3

# FINAL REPORT

## Hospital-Based Surveillance of Severe Acute Respiratory Infections at Tangerang District Hospital

Tintin Martini/ Dewi Lokida

KEMENTERIAN KESEHATAN RI.
BADAN PENELITIAN DAN PENGEMBANGAN KESEHATAN
PUSAT BIOMEDIS DAN TEKNOLOGI DASAR KESEHATAN
JL. PERCETAKAN NEGARA NO. 23, JAKARTA 10560
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## STUDY TEAM

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|---|---|
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# KEMENTERIAN KESEHATAN RI
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**KEPUTUSAN**
**KEPALA PUSAT BIOMEDIS DAN TEKNOLOGI DASAR KESEHATAN**
**NOMOR: HK.03.05/III/2040/2012**

**TENTANG**

**PEMBENTUKAN TIM PELAKSANA PENELITIAN TAHUN 2012**
***DEVELOP CAPACITY BUILDING ON-SITE HOSPITAL BASE SEVERE ACUTE RESPIRATORY INFECTION (SARI) SURVEILANCE (MONITORING SARI PATIENTS).***

**KEPALA PUSAT BIOMEDIS DAN TEKNOLOGI DASAR KESEHATAN**

**Menimbang** :

a. bahwa untuk melaksanakan penelitian *Develop Capacity Building on-Site Hospital Base Severe Acute Respiratory Infection (SARI) Surveilance (Monitoring SARI Patients)*, dengan tujuan membentuk surveilans epidemiologi dan bakteriologi dan *Severe Acute Respiratory Infection* (SARI) di Indonesia, perlu dibentuk Tim Pelaksana Penelitian tahun 2012;

b. bahwa berdasarkan pertimbangan huruf a tersebut di atas, maka dipandang perlu menetapkan Keputusan Kepala Pusat Biomedis dan Teknologi Dasar Kesehatan tentang Pembentukan Tim Pelaksana Penelitian Tahun 2012;

**Mengingat** :

1. Undang-Undang Nomor 23 Tahun 1992 tentang Kesehatan (Lembaran Negara RI Tahun 1992 No. 100, Tambahan Lembaran Negara RI No. 3495);
2. Undang-Undang No. 4 Tahun 1984 tentang Wabah Penyakit Menular (Lembaran Negara RI Tahun 1984 No. 20, Tambahan Lembaran Negara RI No. 3273);
3. Undang-undang Nomor 36 Tahun 2009 tentang Kesehatan (Lembaran Negara RI Tahun 2009 No. 144, Tambahan Lembaran Negara RI No. 5063);
4. Peraturan Pemerintah RI No. 39 Tahun 1995 tentang Penelitian dan Pengembangan Kesehatan (Lembaran Negara Tahun 1995 No. 67, Tambahan Lembaran Negara No. 3605);
5. Peraturan Menteri Kesehatan RI No.657/Menkes/Per/VIII/2009 tentang Pengiriman dan Penggunaan Spesimen Klinik, Materi Biologik dan Muatan Informasinya.
6. Peraturan Menteri Kesehatan RI No.503/Menkes/Per/VIII/2009 tentang Jejaring Lab. Diagnosa Penyakit Infeksi New Emerging dan Re-Emerging.
7. Peraturan Menteri Kesehatan No. 1144/Menkes/Per/VIII/2010 tentang Organisasi dan Tata Kerja Kementerian Kesehatan;
8. Keputusan Menteri Kesehatan No. 1116/Menkes/SK/VIII/2003 tentang Pedoman Penyelenggaraan Sistem Surveilans Epidemiologi Kesehatan;
9. Keputusan Menteri Kesehatan No. 1479/Menkes/SK/X/2003 tentang Pedoman Penyelenggaraan Sistem Surveilans Epidemiologi Penyakit Menular dan Tidak Menular Terpadu;
10. Keputusan Menteri Kesehatan No. 535/Menkes/SK/IX/2006 tentang Pedoman Kesehatan dan Keamanan Lab Mikrobiologik dan Biomedik;
11. Keputusan Menteri Kesehatan Nomor 731/Menkes/SK/VIII/1999 tentang Koordinasi Penyelenggaraan Penelitian dan Pengembangan Kesehatan;
12. Keputusan Menteri Kesehatan Nomor 1179A/Menkes/SK/X/1999 tentang Kebijakan Nasional Penelitian dan Pengembangan Kesehatan;

