CLINICAL, LABORATORY, AND RADIOLOGIC CHARACTERISTICS OF CONFIRMED AVIAN INFLUENZA (H5N1)

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Abstract. This was a cross sectional study to determine the clinical, laboratory and radiologic characteristics of confirmed avian influenza (AI) (H5N1) infection among children and adults. This study was conducted at Sulianti Saroso Infectious Diseases Hospital (SS-IDH), Jakarta among subjects confirmed to have AI infection hospitalized during September 2005 to August 2010. The proportion of confirmed AI patients was 33 out of 321 suspected and probable cases (10.2%). Of 26 subjects analyzed (7 subjects was excluded due to loss of or incomplete medical records), the median ages were 7 years and 25 years in children and adults, respectively (range 1 - 39 years). Prominent clinical features were respiratory symptoms [productive cough (13/13 children; 12/13 adults), dyspnea (12/13 children; 13/13 adults)], and fever (12/13 children; 12/13 adults). Leukopenia was found in 9 subjects in each group. Four children and 7 adults had lymphopenia, while thrombocytopenia was found in 7 children and 10 adults. Two children had an increased ALT, while most adults had an increased AST (10/13) and/or ALT (8/13). Bilateral infiltrates found in most subjects on chest x-ray who had clinical deterioration. Of the 3 children who survived out of 13 children with AI, they all had less severe clinical features and no central nervous system involvement, lymphopenia, thrombocytopenia, or increased creatinine level. None of the adults survived.

Keywords: avian influenza, characteristics, children, adults, Indonesia

INTRODUCTION

The first confirmed human avian influenza (AI) (H5N1) case was reported from Hong Kong in 1997, and since then AI has received a large amount of attention due to its potential to become a global pandemic, such as the Spanish flu pandemic which occurred in 1918 (Yuen *et al*, 1998). The virus is highly species-specific, but in certain conditions can cross the species-barrier and infect humans (Chan, 2002; Wong *et al*, 2006; CDC, 2007). Avian Influenza (H5N1) is usually found in children and young adults, with a high global case fatality rate (CFR) (59.4%) (WHO, 2010). Indonesia has the largest number of human cases worldwide. According to the WHO, as of August 31, 2010, there

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were 168 confirmed human AI cases in Indonesia, with 139 deaths (CFR 82.7%) (WHO, 2010).

The objective of this study was to determine the clinical, laboratory and radiologic characteristics of confirmed AI (H5N1) cases at Sulianti Saroso Infectious Diseases Hospital (SS-IDH), Jakarta, Indonesia during 2005-2010. We also analyzed the characteristics of pediatric patients based on the outcome (survive or death), in order to discover prognostic factors related to mortality (Yuen *et al*, 1998; Apisarnthanarak *et al*, 2004).

MATERIALS AND METHODS

We conducted a cross sectional study using data obtained retrospectively from the SS-IDH medical records between September 2005 and August 2010. The inclusion criterion was a confirmed AI (H5N1) patient referred to SS-IDH; the exclusion criterion was a loss of or incomplete medical records. For each confirmed case that fulfilled the inclusion criterion, we collected standardized information from their medical records, which included demographic, clinical, laboratory, and radiologic characteristics of patients on admission and during hospitalization. This study has been approved by the ethic committees of the Medical School of the University of Indonesia and Sulianti Saroso Infectious Diseases Hospital, Jakarta, Indonesia.

A confirmed AI (H5N1) case was defined as a subject who fulfilled the suspected or probable criteria of infection and whose infection was validated by a positive reverse transcription-polymerase chain reaction for H5N1 performed at the WHO-approved reference laboratory of the National Institute of Health Research and Development in Jakarta (Indonesian Pediatic Society, 2005; Directorate General of Medical Services, 2007; Soepandi *et al*, 2010). Children was defined as subjects aged 0-18 years old at the time of diagnosis (Wiradisuria, 2005).

Leukopenia was defined as a leukocyte count below the cut-off point for age (1-12 months: <5,000/µl; 1-4 years: <6,000/µl; 4-8 years: <5,500/µl; >8 years: <4,500/µl). Lymphopenia was defined as an absolute lymphocyte count <1,500/µl. Thrombocytopenia was defined as a thrombocyte count <150,000/µl (Pesce, 2007).

