The East Jakarta Project: surveillance for highly pathogenic avian influenza A(H5N1) and seasonal influenza viruses in patients seeking care for respiratory disease, Jakarta, Indonesia, October 2011–September 2012

A. D. STORMS[1,2], R. KUSRIASTUTI[3], S. MISRIYAH[3], C. Y. PRAPTININGSIH[4],
M. AMALYA[4], K. E. LAFOND[1], G. SAMAAN[4], R. TRIADA[3], A. D. IULIANO[1],
M. ESTER[4], R. SIDJABAT[3], K. CHITTENDEN[5], R. VOGEL[6],
M. A. WIDDOWSON[1], F. MAHONEY[1] AND T. M. UYEKI[1]*

[1] *Influenza Division. U.S. Centers for Disease Control and Prevention, Atlanta, GA, USA*
[2] *Epidemic Intelligence Service. Centers for Disease Control and Prevention, Atlanta, GA, USA*
[3] *Ministry of Health Republic of Indonesia, Jakarta, Indonesia*
[4] *Influenza Division. U.S. Centers for Disease Control and Prevention, Jakarta, Indonesia*
[5] *United States Agency for International Development, Jakarta, Indonesia*
[6] *USAID/DELIVER PROJECT, John Snow, International, Jakarta Field Office, Jakarta, Indonesia*

SUMMARY

Indonesia has reported the most human infections with highly pathogenic avian influenza (HPAI) A(H5N1) virus worldwide. We implemented enhanced surveillance in four outpatient clinics and six hospitals for HPAI H5N1 and seasonal influenza viruses in East Jakarta district to assess the public health impact of influenza in Indonesia. Epidemiological and clinical data were collected from outpatients with influenza-like illness (ILI) and hospitalized patients with severe acute respiratory infection (SARI); respiratory specimens were obtained for influenza testing by real-time reverse transcription–polymerase chain reaction. During October 2011–September 2012, 1131/3278 specimens from ILI cases (34·5%) and 276/1787 specimens from SARI cases (15·4%) tested positive for seasonal influenza viruses. The prevalence of influenza virus infections was highest during December–May and the proportion testing positive was 76% for ILI and 36% for SARI during their respective weeks of peak activity. No HPAI H5N1 virus infections were identified, including hundreds of ILI and SARI patients with recent poultry exposures, whereas seasonal influenza was an important contributor to acute respiratory disease in East Jakarta. Overall, 668 (47%) of influenza viruses were influenza B, 384 (27%) were A(H1N1)pdm09, and 359 (25%) were H3. While additional data over multiple years are needed, our findings suggest that seasonal influenza prevention efforts, including influenza vaccination, should target the months preceding the rainy season.

Key words: Influenza, influenza (seasonal), avian flu, surveillance.

INTRODUCTION

As of late July 2014, Indonesia had reported more cases of human infection with highly pathogenic avian influenza (HPAI) A(H5N1) virus (197/667 cases worldwide), deaths (165), and the highest cumulative case-fatality proportion (84%) than any country since 2003 [1]. HPAI H5N1 virus is considered to be endemic in poultry in Indonesia, with >11 000 poultry outbreaks reported from 2006 to mid-2012 (USAID Indonesia, unpublished data) [2]. Risk factors for HPAI H5N1 virus infection in humans include direct

* Author for correspondence: T. M. Uyeki, MD, MPH, MPP, Influenza Division, Centers for Disease Control and Prevention,1600 Clifton Rd., NE, MS A-20, Atlanta, GA 30333, USA.
(Email: tuyeki@cdc.gov)

or close exposure to sick or dead infected poultry, and visiting a live poultry market [3].

Jakarta province has reported more human HPAI H5N1 cases than other provinces in Indonesia, accounting for 27% of all cases since the first human infections were detected in 2005 [4]. East Jakarta district is one of five districts in Jakarta and its residents are at risk for poultry-to-human HPAI H5N1 virus transmission because the district is a major entry point for poultry shipments from other parts of Java. The majority of Jakarta's poultry collector yards and slaughterhouses are located in East Jakarta district, and there are also many traditional live bird markets. HPAI H5N1 viruses have been detected in live poultry markets in this district [5–7].

While there are some data on the epidemiology and seasonal patterns of influenza virus infection in Indonesia, data on the public health impact of influenza are limited [8, 9]. To date, there are no estimates of severe disease caused by seasonal influenza virus infections in Indonesia, including the burden of hospitalizations or deaths. Although there is a national influenza surveillance system in place, it focuses on specimen collection for virological surveillance [10]. Published surveillance data suggests that influenza viruses circulate throughout the year in Indonesia, with peaks of influenza activity during the rainy season [8, 9].

To address gaps in knowledge about the public health impact of influenza in Indonesia, enhanced surveillance for HPAI H5N1 and seasonal influenza viruses was implemented in East Jakarta district. The objectives of this surveillance were to assess the prevalence and epidemiology of seasonal influenza and HPAI H5N1 virus infections in patients seeking care for respiratory illness in outpatient and inpatient settings, and to describe the characteristics of patients with laboratory-confirmed infections. We present data for the first 12 months of enhanced surveillance.

METHODS

Six hospitals and four outpatient clinics were selected from health facilities in East Jakarta district. The participating hospitals were all large general hospitals (>200 beds). Three of the hospitals were private and three were public, and they were among the facilities with highest numbers of admissions for pneumonia in East Jakarta district in 2010 [11]. The outpatient clinics are all 'subdistrict' rather than 'village' clinics to promote a higher volume of monthly visits for respiratory illness and to ensure sufficient availability of staff for surveillance activities. At each site, surveillance teams consisting of one or two physicians, a nurse, medical records officer, and at hospital sites, a laboratorian, were trained on the methodology for conducting surveillance. At all 10 sites, patients of all ages were screened, and all consenting individuals were enrolled. After a 2-month pilot phase for facilitating staffing and logistical issues, the project was implemented on 1 October 2011.

