medical care [10,24] and estimates of disease burden in the community, based on passive surveillance case detection, need to account for health care utilization and other factors such as subject refusal [28]. We adjusted our incidence estimates to account for health care utilization of persons with ILI to account for this bias. However, the healthcare utilization percentage used for adjustment in this study was derived from an unpublished survey that was conducted after our study (2014) with a limited sample size. In 2014, the national health security program (JKN) for Indonesian universal health care was launched to increase healthcare utilization in general, including for persons with ILI.

The three community health centers that participated in ILI surveillance were open 5 days per week, and it is possible that some persons with ILI were missed if the centers were open 7 days a week. Therefore, our adjusted incidence estimates likely underestimate the incidence of ILI and influenza in the community. Moreover, healthcare utilization depends on access to medical services, which may vary by location, while we assumed the same level for the whole study area. Therefore, the adjustments made in this study might not fully address health-seeking behavior that differs temporally and geographically.

In addition, the confidence intervals of the incidence estimates were calculated using the WHO method, which does not address uncertainty in the proportion of ILI cases that present to included clinics and could lead to further imprecision of the incidence estimates. We also did not assess asymptomatic influenza virus infections, and since enrollment and testing for influenza required meeting the ILI case definition, symptomatic individuals with influenza virus infection without ILI and who sought medical care were not captured. Therefore, our estimates of symptomatic influenza incidence may underestimate the overall burden of influenza in the community.

The refusal rate was very low; however, we did not record the number and the characteristics of the refusal group and were unable to adjust for the percentage of persons who declined to participate in the study. We assumed that refusals occurred similarly across age groups. To estimate the population at risk, we considered a fixed cohort population, which may have changed over the study period. Overall, the study population in these two areas was relatively small and might limit the generalizability of findings to other areas of Indonesia.

Table 4. Estimated age-specific number of influenza cases, population size in Bandung district, Indonesia, 2009–2011, and community health care utilization (CHCU) from Praptiningsih *et al.* [27]

Year	Age category (year)	No of non-influenza	Adjusted numerator*	No of influenza A	Adjusted numerator	No of influenza B	Adjusted numerator	Total ILI	Adjusted numerator	No of population	CHCU# (%)
2009	0–5	132	404	18	55	11	34	161	493	8,511	32.7
	6–15	151	335	45	100	16	35	212	470	34,217	45.1
	16–50	174	642	21	77	11	41	206	760	96,766	27.1
	51–65	24	89	2	7	1	4	27	100	16,957	27.1
	>65	4	18	0	0	0	0	4	18	6,573	21.7
	Total	485	1,459	86	258.6	39	117	610	1,835	163,024	33.3
2010	0–5	269	823	27	83	5	15	301	921	8,511	32.7
	6–15	437	968	50	111	36	80	523	1,159	34,217	45.1
	16–50	480	1,771	41	151	17	63	538	1,985	96,766	27.1
	51–65	33	122	4	15	0	0	37	136	16,957	27.1
	>65	3	14	0	0	0	0	3	14	6,573	21.7
	Total	1,222	3,675	122	366.9	58	174	1,402	4,216	163,024	33.3
2011	0–5	212	649	16	49	1	3	229	701	8,511	32.7
	6–15	326	722	52	115	3	7	381	844	34,217	45.1
	16–50	418	1,542	51	188	3	11	472	1,741	96,766	27.1
	51–65	49	181	4	15	0	0	53	196	16,957	27.1
	>65	2	9	1	5	0	0	3	14	6,573	21.7
	Total	1,007	3,029	124	372.9	7	21	1,138	3,422	163,024	33.3

#CHCU: community health care utilization as percentage of population who came for influenza-like illness (ILI) from another study by Praptiningsih *et al.* [27]
*The adjusted numerator was calculated by dividing the number of cases for each age group by CHCU percentages

Conclusion

The estimated mean annual incidence of influenza A and B, adjusted for health care utilization, was 1.6 (95%CI: 1.3–2.0) and 0.7 (95%CI: 0.5–1.0) per 1,000 persons, respectively, with the most affected group being young and school-age children in West Java, Indonesia. Therefore, these populations are potential targets for influenza vaccination. This study reiterates the importance of pediatric populations in lower and middle-income countries as a target for influenza vaccination and other prevention measures.

Ethics approval

Participation was voluntary, and all subjects provided written informed consent. All data were kept confidential and data analysis was performed on de-identified data. The study was approved by the Colorado Multiple Institutional Review Board (COMIRB) and the Ethical Committee of Faculty of Medicine, Universitas Padjadjaran, Bandung, Indonesia by ethical clearance letter number 50/UN6.C1.3.2/KEPK/PN/2016.

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Competing interests

All the authors declare that there are no conflicts of interest. The views expressed are those of the authors and do not necessarily reflect the official policy of the Centers for Disease Control and Prevention.

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Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

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