Delayed antiviral therapy was defined as oseltamivir given >48 hours after the onset of symptoms (WHO, 2007). Acute respiratory distress syndrome (ARDS) was defined as a ratio of PaO_2(kPa,mmHg)/FiO_2<200 (Ware and Matthay, 2000). Acute lung injury (ALI) was defined as ratio of PaO_2(kPa,mmHg)/FiO_2 of 200-300 (Ware and Matthay, 2000). Liver dysfunction was defined as a total serum bilirubin ≥4 mg/dl or an ALT ≥2 times the upper limit of normal (Goldstein *et al*, 2005; Pesce, 2007). Renal dysfunction was defined as a serum creatinine greater than the cut-off point for age (7 days - 12 months: ≥1.59 mg/dl; 1-11 years: ≥1.13 mg/dl; >11 years: ≥1.59 mg/dl) (Leuteurtre *et al*, 1999, 2003). Multiple organ dysfunction syndrome (MODS) was defined as dysfunction of ≥2 organ systems (Goldstein *et al*, 2005). Pneumonia was defined as fever, dyspnea, and more than one of the following respiratory symptoms: tachypnea, cough, nasal flaring, retractions, ronchi or decreased breath sounds (Said, 2008).

Direct contact history was defined as direct contact with sick or dead poultry during the incubation period (Giriputro *et al*, 2008). Indirect contact history was

Table 1
Demographic characteristics of confirmed AI cases.

Characteristics	Children (0-18 years) *N*=13	Adults (>18 years) *N*=13
Median age (range in years)	7 (1.7 - 16)	25 (20 - 39)
Sex ratio (male : female)	8:5	5:8
Contact history		
Direct	3	1
Indirect	9	4
None	1	8
Living area (province)		
DKI Jakarta	5	7
West Java	5	4
Banten	3	2

defined as contact with contaminated environments, including fertilizer or an animal market (Giriputro *et al*, 2008). Radiologic findings were defined by chest radiograph abnormality: unilateral infiltrates were referred to as infiltrates found in one hemithorax, bilateral infiltrates were referred to as infiltrates located in both hemithoraxes, extensive bilateral infiltrates were referred to as infiltrates found in both hemithoraxes comprising ≥50% of the lung. Extensive consolidation was referred to as consolidation in ≥50% of the lung area (Soepandi *et al*, 2010).

All data were analyzed using Statistical Package for the Social Sciences version 17.0 for windows PC (SPSS, Chicago, IL). The unpaired *t*-test was used to compare numerical variables with normal distribution, while data with abnormal distribution were compared using the Mann-Whitney test. The Pearson chi-square test or Fisher exact test were used to compare categorical variables.

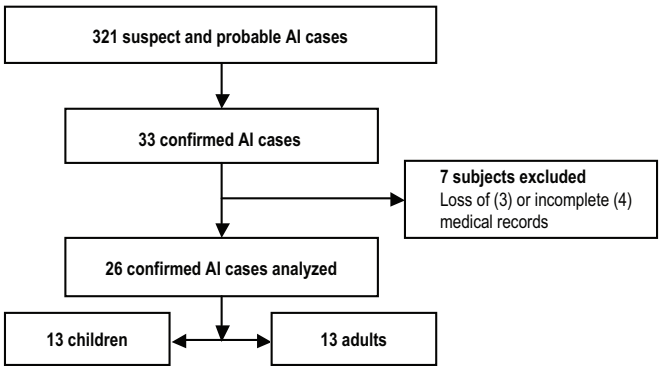

Fig 1–Subject flow chart.

RESULTS

Patients

During September 2005-August 2010, there were 33 confirmed AI cases out of 321 suspect and probable cases (10.2%) managed at SS-IDH. Seven subjects were excluded due to loss of or incomplete medical records, so the final analysis was of 26 subjects (Fig 1).

Of the 26 subjects (Table 1), the ratio of children to adults was 1:1. The median ages were 7 years and 25 years in children

Table 2
Clinical characteristics of confirmed AI cases.