At the four outpatient clinics, surveillance for influenza-like illness (ILI) was conducted Monday–Friday in general medicine clinics and Integrated Management of Childhood Illness (IMCI) clinics for children aged <5 years. Physicians and nurses identified ILI cases by screening temperatures and conducting interviews of patients or their parents during their regular clinical encounters. ILI was defined as a measured temperature ⩾38 °C and either cough or sore throat. At the six hospitals, surveillance for severe acute respiratory infection (SARI) was conducted daily in adult medicine and paediatric wards. SARI was based on the IMCI case definition for pneumonia or severe pneumonia for patients aged <5 years [12], and for patients aged ⩾5 years was defined as fever (either measured temperature ⩾38 °C or subjective complaint) and at least one of the following: cough, sore throat, or shortness of breath. ILI surveillance was only conducted in outpatient clinics and SARI surveillance was only conducted in hospitals. SARI cases were identified in a multistep process: (1) medical records officers compiled all admissions to the adult medicine and paediatric wards within the previous 24 h, (2) surveillance nurses reviewed admission diagnoses of all new patients to identify those with a respiratory diagnosis or chief complaint (e.g. pneumonia, asthma) or fever, (3) surveillance nurses interviewed staff in surveillance wards to identify additional eligible patients, and (4) surveillance staff conducted targeted interviews with potential cases identified from previous steps, exclusively to determine if they met the SARI case definition.

Outpatients or hospitalized patients who met the ILI or SARI case definitions and consented to participate were interviewed using standardized case forms to collect demographic and basic clinical data and ascertain any history of poultry exposures within 7 days of illness onset. We chose 7 days to capture the incubation period for the majority of cases of avian-to-human transmission of H5N1 virus [13, 14]. For SARI cases, data were also collected on comorbidities, hospitalization course, and discharge

information. Nasal and throat swabs taken from each patient were combined and refrigerated at 2–8 °C before transport (Monday–Friday) to two laboratories in Jakarta for testing by real-time reverse transcription–polymerase chain reaction (rRT–PCR) assay for the presence of influenza viruses using primers and probes for influenza A and B; specimens positive for influenza A were subtyped for H3, seasonal H1, pandemic H1 (which are the influenza A virus subtypes that have been in general circulation among humans worldwide and in Indonesia in recent years), and H5. An aliquot of all original respiratory specimens was sent by both laboratories [Provincial Health Laboratory of DKI Jakarta and the Infectious Disease Hospital (RSPI) Sulianti Saroso Laboratory] to the National Influenza Centre (NIC) at the National Institute of Health Research and Development (NIHRD) in Jakarta for repeat RT–PCR testing of a proportion of positive and negative specimens, for quality control purposes.

Data for ILI and SARI patients were entered at each site into an online reporting system. Each site also completed a weekly aggregate report that included the total number of visits or admissions by age group (all diagnoses) to the clinics or wards where surveillance was conducted. Laboratory specimens were linked to epidemiological data using a unique ID number assigned to each case and testing results were also entered into the online reporting system. All data were stored in a MySQL database hosted by the Jakarta Provincial Health Office. Monthly supervision visits were conducted for each site, with quarterly review meetings to share data and provide feedback to all sites and other stakeholders.

Descriptive statistics and bivariate analyses were calculated for epidemiological and clinical data. Poultry contact data were used to determine the proportion of cases that met the Indonesia 'suspect H5N1 infection' case definition [15]. Preliminary rates of hospitalized influenza-positive SARI cases for the general population of East Jakarta district were calculated by using information on severe respiratory illness obtained from a health utilization study (HUS) that was conducted in the district. For the rate calculation we adjusted the number of influenza-positive SARI cases by taking into account the proportion of SARI cases that were not tested for influenza. For the population denominator, we adjusted (i.e. multiplied) the 2012 population projections for East Jakarta [16], by the proportion of all persons that were hospitalized for severe respiratory illness at the six SARI surveillance sites (identified by

the HUS) as opposed to elsewhere. We calculated 95% confidence intervals (CI) around the rate estimates using the continuity-corrected score method [17].

Descriptive statistics and bivariate analyses were conducted using SPSS Statistics v. 20 (SPSS Inc., USA). Rate analyses were conducted using SAS v. 9.3 (SAS Institute Inc., USA).

Ethical standards

This surveillance project was considered to be routine public health surveillance by the Indonesian Ministry of Health and by the Centers for Disease Control and Prevention (CDC) Institutional Review Boards (IRBs) and was exempt from formal review. The Health Utilization Study (HUS) was approved by University of Indonesia and CDC IRBs. Written consent was obtained from all SARI and ILI cases before completion of case forms and specimen collection. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

RESULTS

During October 2011–September 2012, surveillance sites identified 3390 (2%) ILI cases out of 173 508 visits to the general and IMCI outpatient clinics, and 1934 (3%) SARI cases, out of 64 538 patients admitted to adult medicine and paediatric hospital wards. By site, the proportion of ILI cases out of total outpatient visits ranged from 1% to 3%, and the proportion of SARI cases out of total admissions ranged from 2% to 5%. As a result of the volume of patients cared for at each site, the proportion of cases contributed by each site varied for both ILI surveillance (17–32%) and SARI surveillance (12–28%). A majority of patients who met the ILI and SARI case definitions participated in this surveillance. Of the 3325 (98·1%) ILI cases with completed forms, the median age was 5 years [interquartile range (IQR) 2–10 years] and 1763 (53%) cases were female (Tables 1, 2). Of the 1870 (96·7%) SARI cases with completed forms, the median age was 17 years (IQR 2–47 years) and 901 (48·2%) cases were female. Overall, adults accounted for half of all SARI cases, but only 16% of ILI cases (Table 1). The ≥65 years age group accounted for the smallest proportion of cases enrolled, particularly for ILI cases.