# KEMENTERIAN KESEHATAN RI
## BADAN PENELITIAN DAN PENGEMBANGAN KESEHATAN
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MEMUTUSKAN

MENETAPKAN :

KESATU : Membentuk Tim Pelaksana Penelitian *Surveillance of Severe Acute Respiratory Infections in Three District Hospitals in Three Provinces* (Banten, West Java and DKI Jakarta), dengan Susunan Tim sebagaimana tercantum dalam lampiran keputusan ini;

KEDUA : Tim Pelaksana Penelitian *Surveillance of Severe Acute Respiratory Infections in Three District Hospitals in Three Provinces* (Banten, West Java and DKI Jakarta) mempunyai tugas sebagai berikut :

1) Melaksanakan Penelitian *Surveillance of Severe Acute Respiratory Infections in Three District Hospitals in Three Provinces* (Banten, West Java and DKI Jakarta);
2) Menyusun laporan kemajuan/triwulan ; elitian *Surveillance of Severe Acute Respiratory Infections in Three Di ct Hospitals in Three Provinces* (Banten, West Java and DKI Jakarta) secara berkala, dan menyampaikan kepada Kepala Pusat Biomedis dan Teknol Dasar Kesehatan;
3) Menyusun Laporan Akhir Penelitian *Surveil of Severe Acute Respiratory Infections in Three District Hospitals in Th rovinces*,

KETIGA : Dalam melaksanakan tugasnya, Tim Pelaksana elitian *Surveillance of Severe Acute Respiratory Infections in Three District Hospitals in Three Provinces* (Banten, West Java and DKI Jakarta) bertang ngjawab kepada Kepala Pusat Biomedis dan Teknologi Dasar Kesehatan ser wajib menyampaikan laporan kemajuan/triwulan dan laporan akhir penelitian secara pertanggungjawaban pelaksanaan kegiatan;

KEEMPAT : Biaya pelaksanaan penelitian dibebankan pada Bantuan Luar Negeri – WHO dengan Reg. File : INS-2012-CB-DFC-3018;

KELIMA : Keputusan ini mulai berlaku sejak tanggal 1 April s.d. 31 Desember 2012, dengan ketentuan apabila dikemudian hari ternyata terdapat kekeliruan dalam penetapan ini akan diadakan perbaikan dan perubahan sebagaimana mestinya.

Ditetapkan di Jakarta
Pada tanggal 2 April 2012

Kepala,

Drs. Ondri Dwi Sampurno, M.Si.Act
NIP 19621112 198803 1001

# KEMENTERIAN KESEHATAN RI
## BADAN PENELITIAN DAN PENGEMBANGAN KESEHATAN
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Lampiran : Keputusan Kepala Pusat Biomedis dan Teknologi Dasar Kesehatan.
Nomor : HK.03.05/III/2040/2012
Tanggal : 2 April 2012

**PEMBENTUKAN TIM PELAKSANA PENELITIAN TAHUN 2012**

**DEVELOP CAPACITY BUILDING ON-SITE HOSPITAL BASE SEVERE ACUTE RESPIRATORY INFECTION (SARI) SURVEILLANCE (MONITORING SARI PATIENTS).**

| | | | |
|---|---|---|---|
| 1. | dr. Titin Martini, Sp.P | : | Peneliti/Ketua Pelaksana Penelitian |
| 2. | dr. Bowi Lokida, SpPK | : | Peneliti |
| 3. | dr. Ujiani Edi P., Sp.A | | Peneliti |
| 4. | dr. Fantientina Panjaitan, Sp.A | | Peneliti |
| 5. | dr. Khumaedi, Sp.A | : | Peneliti |
| 6. | Ariani Intan, Sp PD | : | Peneliti |
| 7. | Siti Napsiah | : | Pembantu Peneliti |
| 8. | Sukismiyati | : | Pembantu Peneliti |
| 9. | Martina | : | Pembantu Peneliti |

Kepala,

Drs. Ondri Dwi Sampurno, M.Si ,Apt
NIP 19621119 198803 100 1

# KEMENTERIAN KESEHATAN RI
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Lampiran 2
Keputusan Kepala Pusat Biomedis dan Teknologi Dasar Kesehatan
Nomor : HK.03.05/III/2040/2012
Tanggal : 2 April 2012

JUDUL PENELITIAN : DEVELOP CAPACITY BUILDING ON-SITE HOSPITAL BASE SEVERE ACUTE RESPIRATORY INFECTION (SARI) SURVEILANCE (MONITORING SARI PATIENTS).