Clinical characteristics	Total (*N*=26)	Children (*N*=13)	Adults (*N*=13)	*p*-value
Respiratory manifestations				
Productive cough[a]				
On admission	22	11	11	1.000
During hospitalization	25	13	12	1.000
Rhinorhea[a]				
On admission	4	3	1	0.593
During hospitalization	6	4	2	0.645
Sore throat[a]				
On admission	3	2	1	1.000
During hospitalization	5	2	3	1.000
Dyspnea[a]				
On admission	19	10	9	1.000
During hospitalization	25	12	13	1.000
CNS manifestations				
Seizures[a]				
On admission	1	1	0	1.000
During hospitalization	2	1	1	1.000
Decreased conciousness[a]				
On admission	4	2	2	1.000
During hospitalization	10	4	6	0.420
Headache[a]				
On admission	3	1	2	1.000
During hospitalization	4	1	3	0.593
Gastrointestinal manifestations				
Vomiting[a]				
On admission	2	2	0	0.480
During hospitalization	7	5	2	0.378
Diarrhea[a]				
On admission	1	1	0	1.000
During hospitalization	5	1	4	0.322
Abdominal pain				
On admission	0	0	0	NA
During hospitalization[a]	2	1	1	1.000
Other manifestations				
Fever[a]				
On admission	10	7	3	0.226
During hospitalization	24	12	12	1.000
Fatique				
On admission[a]	12	6	6	1.000
During hospitalization[b]	13	7	6	0.695
Rash[a]				
On admission	1	1	0	1.000
During hospitalization	1	1	0	1.000
Mucosal bleeding				
On admission	0	0	0	NA
During hospitalization[a]	3	1	2	1.000
Complications				
ARDS[b]	16	9	7	0.420
ALI[a]	6	1	5	0.160
MODS[a]	13	5	8	0.239
Outcome				
Death[a]	23	10	13	0.220

CNS, central nervous system; ARDS, acute respiratory distress syndrome; ALI, acute lung injury; MODS, multiple organ dysfunction syndrome; NA, not analyzed; [a]*p*-value using Fisher exact test; [b]*p*-value using Pearson chi-square test.

Table 3
Laboratory characteristics of confirmed AI cases.

	Children (0-18 years) *N*=13	Adults (>18 years) *N*=13	*p*-value
Hemoglobin (g/dl) [a]	11.8 (SD 1.80)	14.1 (SD 1.85)	0.040
Hematocrit (%) [a]	35.6 (SD 5.03)	41.5 (SD 5.15)	0.007
Leukocytes ($x10^3$)(/µl) [b]	3.80 (1.90 - 31.70)	4.34 (1.00 - 11.00)	0.397
Thrombocytes ($x10^3$)(/µl) [b]	141 (106 - 436)	128 (49 - 424)	0.124
Absolute lymphocytes (/µl) [b]	1,360 (532 - 3,950)	650 (252 -1,100)	0.021
Peak AST (U/l) [b]	270 (26 - 741)	383 (50 - 1,193)	0.391
Peak ALT(U/l) [b]	65 (10 - 152)	131 (36 - 439)	0.035
Peak BUN level (mg/dl) [b]	36 (17 - 163)	72 (30 - 115)	0.067
Peak creatinine level (mg/dl) [b]	0.88 (0.23 - 2.70)	1.25 (0.99 - 6.21)	0.035

Normal data distribution presented as mean (SD, standard deviation); abnormal data distribution presented as median (range); [a]*p*-value using unpaired *t*-test; [b]*p*-value using Mann-Whitney test.

and adults, respectively (range 1 - 39 years). The contact history was positive for contact with a human AI cases (1 subject), domestic poultry (8 subjects), poultry living nearly (3 subjects) and an egg seller (1 subject).

Clinical, laboratory, and radiologic features

The clinical manifestations of subjects on admission and during hospitalization are shown in Table 2**.** Prominent clinical features among children and adults were: productive cough (13/13 children; 12/13 adults), dyspnea (12/13 children; 13/13 adults) and fever (12/13 children; 12/13 adults). All three survivors were children. Deaths occurred mostly on day 10 (range 6-20 days) after the onset of clinical symptoms.