Table 1. *Distribution of ILI and SARI cases by age group, sex, and district of residence. East Jakarta District, Jakarta, Indonesia, October 2011–September 2012*

Characteristic	ILI (N = 3325) n (%)	SARI (N = 1870) n (%)
Female	1763 (53·0)	901 (48·2)
<2 years	732 (22·0)	443 (23·7)
2–4 years	627 (18·9)	206 (11·0)
5–17 years	1429 (43·0)	306 (16·4)
18–49 years	472 (14·2)	580 (31·0)
50–64 years	56 (1·7)	214 (11·4)
⩾65 years	9 (0·3)	121 (6·5)
Resident of East Jakarta District (all ages)	3176 (95·5)	1203 (64·3)

ILI, Influenza-like illness; SARI, severe acute respiratory infection.

Of 3278 respiratory specimens collected from ILI cases (96·7%) and tested for influenza viruses, 1131 (34·5%) ILI cases were positive. Of 1787 respiratory specimens collected from SARI cases (92·4%) and tested for influenza, 276 (15·4%) were positive. In influenza-positive ILI cases, the median age was 7 years (IQR 4–17) and 606 (53·6%) cases were female. In influenza-positive SARI cases, the median age was 25 years (IQR 4–45) and 136 (49·3%) were female. For ILI cases, the proportion positive increased substantially with increasing age, from 17% in children aged <2 years to 67% for adults aged 50–64 years. For SARI cases, the proportion positive between age groups showed less variation, from 10% in children aged <2 years to 21% in adults aged 50–64 years (Fig. 1).

The proportion of ILI and SARI cases that tested positive for influenza varied markedly by month (Fig. 2a, b). By contrast, there were no clear seasonal differences in total SARI or ILI cases as a proportion of total patients visiting surveillance sites (Fig. 2c). In ILI specimens, the weekly proportion testing positive for influenza viruses was >10% during mid-November 2011 until the end of May 2012 (46% of all ILI specimens tested positive for that period) (Fig. 2a). The influenza virus proportion positive in ILI cases increased substantially after the first week of December and peaked at 76% during the third week of January 2012. For SARI, the proportion positive for influenza virus infection was >10% during early December 2011 until mid-May 2012 (23% of all SARI specimens tested positive for that period) (Fig. 2b). In SARI cases, the influenza virus

proportion positive also increased substantially after the first week of December and peaked at 36% during the second week of February 2012. For both ILI and SARI, there were also variations in the timing of peak activity by influenza virus type and subtype (Fig. 3a, b), with A(H1N1)pdm09 dominating at the end of 2011, followed by H3, and then influenza B. For ILI, 536 (47%) of influenza viruses were influenza B, 301 (27%) were A(H1N1)pdm09, and 298 (26%) were H3. For SARI, 132 (48%) of influenza viruses were influenza B, 83 (30%) were A(H1N1)pdm09, and 61 (22%) were H3. No HPAI H5N1 virus infections were identified in 598 ILI specimens and 144 SARI specimens testing positive for influenza A, and subsequently tested for H5.

Of 276 influenza-positive SARI cases, 180 (65%) sought care at another facility before admission compared to 1101 (73%) of 1511 influenza-negative cases (Table 2). There were 55 (20%) influenza-positive and 282 (19%) influenza-negative SARI cases that reported having at least one underlying condition associated with higher risk of influenza virus complications (i.e. diabetes, chronic obstructive pulmonary disease, asthma, cardiovascular disease, chronic kidney disease, chronic liver disease, cancer, pregnancy). For influenza-positive and influenza-negative SARI cases, the two underlying conditions that were most prevalent were asthma (11% and 9%, respectively) and diabetes (7% and 5%, respectively), with no significant differences regarding comorbidities by influenza test status ($P = 0.62$). None of the influenza-positive SARI cases reported receiving influenza vaccination in the previous 12 months compared to 20 (1·3%) of influenza-negative SARI cases; this difference was not statistically significant ($P = 0.06$).

Discharge data were available for 271 (98·2%) of influenza-positive and 1477 (97·7%) of influenza-negative SARI cases (Table 3). Of the influenza-positive cases, three (1%) were admitted to an intensive care unit and four (2%) received mechanical ventilation. Three (1%) influenza-positive and 57 (4%) influenza-negative SARI cases died ($P = 0.02$). Only 1% of influenza-positive and 0·4% of influenza-negative SARI cases received oseltamivir treatment.

A high proportion of ILI and SARI cases had a history of poultry contact in the 7 days before symptom onset (34% and 21%, respectively). In addition, 398 (12%) of ILI and 143 (8%) of SARI cases reported having poultry exposures that met the 'suspected H5N1' case definition in Indonesia (i.e. touching healthy, sick or dead poultry, touching poultry

Table 2. *Comorbidities and clinical characteristics of influenza-positive and influenza-negative hospitalized SARI cases. East Jakarta District, Jakarta, Indonesia, October 2011–September 2012*

	Influenza-positive SARI cases* (N = 276)	Influenza-negative SARI cases* (N = 1511)	P value
Age, years, median (IQR)	25 (4–45·8)	16 (2–39)	<0·01
Any comorbidity	55 (19·9)	282 (18·7)	0·62
Diabetes	19 (6·9)	79 (5·2)	0·27
COPD	5 (1·8)	57 (3·8)	0·10
Asthma	30 (10·9)	136 (9·0)	0·33
Cardiovascular disease	11 (4·0)	50 (3·3)	0·57
Chronic kidney disease	2 (0·7)	13 (0·9)	1·0
Chronic liver disease	2 (0·7)	13 (0·9)	1·0
Cancer	0 (0)	0 (0)	n.a.
Pregnancy†	2 (3·9)	7 (3·0)	0·67
Influenza vaccination in past 12 months,	0 (0)	19 (1·3)	0·06
Active smoker	33 (12·0)	204 (13·5)	0·48
Sought care before admission	180 (65·2)	1101 (73·1)	<0·01

SARI, severe acute respiratory infection; IQR, interquartile range; COPD, chronic obstructive pulmonary disease, n.a., not applicable.