JUMLAH HONOR TIM PELAKSANA PENELITIAN TAHUN 2012

| | | | | |
|---|---|---|---|---|
| 1. | Peneliti | : Jumlah honor yang diterima per-jam, per-minggu sebesar | =Rp. | 30.000 |
| 2. | Pembantu Peneliti | : Jumlah honor yang diterima per-jam, per-minggu sebesar | =Rp. | 20.000 |

Kepala,

Drs. Ondri Dwi Sampurno, M.Si., Apt
NIP 19521119 198803 100 1

# FOREWORDS

This study has been conducted at Tangerang District Hospital from April to December 2012. The study activity aims to conduct a hospital-based surveillance of adults and children who are hospitalized for severe acute respiratory infections (SARI). The results is to better understand spectrum of clinical features, etiologies, severity of illness and risk factors in a district hospital in Indonesia.

The project is being supported through a combination of grants from the WHO (funding source USAID) and the REDI Center (funding source MOH Singapore). Appreciation is extended for the laboratory support from National Insitute of Health Research and Development. A special thank you is extended to Regional Emerging Disease Intervention (REDI) Center in Singapore for its support in the protocol development process, the study implementation, until the final report writing.

# Contents

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## FIGURE

## *I.* BACKGROUND

A hospital-based surveillance of children and adults hospitalized for severe acute respiratory infections (SARI) to better understand spectrum of clinical features, including severity of illness, etiologies and risk factors for severe disease and mortality in a district hospital in Indonesia has been conducted.

Eligible children and adults who are hospitalized will be enrolled, with informed consent, if they meet the study case definition, over a period of one year. Lab specimens will be collected and analyzed to determine viral and microbial pathogens, and clinical management and outcomes will be recorded during hospitalization and at discharge. Data from this initial phase will help to better understand the scope and extent of the problem of severe acute respiratory infections in this district hospital. This will in turn contribute to identify and develop strategies and interventions, as well as inform the design and feasibility of subsequent studies to implement and evaluate these strategies in the future.

Ultimately, the long-range goal of this project is to improve outcomes in patients with severe acute respiratory infection through accurate case management and appropriate integration of clinical surveillance and laboratory diagnosis. This is line with national and global recommendations to address the burden posed by severe acute respiratory infections on populations and health systems, particularly in high burden countries such as Indonesia[1] [2].

## *II.* LITERATURE RESEARCH

**Burden and affected populations:** Despite major advances in prevention, care and treatment of infectious diseases, they remain a major cause of mortality and morbidity globally, particularly those of the respiratory and gastrointestinal tract. Acute respiratory infections are estimated to cause 4.2 million deaths annually – almost all due to lower respiratory infections, mostly pneumonia[3]. Most of these occur in children, the elderly and immune-compromised individuals.

Almost half of the deaths occur in children under 5 years. Although lower income countries are disproportionately affected, acute respiratory infections are among the top

five leading causes of death, regardless of country income level. In addition, it is also the leading cause of morbidity in developing countries as measured by years lost due to disease or disability-adjusted life-years (DALY), accounting for 94.5 million DALYs[3].