Laboratory findings of the subjects are shown in Table 3. Using WHO criteria, anemia were found in 7 children and 2 adults. Leukopenia was found in 9 subjects in both groups. Thrombocytopenia was found in 7 children and 10 adults. Lymphopenia was found in 4 children and 7 adults. An elevates AST level was found in 7 children and 10 adults, and an elevated ALT level was found in 8 adults, and 2 children. Postmortem examinations were not performed on any of the subjects.

Table 4 shows the chest radiograph findings; bilateral infiltrates were seen in children and adults. Other findings included bilateral pleural effusions, unilateral infiltrates, consolidation and pneumothoraxes. A CT of the chest was performed in 1 pediatric patient, which revealed consolidation of the right posterior lobe.

There were only 3 survivors, all children. Table 5 shows the characteristics of children by outcome. No lymphopenia, thrombocytopenia, or increased creatinine levels were found in childen who survived. Two out of three survivors had normal radiological fendings. Delayed oseltamivir therapy were not different between the two groups. ARDS was the main cause of death.

The factors associated with mortality are shown in Table 6. No adults survived. Two out of 3 subjects <5 years old died and 8 out of 10 subjects aged 5-18 years died. Sixteen out of 18 subjects with leukopenia

Table 4
Characteristics of chest radiographs among AI confirmed cases.

	Total *N*= 21	Children *N*= 12	Adults *N*= 9	*p*-value
Bilateral pleural effusion[a]				
On admission	4	1	3	0.545
During hospitalization	7	3	4	1.000
Consolidation				
On admission	0	0	0	NA
During hospitalization[a]	1	1	0	1.000
Unilateral infiltrates[a]				
On admission	2	1	1	1.000
During hospitalization	7	3	4	1.000
Bilateral infiltrates				
On admission[a]	8	4	4	1.000
During hospitalization[b]	15	8	7	0.691
Extensive bilateral infiltrates[a]				
On admission	2	1	1	1.000
During hospitalization	14	7	7	1.000
Air bronchogram				
On admission	0	0	0	NA
During hospitalization[a]	2	0	2	0.480
Pneumothorax[a]				
On admission	1	0	1	1.000
During hospitalization	4	1	3	0.593

NA, not analyzed; [a]*p*-value using Fisher exact test; [b]*p*-value using Pearson chi-square test

died, all 11 subjects with lymphopenia died and all 17 subjects with thrombocytopenia died. Twenty-three out of 25 subjects with pneumonia were died. Of the 2 subjects who were given oseltamivir more than 48 hours after the onset of symptems, 1 died and 1 survived.

DISCUSSION

We determined the clinical, laboratory and radiologic finding among confirmed AI cases at SS-IDH, Jakarta, Indonesia, during 2005-2010. The most prominent clinical feature among subjects was respiratory symptoms, *ie*, productive cough and dyspnea, both in children and adults. Fever was also noted in 24 out of 26 subjects. These findings are similar to previous studies (Hien *et al*, 2004; Chotpitayasunondh *et al*, 2005; Soepandi *et al*, 2010). The first study to present the clinical spectrum, natural history and complications of AI infection in humans was by Yuen *et al* (1998), they noted respiratory symptoms as the chief complaint in most cases. The lack of pathognomonic signs and symptoms makes the diagnosis of AI difficult to established (Wong *et al*, 2006). Respiratory symptoms are the most prominent clinical manifestation in early stages of the disease. These might be explained by postmortem examination in Hong Kong, which showed early

Table 5
Comparison of characteristics among children with AI by outcome.