Values given are *n* (%), unless stated otherwise.

* SARI cases with case form completed and tested for influenza.

† Denominator includes women aged 18–49 years (232 influenza negative and 51 influenza positive).

products, slaughtering/killing poultry or contact with chicken manure). For ILI and SARI influenza-positive cases these proportions were 14% and 5%, respectively, compared to 11% and 9% of influenza-negative cases. Additional poultry exposures are described in Table 4.

The overall estimated rate of hospitalized influenza-positive SARI cases in East Jakarta district was 12·8 cases/100 000 person-years (pyr) (95% CI 8·2–23·1). By age group the hospitalization rates/100 000 pyr were 37·2 (95% CI 20·9–76·7) in children aged <5 years, 10·4 (95% CI 5·5–22·9) in those aged 5–19 years, 9·5 (95% CI 5·7–18·4) in those aged 20–64 years and 20·3 in those aged ⩾65 years (95% CI 7·5–61·8).

DISCUSSION

We describe the findings of an enhanced influenza surveillance system focusing on patients seeking medical care for acute respiratory disease in an urban district of Jakarta, Indonesia during October 2011 to September 2012. Overall, >3200 ILI and >1700 SARI cases were tested and more than 34% and 15%, respectively, were positive for seasonal influenza viruses. The prevalence of Influenza virus infections was highest during December–May.

No human cases of infection with HPAI H5N1 virus were identified through this enhanced surveillance system despite the high proportion of people that reported contact with poultry and the high prevalence of HPAI H5N1 viruses circulating in poultry [6]. During 2011–2012, Indonesia reported 12 and nine HPAI H5N1 cases, respectively [1]. HPAI H5N1 poultry outbreaks in backyard poultry typically peak in January or February during most years in Indonesia (USAID Indonesia, unpublished data). Although HPAI H5N1 cases have usually been identified in people who were tested due to clinical suspicion, the national influenza surveillance system in Indonesia identified two HPAI H5N1 cases in patients with SARI in 2008–2009 [10]. Surveillance conducted by the Naval Medical Research Unit 2 laboratory identified an additional 10 cases of HPAI H5N1 during 2005–2007 [9]. Since respiratory specimens from 5065 patients that met the SARI or ILI case definitions were tested for influenza, and none of the 744 influenza A-positive specimens were positive for H5, it is likely that few symptomatic HPAI H5N1 virus infections occurred in this population seeking medical care during the surveillance period.

Seasonal influenza was associated with a substantial amount of illness in people seeking care for acute respiratory disease in East Jakarta district as indicated by the high proportion of influenza virus infections
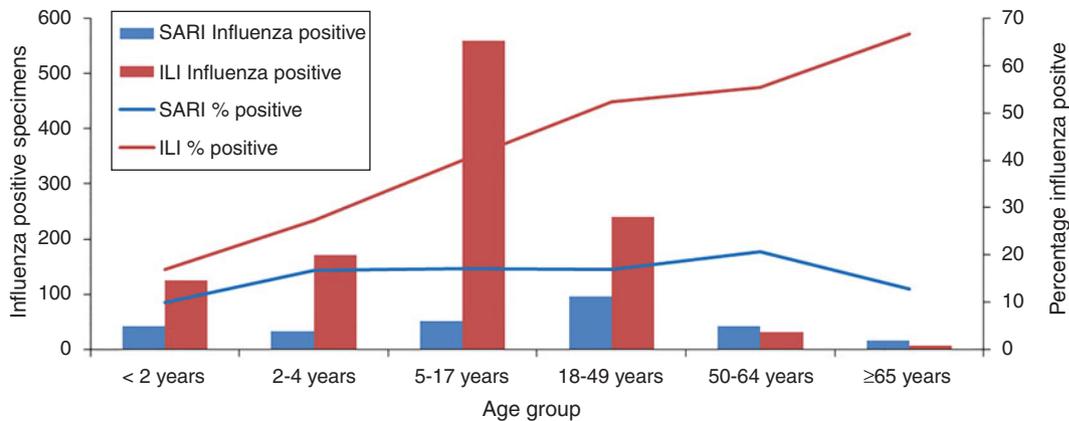
Fig. 1. Percentage of influenza-positive influenza-like illness (ILI) and severe acute respiratory infection (SARI) cases by age group. East Jakarta District, Jakarta, Indonesia, October 2011–September 2012.

detected in SARI and ILI case-patients and the rate of hospitalized influenza-associated SARI. Our preliminary rates are similar to those published in a meta-analysis by Nair *et al.* [18] who estimated the incidence of influenza-associated severe acute lower respiratory infection in children aged <5 years in South East Asia to be 1 (0–6)/1000 pyr. Similar to East Jakarta, the sources from South East Asia included in the meta-analysis used data collected mostly from hospitalized patients. Our estimates were also similar to rates published from Bangladesh for SARI associated with influenza in children aged ≥5 years (1·2/10 000 pyr) [19] but the rates in Bangladeshi children aged <5 years were much higher (5·9/1000 pyr). By contrast to East Jakarta, the method for rate calculation in Bangladesh focused on identifying the number of influenza-positive outpatients who were later admitted to hospital; it is unclear how this different method compares to the one we used. In addition, in the Bangladesh study, surveillance was only conducted 2 days per month, and these data were extrapolated to non-surveillance days. Our findings are also lower than those published from Kenya in children aged <5 years (2·9–4·7/1000 pyr) and ≥5 years (0·21–0·24/1000 pyr) [20]. However, the estimates from Kenya adjusted for the proportion of patients that did not seek medical care (i.e. non-hospitalized SARI) and are therefore expected to be higher. We expect to update our preliminary burden estimates after data from more surveillance years are available.