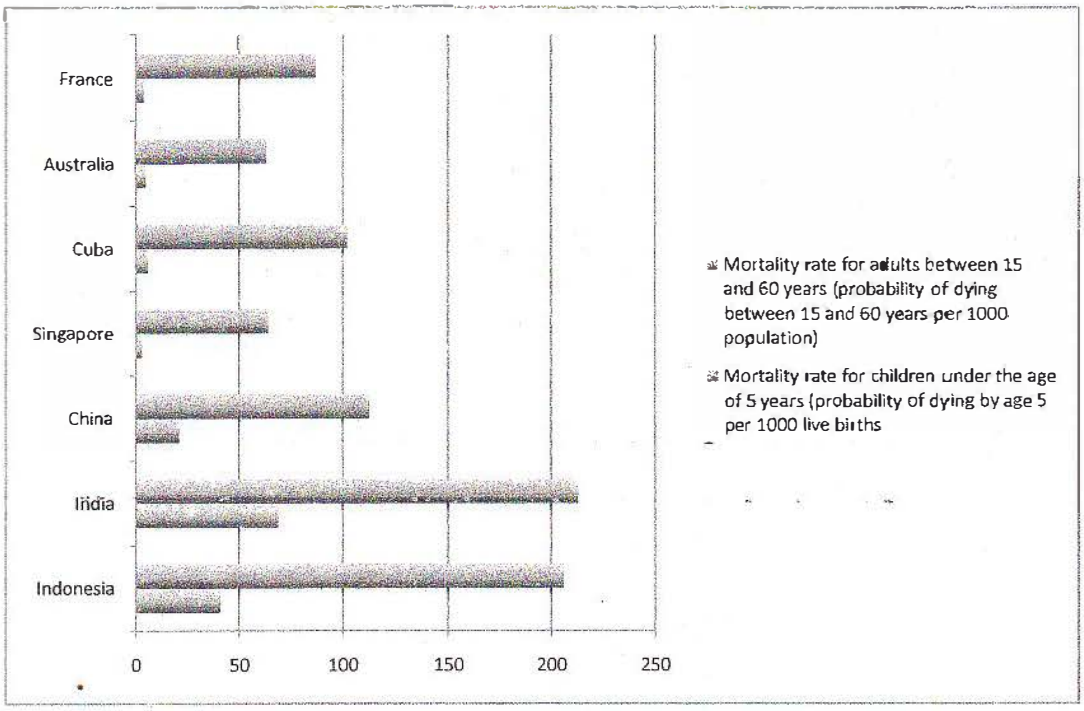


**Figure 7. Comparison of mortality rates for children under the age of 5 years and adults between 15 and 60 years for Indonesia and selected countries. WHO 2008 (World Health Statistics, WHO 2010)[4]**

Despite remarkable progress in terms of economic development and advancement in the last decade, Indonesia continues to struggle with a high infectious disease burden and higher mortality rates compared to more populous or prosperous neighbors and countries[4] (Figure 1).

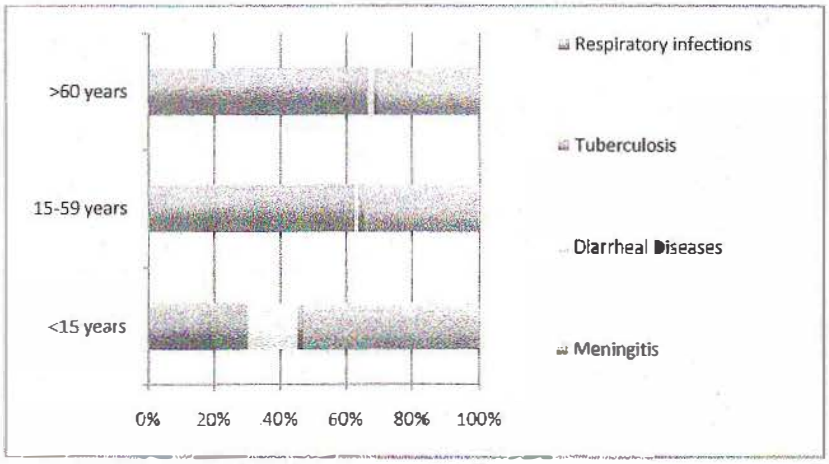


**Figure 8. Distribution of total mortality due to select infectious diseases in Indonesia, WHO 2008[4]**

A significant proportion of this mortality is due to preventable infectious diseases. In fact, respiratory infections (mostly lower tract infections) and tuberculosis account for more than half the total mortality due to infectious diseases in adults and up to a third of total mortality due to infectious diseases in children under the age of 15 years (Figure 2).