Characteristics	Survived (*N*=3)	Died (*N*=10)
Median age (range in years)	6.3 (3-9)	8 (1.7-16)
Sex ratio (M:F)	2:1	3:2
Clinical features during hospitalization		
Respiratory manifestations		
Productive cough	3	10
Rhinorrhea	-	4
Sore throat	1	1
Dyspnea	2	10
CNS manifestations		
Seizure	-	1
Decreased consciousness	-	4
Headache	-	1
Gastrointestinal manifestations		
Vomiting	1	4
Diarrhea	-	1
Abdominal pain	-	1
Other symptoms		
Fever	2	10
Fatique	1	6
Rash	-	1
Mucosal bleeding	-	1
Chills	-	1
Loss of appetite	-	1
Laboratory features on admission		
Hemoglobin (g/dl)	12.5 (11.2-13.1)	11.4 (8-15.4)
Hematocrit (%)	38 (33-40)	34 (28-46)
Leukocytes ($x10^3$)(/ml)	4.5 (3.8-7.1)	3.7 (1.9-31.7)
Thrombocytes ($x10^3$)(/ml)	262 (192-270)	136 (106-436)
Lymphocytes (/ml)	1,900 (1,775-2,025)	905 (532-3,950)
Peak AST level (U/l)	70 (43-97)	394 (26-741)
Peak ALT level (U/l)	87 (22-152)	65 (10-147)
Peak BUN level (mg/dl)	22.5 (17-28)	52 (17-163)
Peak creatinine level (mg/dl)	0.32 (0.23-0.42)	0.94 (0.70-2.70)
Radiological findings		
Bilateral pleural effusions	-	3
Consolidation	1	-
Unilateral infiltrate	1	2
Bilateral infiltrates	1	7
Extensive bilateral infiltrates	-	7
Pneumothorax	-	1
Therapy		
Oseltamivir (range of day given)	3 (2-8)	8 (5-16)
Complicaions		
ARDS/ALI	-	10
MODS	-	5

M, male; F, female; -, no; ARDS, acute respiratory distress syndrome; ALI, acute lung injury; MODS, multiple-organ dysfunction syndrome.

Table 6
Factors associated with poor outcomes in AI.

		Outcome		Total	*p*-value	RR (95%CI)
		Died	Survive			
Age	Adults	13	0	13	0.220	1.30 (0.96-1.75)
	Children	10	3	13		
Childhood age groups	5-18 years	8	2	10	1.000	1.20 (0.51-2.83)
	<5 years	2	1	3		
Pneumonia	Yes	23	2	25	0.115	
	No	0	1	1		
Leukopenia	Yes	16	2	18	1.000	1.01 (0.74-1.38)
	No	7	1	8		
Lymphopenia	Yes	11	0	11	0.238	1.25 (0.97-1.61)
	No	12	3	15		
Thrombocytopenia	Yes	17	0	17	0.032	1.50 (0.94-2.38)
	No	6	3	9		
Delayed oseltamivir use	Yes	21	2	23	0.230	1.83 (0.45-7.34)
	No	1	1	2		

p-value using the Fisher exact test

viral replication was isolated to the lungs (To *et al*, 2001). For clinicians, especially in endemic areas, it is crucial to obtain information about contact history when encountering patients with respiratory tract infections, even though, other studies have reported atypical AI infections among humans, presenting as diarrhea and encephalopathy without respiratory symptoms (Apisarnthanarak *et al*, 2004; De Jong *et al*, 2005; Wong *et al*, 2006).

Gastrointestinal symptoms were noted in our study: vomiting was seen in 5 children and 2 adults also diarrhea was seen in 1 child and 4 adults. Hien *et al* (2004) found diarrhea was the most reported symptom among their 8 pediatric patients. Diarrhea was also reported in one child from Thailand, whose RT-PCR test detected RNA virus in the lungs, colon and spleen with isolated replication in the lungs and colon (Chokephaibulkit *et al*, 2005). Central nervous system (CNS) involvement was also reported in this study. Previous studies rarely described CNS involvement, but some studies have reported seizures, psychosis, stupor and coma (Steininger *et al*, 2003; Maricich *et al*, 2004; De Jong *et al*, 2005). One study suggested influenza infections can precipitate seizures in children, complicated by encephalitis, which is rare; its pathogenesis is not fully understood (Studahl, 2003).

Avian influenza (H5N1) patients usually developed rapid clinical deterioration and fatal outcomes. In this study, deaths were mostly due to ARDS, which usually occured on day 7 (range 2-11 days). Another study reported ARDS happened on day 6 (range 4-13 days) (Chotpitayasunondh *et al*, 2005). ARDS survival rates have been 60-85%, but ARDS caused by AI infections has a poorer survival rate (43%) (Ware and Matthay, 2000; Johnson, n.d.).