In ILI patients, school-aged children (5–17 years) comprised the highest number of influenza-positive ILI cases as well as the largest age group of ILI patients. However, the proportion of influenza-positive ILI cases was highest in the 18–49 years age

group. The highest number of SARI patients and influenza-positive SARI patients was in persons aged 18–49 years, whereas the proportion of influenza cases was highest in those aged 50–64 years. The age distribution of the Indonesian population may partially explain these frequencies since persons aged 20–49 and 5–19 years are the most predominant age groups in the general population of East Jakarta [16]. However, it is unclear if the role of health-seeking behaviours in this community could also be a factor. The prevalence of chronic medical conditions in SARI-associated influenza patients was lower than in other countries, which may be partially explained by the small number of SARI cases aged ≥65 years, since chronic medical conditions increase with advanced age. In this surveillance system we found that 3% of inpatients out of total admissions and 2% of outpatients out of total visits met the SARI and ILI case definitions, respectively. Although there is a paucity of published data about these proportions in other settings, a few surveillance reports from other countries have identified proportions that are broadly consistent with our findings [21, 22].

There was clear temporal variation in the proportion of specimens that tested positive for influenza viruses. The months with the highest proportion of influenza-positive specimens (>20%) were November/December–April/May, which for the most part coincides with the rainy season in Jakarta (usually November–March) [16, 23]. This is consistent with previous findings from influenza surveillance in Indonesia [8, 9, 24] and other tropical countries in the region [25–27], suggesting that prevention efforts such as influenza vaccination programmes should target the months preceding the rainy season.
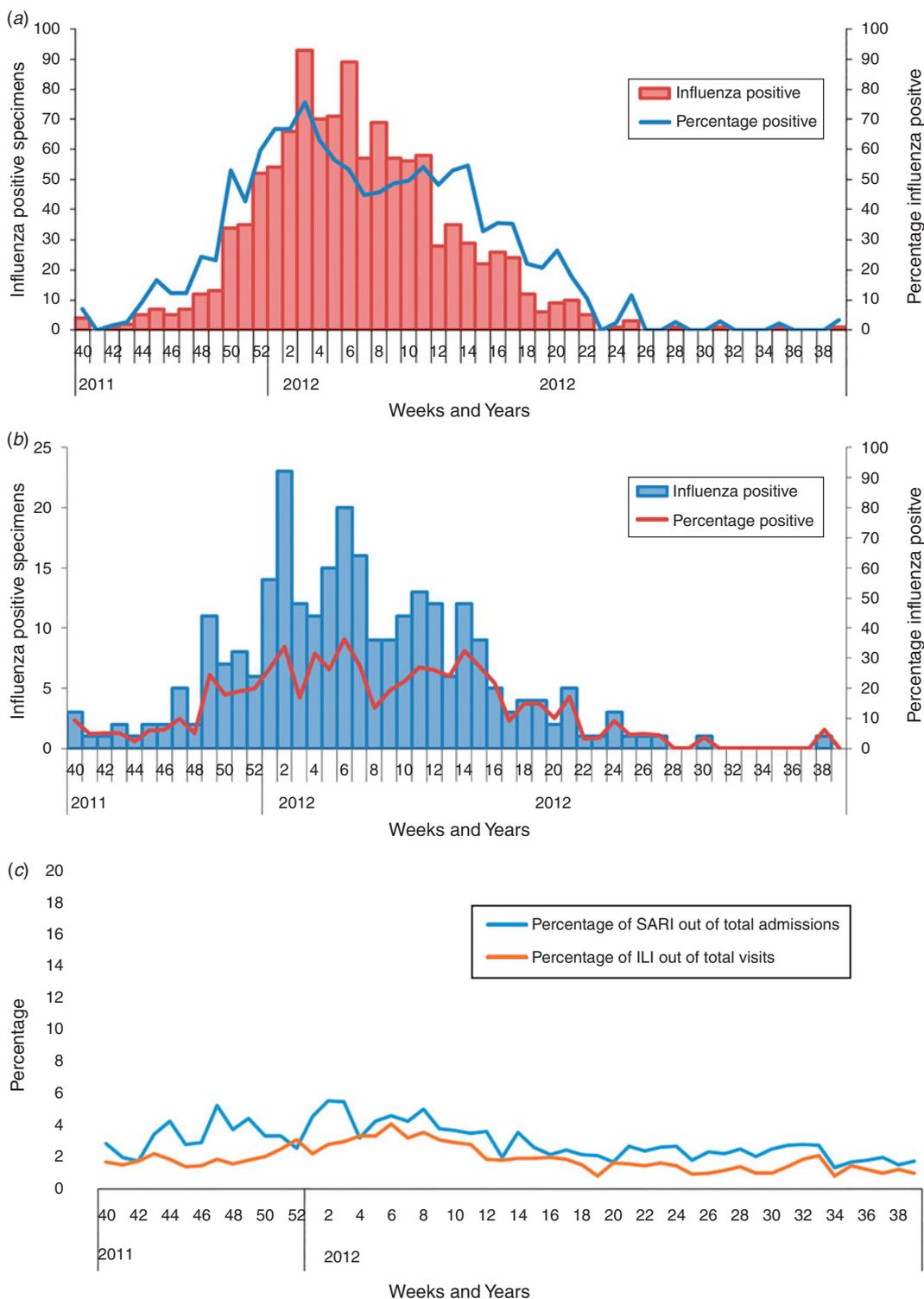
Fig. 2. (*a*) Influenza-positive influenza-like illness (ILI) cases by epidemiological week. Cases by date of illness onset. (*b*) Influenza-positive severe acute respiratory infection (SARI) cases by epidemiological week. Cases by date of illness onset. (*c*) Percentage of SARI cases out of total admissions and ILI cases out of total visits, by epidemiological week. Cases by date of presentation. East Jakarta District, Jakarta, Indonesia, October 2011–September 2012.
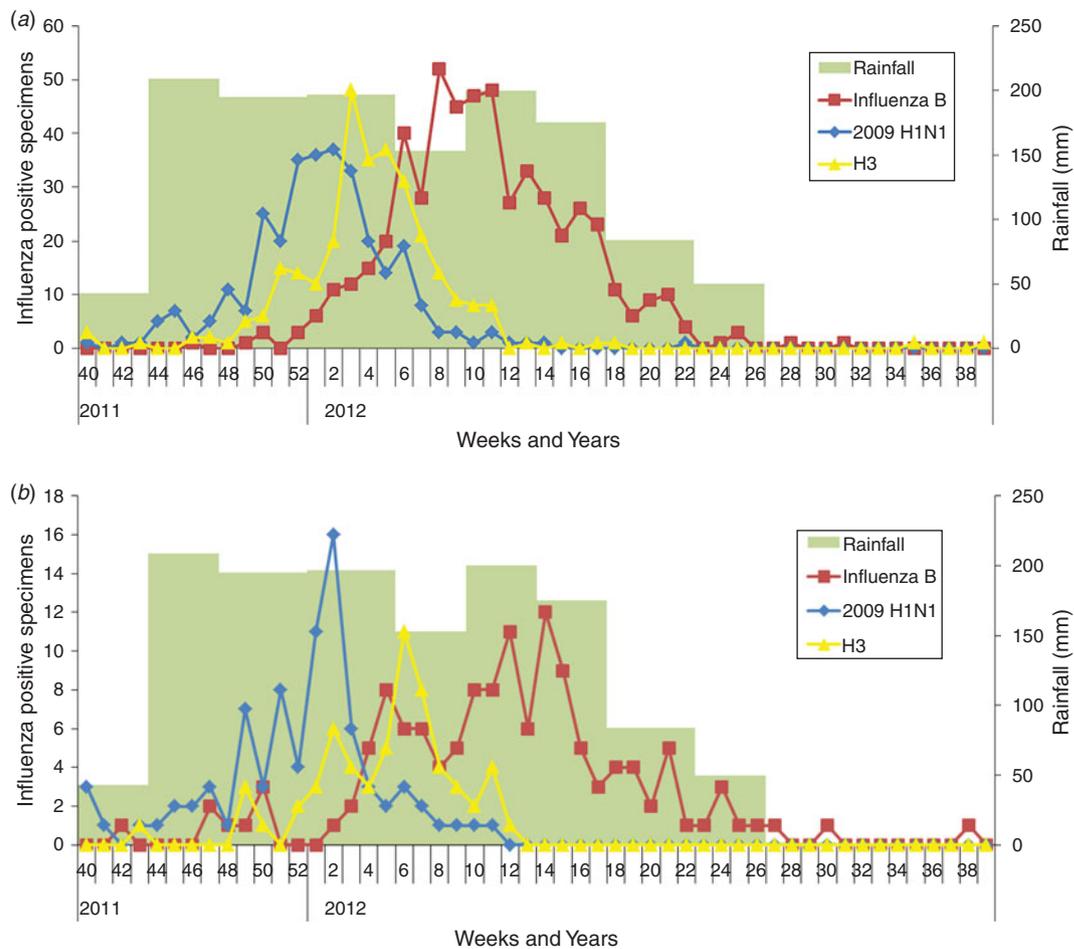
Fig. 3. Influenza-positive specimens from (*a*) influenza-like illness cases and (*b*) severe acute respiratory infection cases by type/subtype and rainfall by epidemiological week. Cases by date of presentation. East Jakarta District, Jakarta, Indonesia, October 2011–September 2012.