Previous studies have concluded that laboratory findings with AI infection

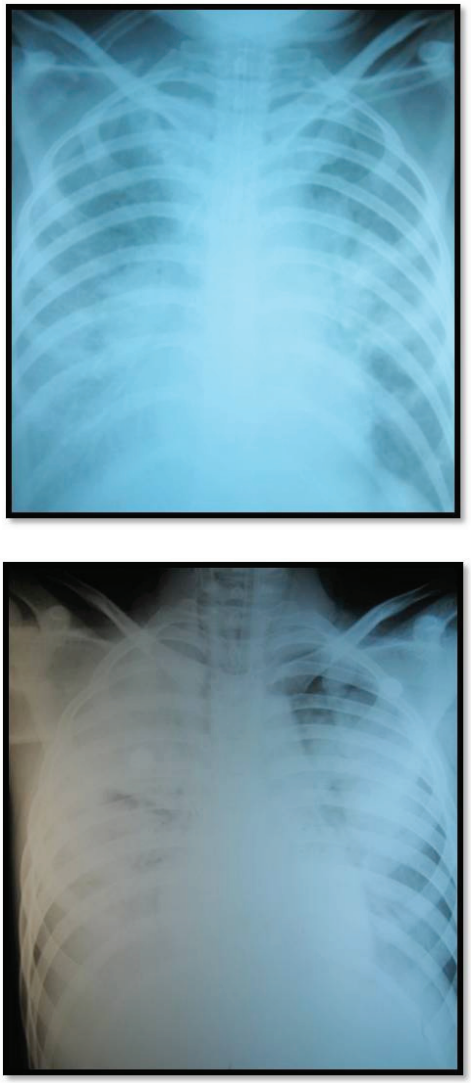

Fig 2–Chest radiograph of AI patients showing extensive bilateral infiltrates.

include leukopenia, lymphopenia, thrombocytopenia, elevated aminotransferases, and elevated creatinine levels (Yuen *et al*, 1998; Chan, 2002; Hien *et al*, 2004; Oner *et al*, 2006; The Writing Committee of WHO, 2005). In this study, all subjects with lymphopenia or thrombocytopenia died. These findings are similar to a study from Thailand, which reported increased mortality related to leukopenia, thrombocytopenia, and lymphopenia on admission (Chotpitayasunondh *et al*, 2005). An elevated of AST level was seen more frequently than an elevated ALT level among our pediatric subjects, similar to a study by Oner *et al* (2006).

Hematologic abnormalities have been related to ARDS and death (Wong *et al*, 2006). In severe cases, pancytopenia, prolonged clotting time and an elevated aminotransferase level usually were noted before respiratory failure (Chan, 2002). These conditions are due to hypercytokinemia resulting in reactive hemophagocytic syndrome (To *et al*, 2001). A previous study reported a correlation between lymphopenia, high levels of chemokine and cytokine with high viral levels in the respiratory tract (De Jong *et al*, 2006).

Most subjects in this study had radiologic abnormalities, only two survivors had normal radiologic findings. Bilateral infiltrates were frequently found among children and adults; these progressed to extensive bilateral infiltrates in 14 out of 21 subjects. Pleural effusions have been rarely reported in other studies, some studies described them as being more common among adults (Yuen *et al*, 1998; Hien *et al*, 2004). In this study, right lower lobe consolidation was found in 1 child, similar to a previous study, which reported consolidation mostly appeared in the lower lobes (Yuen *et al*, 1998). A pneumothorax was found in 1 child and 2 adults in this study, which was related to a mechanical ventilator, similar to other studies (Hien *et al*, 2004; Chotpitayasunondh *et al*, 2005). Qureshi *et al* (2006) found multifocal consolidation and pneumothorax among AI patients are associated with a higher mortality; however, our study found nonspecific radiological

finding were related to higher mortality.

All 3 survivors were children, so in order to identified prognostic factors, we compared characteristics between surviving and non-surviving children. On average, death occurred 9 days after the onset of symptoms (range 6-20 days). All survivors has respiratory symptoms as their chief complaint and had a less severe clinical manifestation. Central nervous system (CNS) involvement (seizures, decreased consciousness, headache) occurred only in non-surviving children. According to Chiu *et al* (2001), 19.5% of patients hospitalized due to influenza A infections have seizures. This is greater than the percentages of patients hospitalized due to influenza B, parainfluenza, adenovirus and respiratory-syncytial virus (RSV) combined. The pathogenesis of this is still unknown, but Chiu *et al* (2001), Morshima *et al* (2002) and Studahl *et al* (2003) found a novel amino acid substitution on influenza A hemagglutinin, which might contribute to the viral tropism of the CNS, which then causes encephalitis or encephalopathy.