Table 3. *Clinical outcomes of influenza-positive and influenza-negative hospitalized SARI cases. East Jakarta District, Jakarta, Indonesia, October 2011–September 2012*

	Influenza-positive SARI cases* ($N = 271$)	Influenza-negative SARI cases* ($N = 1477$)	*P* value
Days of hospital stay, median (IQR)	4 (3–6)	5 (3–7)	<0·01
ICU admission	3 (1·1)	45 (3·1)	0·07
Mechanical ventilation	4 (1·5)	32 (2·2)	0·46
Received oseltamivir treatment	3 (1·1)	5 (0·4)	0·13
Died	3 (1·1)	57 (3·9)	0·02

SARI, Severe acute respiratory infection; IQR, interquartile range; ICU, intensive care unit.
Values given are *n*(%), unless stated otherwise.
* SARI cases with case form and discharge form completed and tested for influenza.

Few (1%) influenza-associated SARI cases received oseltamivir treatment. This finding might have been the result of clinicians following guidelines in Indonesia which recommend oseltamivir only for suspected H5N1 cases [28]. Although hospitals had early access to results for influenza testing (within 2 days after specimen collection in 30% of cases, and within 4 days in 63% of cases), we cannot assess from our data the impact that knowledge, attitudes and practices of Indonesian clinicians may have played in

Table 4. *History of poultry exposure in ILI and SARI cases in the 7 days prior to illness onset. East Jakarta District, Jakarta, Indonesia, October 2011–September 2012*

Exposure	ILI cases (N = 3325) n (%)	SARI cases (N = 1870) n (%)
Any history of poultry contact	1143 (34·4)	396 (21·2)
Touched healthy poultry*	139 (4·2)	79 (4·2)
Touched sick poultry*	10 (0·3)	12 (0·6)
Touched dead poultry*	5 (0·2)	4 (0·2)
Touched poultry products*	285 (8·6)	75 (4·0)
Slaughtered or cleaned poultry*	22 (0·7)	26 (1·4)
Contact with chicken manure*	17 (0·5)	31 (1·7)
Owns poultry	401 (12·1)	244 (13·0)
Visited live poultry market	519 (15·6)	75 (4·0)
Poultry die-offs in neighbourhood	48 (1·4)	56 (3·0)
Met the H5N1 suspect case definition	398 (12·0)	143 (7·6)

ILI, Influenza-like illness; SARI, severe acute respiratory infection.