Although no specific radiological features were associated with higher mortality, all subjects with bilateral pleural effusions died, while one subject with pulmonary consolidation had clinical improvement and was discharged. Soepandi *et al* (2010) previously reported consolidation of the middle lobe and bronchial dilatation which had partial resolution on serial CT-scans along with clinical improvement.

Of the 26 subjects analyzed, 2 out of 3 subjects aged <5 years died and 8 out of 10 subjects aged 5-18 years and all adults died. It appears older subjects had a higher mortality rate. Previous studies, also found patients aged <5 years had less severe clinical manifestations than older patients (Yuen *et al*, 1998; Steininger *et al*, 2003; Kandun *et al*, 2006). No theory explains this phenomenon. Our hypothesis is antigenic shift produced a novel, alien influenza subtype. When this virus infects humans, it triggers an exaggerated, fatal immune response by the host (Rouphael *et al*, 2007). Avian influenza infection can induce cytotoxic Th1 and activate macrophages to proliferate T-cells and natural killer (NK) cells, which is followed by release of proinflammatory mediators (TNF-α, IL-6, oxygen free radicals, coagulation factors) (Kandun *et al*, 2006; Petrosino, 2007). A complete or advanced immune system has not yet been established in children <5 years old, which makes the immune response less fatal to the host, in contrast to immunocompetent adults who develop a cytokine storm (Petrosino, 2007).

Leukopenia, lymphopenia, thrombocytopenia, and pneumonia are often found among AI patients. In this study, death occurred in 16 out of 18 leukopenia subjects, and 7 out of 8 subjects without leukopenia. Lymphopenia was found in 11 subjects, and thrombocytopenia was found in 17 subjects, all of whom died. These findings confirm previous studies that found lymphopenia, thrombocytopenia and increased aminotransferase level were poor prognostic factors in AI infection (Yuen *et al*, 1998; Chan, 2002; Hien *et al*, 2004; The Writing Committee of WHO, 2005; Oner *et al*, 2006). Pneumonia occurred in 25 subjects, of whom 23 died. In this study, 95% confidence intervals for relative risk (RR) for all independent variables exceeded 1, which means none of these variables could be established as prognostic factors. However, observing the trends shows subjects of adult age, lymphopenia, thrombocytopenia, and pneumonia tended to have increased

mortality.

Previous studies found giving oseltamivir within the first 48 hours of onset of symptoms resulted in increased survival (Welliver *et al*, 2001; Hayden *et al*, 2004; Oner *et al*, 2006; WHO, 2007; Kandun *et al*, 2008; Adisasmito, 2010). Twenty-three out of 26 subjects in this study had a delay in being giving oseltamivir, and 21 out of 23 of these subjects died. Only 2 subjects were given oseltamivir promptly; 1 lived and 1 died due to ALI and MODS. Complications, such as ARDS, ALI and MODS, only occurred in fatal cases. Ware and Matthay (2000) stated accelerated proliferation of type-2 alveolar cells was crucial for resolution of ARDS. These may explain the reason for low survival in ARDS due to AI infection, since α-2,3 sialic acid receptors are mainly found in type-2 alveolar cells (Ware and Matthay, 2000; Cerna *et al*, 2002). The small sample size limits this study, which made correlations between variables and outcomes impossible to determine. Information obtained from this study could be used as preliminary data for other studies or as a hypothesis-generating study.

In conclusion, there were no differences in clinical, laboratory or radiologic findings among confirmed AI cases between children and adults. Prominent clinical features were respiratory symptoms (productive cough and dyspnea) and fever. Laboratory findings included leukopenia, lymphopenia, thrombocytopenia, and elevated aminotransferase levels (mainly AST). The main radiological findings were bilateral infiltrates, which extensively deteriorated in most cases suggesting severe pneumonia. Patients who were adults, had lymphopenia, thrombocytopenia, or pneumonia tended to have higher mortality.

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