* Poultry contact included in the current H5N1 suspect case definition.

regards to oseltamivir prescribing for seasonal influenza. In addition, we did not assess oseltamivir availability at surveillance sites. However, this finding highlights the importance of increasing awareness in clinicians and policy makers about the potential complications of seasonal influenza which can lead to hospitalizations, the risk of nosocomial infections, and the clinical benefit of oseltamivir treatment, especially when administered soon after illness onset [29, 30]. In addition, isolation practices for influenza-positive hospitalized patients were not assessed in this project. Availability of rapid influenza diagnostic tests would allow early identification of influenza and potentially facilitate antiviral treatment of influenza patients. However, such rapid influenza diagnostic tests lack sensitivity compared to RT–PCR [31]. Recently, rapid molecular assays and multi-pathogen PCR assays for detection of influenza viruses have become available, but may not be economically feasible for use in Indonesia [32, 33].

Only 31 patients were identified as suspected HPAI H5N1 cases by clinicians in the surveillance sites over the 12-month period, mostly based on clinical suspicion (of note, only three of these patients were reported to have received oseltamivir). However, 12% and 8% of all ILI and SARI patients, respectively (i.e. 541

persons) met the suspected HPAI H5N1 case definition in Indonesia based on poultry exposure history. Since the prevalence of poultry exposure is high in many areas of Indonesia, the usefulness of the 'suspected H5N1' case definition (respiratory symptoms and poultry exposure) should be evaluated. For example, epidemiological and clinical information from confirmed HPAI H5N1 cases in Indonesia could be incorporated into the suspected HPAI H5N1 case definition to improve specificity [34–36]. In addition, specificity could also be increased if clinicians throughout Indonesia were informed if HPAI H5N1 viruses are circulating in poultry in areas where they see patients.

Limitations to this project include that our surveillance was limited to one district in western Java and these findings might not be generalizable to all of Indonesia. In addition, there was some variability in surveillance activities at different sites. For example, some sites optimized their case-finding and reporting strategies earlier than others, which resulted in lower case detection, especially at the start of the project. For this reason, we excluded data from the first 2 months of surveillance (i.e. pilot period during August and September 2011). Other limitations include that we only captured cases that sought medical care at surveillance sites, and it is possible that we may have under-detected some influenza virus infections in persons that did not seek care, did not meet the case definitions for ILI or SARI, or if ILI and SARI patients were not shedding detectable influenza viruses in the upper respiratory tract when sampled. Since we were not able to conduct comprehensive ILI or SARI case-finding at all healthcare facilities in East Jakarta district, we would not have been able to capture any H5N1 cases that presented to facilities not included in our surveillance. In addition, some data collected were based on patients' self-reports and may not have been recalled accurately. Although we calculated confidence intervals around the preliminary rate calculations in order to account for sampling error, all these factors related to data collection could result in potential sources of error. As noted above, comparisons with previously published rates are limited by the methodological differences in influenza surveillance and rate calculation at other sites.

CONCLUSION

Although much attention has been focused upon the high mortality from human infection with HPAI H5N1 virus in Indonesia, we did not identify any

HPAI H5N1 virus infections in patients with a high prevalence of poultry exposures who presented to medical care for ILI or SARI. However, a substantial number of seasonal influenza virus infections were identified in SARI and ILI patients, indicating that seasonal influenza is a significant contributor to acute respiratory disease requiring hospitalization and in the outpatient setting in the Jakarta area. The impact of influenza was particularly high during the rainy season, indicating a potential target period for timing of influenza vaccination programmes in this tropical setting. Multi-year data are needed to better define disease burden, seasonality, and the economic impact of seasonal influenza in this area in order to guide interventions.

ACKNOWLEDGEMENTS

DECLARATION OF INTEREST

None.

REFERENCES

1. **World Health Organization.** Cumulative number of confirmed human cases of avian influenza A(H5N1)reported to WHO. (http://www.who.int/influenza/human_animal_interface/H5N1_cumulative_table_archives/en/). Accessed 6 November 2014.

2. **Food and Agriculture Organization of the United Nations.** Approaches to controlling, preventing and eliminating H5N1 highly pathogenic avian influenza in endemic countries. Animal Production and Health Paper, 2011 (http://www.fao.org/docrep/014/i2150e/i2150e00.htm).

3. **Zhou L, *et al.*** Risk factors for human illness with avian influenza A (H5N1) virus infection in China. *Journal of Infectious Diseases* 2009; **199**: 1726–1734.

4. **Directorate-General of Disease Control and Environmental Health, Indonesia Ministry of Health.** Disease Control and Environmental Health Annual Profile. (Report Number 351·770·2 IND P). 2012 (http://www.slideshare.net/budi_hermawan_a/profil-pppl2012).

5. **Yupiana Y, *et al.*** Risk factors of poultry outbreaks and human cases of H5N1 avian influenza virus infection in West Java Province, Indonesia. *International Journal of Infectious Diseases* 2010; **14**: e800–805.

6. **Indriani R, *et al.*** Environmental sampling for avian influenza virus A (H5N1) in live-bird markets, Indonesia. *Emerging Infectious Diseases* 2010; **16**: 1889–1895.

7. **Azhar M, *et al.*** Poultry H5N1 outbreaks in the countryside, human deaths in Jakarta: are mega-cities sinks for avian influenza viruses? *Options for the Control of Influenza VIII*. Cape Town, South Africa, 2013.

8. **Beckett CG, *et al.*** Influenza surveillance in Indonesia: 1999–2003. *Clinical Infectious Diseases* 2004; **39**: 443–449.

9. **Kosasih H, *et al.*** Surveillance of influenza in Indonesia, 2003–2007. *Influenza and Other Respiratory Viruses* 2013; **7**: 312–320.

10. **Ramadhany R, *et al.*** Proportion of influenza cases in severe acute respiratory illness in Indonesia during 2008–2009. *Medical Journal of Indonesia* 2010; **19**: 264–267.

11. **DKI Jakarta Provincial Health Office.** Surveillance and epidemiology. (http://surveilans-dinkesdki.net/). Accessed 3 August 2011.

12. **World Health Organization.** *Handbook: IMCI Integrated Management of Childhood Illness*, 2005 (http://www.who.int/maternal_child_adolescent/documents/9241546441/en/index.html).

13. **Huai Y, *et al.*** Incubation period for human cases of avian influenza A(H5N1) infection, China. *Emerging Infectious Diseases* 2008; **14**: 1819–1821.

14. **Writing Committee of the Second World Health Organization Consultation on Clinical Aspects of Human Infection with Avian Influenza.** Update on avian influenza A (H5N1) virus infection in humans. *New England Journal of Medicine* 2008; **358**: 261–273.

15. **Directorate-General of General Medical Services, Indonesian Ministry of Health.** Clinical management guideline for avian influenza A/H5N1 cases in hospitals. 2010 (http://www.depkes.go.id/downloads/flu_H1N1/tata_laksana_avian_influenza.pdf).

16. **BPS-Statistics Indonesia, East Jakarta Administration.** East Jakarta Area Statistics 2013 (http://www.depkes.go.id/downloads/flu_H1N1/tata_laksana_avian_influenza.pdf).

17. **Vollset SE.** Confidence intervals for a binomial proportion. *Statistics in Medicine* 1993; **12**: 809–824.

18. **Nair H, *et al.*** Global burden of respiratory infections due to seasonal influenza in young children: a systematic review and meta-analysis. *Lancet* 2011; **378**: 1917–1930.

19. **Azziz-Baumgartner E, *et al.*** Incidence of influenza-like illness and severe acute respiratory infection during three influenza seasons in Bangladesh, 2008–2010. *Bulletin of the World Health Organization* 2012; **90**: 12–19.

20. **Fuller JA, *et al.*** Estimation of the national disease burden of influenza-associated severe acute respiratory illness in Kenya and Guatemala: a novel methodology. *PLoS ONE* 2013; **8**: e56882.

21. **Members of the Western Pacific Region Global Influenza Surveillance and Response System.** Epidemiological and virological characteristics of influenza in the Western pacific region of the World Health Organization, 2006–2010. *PLoS ONE* 2012; **7**: e37568.

22. **Nachtnebel M, *et al.*** Lessons from a one-year hospital-based surveillance of acute respiratory infections in Berlin- comparing case definitions to monitor influenza. *BMC Public Health* 2012; **12**: 245.

23. **Bureau of Meteorology, Climatology, and Geophysics.** Pondok Betung, Tangerang. Direct data request. Obtained 5 June 2014.

24. **Yamaoka M, *et al.*** Virological surveillance of human influenza in Indonesia, October 2008-March 2010. *Microbiology and Immunology* 2011; **55**: 514–517.

25. **Hampson AW.** Epidemiological data on influenza in Asian countries. *Vaccine* 1999; **17** (Suppl. 1): S19–23.

26. **Hasegawa G, *et al.*** Influenza virus infections in Yangon, Myanmar. *Journal of Clinical Virology* 2006; **37**: 233–234.

27. **Nguyen HL, *et al.*** Epidemiology of influenza in Hanoi, Vietnam, from 2001 to 2003. *Journal of Infection* 2007; **55**: 58–63.

28. **Kosasih H, *et al.*** Managing seasonal influenza: oseltamivir treatment policy in indonesia? *Acta Medica Indonesiana* 2014; **46**: 58–65.

29. **Hsu J, *et al.*** Antivirals for treatment of influenza: a systematic review and meta-analysis of observational studies. *Annals of Internal Medicine* 2012; **156**: 512–524.

30. **Muthuri SG, *et al.*** Impact of neuraminidase inhibitor treatment on outcomes of public health importance during the 2009–2010 influenza A(H1N1) pandemic: a systematic review and meta-analysis in hospitalized patients. *Journal of Infectious Diseases* 2013; **207**: 553–563.

31. **Chartrand C, *et al.*** Accuracy of rapid influenza diagnostic tests: a meta-analysis. *Annals of Internal Medicine* 2012; **156**: 500–511.

32. **Bell JJ, Selvarangan R.** Evaluation of the Alere I influenza A&B nucleic acid amplification test by use of respiratory specimens collected in viral transport medium. *Journal of Clinical Microbiology* 2014; **52**: 3992–3995.

33. **Pettit N, *et al.*** Comparison of turnaround time (TAT) and time to oseltamivir discontinuation between two respiratory viral panel testing (RVP) methodologies. *Journal of Medical Microbiology* 2015; **64**: 312–313.

34. **Sedyaningsih ER, *et al.*** Epidemiology of cases of H5N1 virus infection in Indonesia, July 2005-June 2006. *Journal of Infectious Diseases* 2007; **196**: 522–527.

35. **Kandun IN, *et al.*** Three Indonesian clusters of H5N1 virus infection in 2005. *New England Journal of Medicine* 2006; **355**: 2186–2194.

36. **Kandun IN, *et al.*** Factors associated with case fatality of human H5N1 virus infections in Indonesia: a case series. *Lancet* 2008; **372**: 744–749.