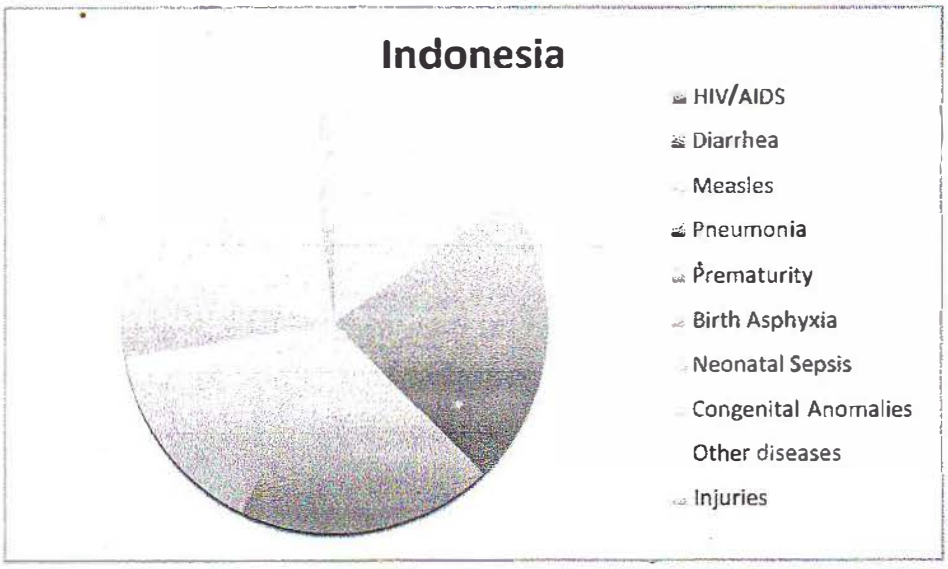


**Figure 9. Distribution of causes of mortality for children under five years in Indonesia. (World Health Statistics 2010)[4]**

For children under 5 years in Indonesia, about 1 in five deaths is estimated to be attributable to lower respiratory infections (Figure 3). More children in this age group die

from pneumonia and diarrheal diseases in Indonesia than compared to most of its neighbors (Figure 4).

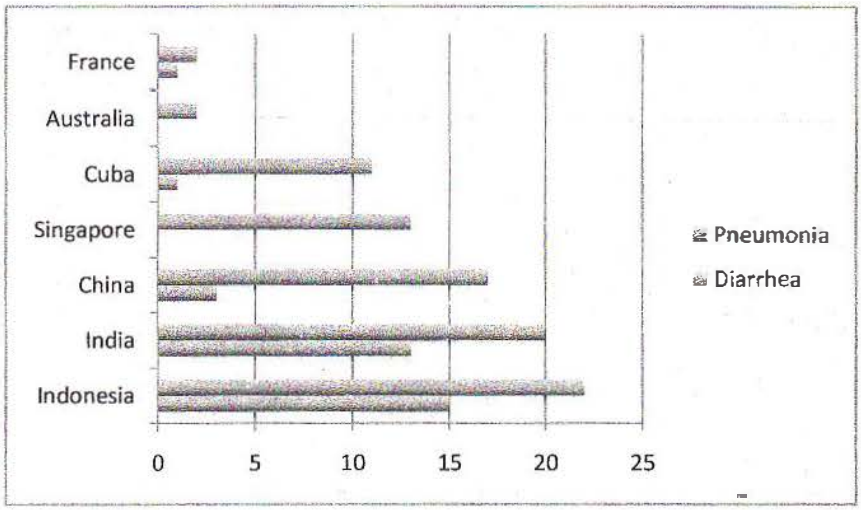


**Figure 10. Comparison of proportions of deaths due to pneumonia and diarrheal diseases in children under 5 years for Indonesia and selected countries. WHO 2008 (World Health Statistics 2010)[4]**

The Ministry of Health has reported that pneumonia is the second leading cause of death in children under the age of 5. The Ministry also reports that pneumonia is among the top ten leading causes of hospital admissions and that case fatality rates among hospital admissions is highest for pneumonia than from any other cause (Table 1).[5] Attempts to study risk factors underlying SARI and pneumonia have identified lack or delayed access to health care, poor nutritional status and exposure to environmental pollutants as possible risk factors among others[2].

**Table 2 Leading causes of hospital admissions and case fatality rates, Indonesia, 2010**
**Excerpt from "Profil Kesehatan Indonesia 2010, Indonesia Ministry of Health" [5]**

| Cause of Admission | Number | Deaths | Case Fatality Rate |
|---|---|---|---|
| Diarrhea/Acute Gastroenteritis | 71889 | 1289 | 1.79 |
| Dengue | 59115 | 328 | 0.55 |
| Typhoid/Paratyphoid | 41081 | 274 | 0.67 |
| Pregnancy related conditions | 40636 | 276 | 0.68 |
| Dyspepsia | 24716 | 166 | 0.67 |
| Injuries and trauma | 21733 | 605 | 2.78 |
| Pulmonary hypertension | 19874 | 955 | 4.81 |
| Intracranial hemorrhage | 19381 | 1025 | 5.29 |
| Acute upper respiratory infections | 17918 | 589 | 3.29 |
| Pneumonia | 17311 | 1315 | 7.60 |

Despite the recognition of the burden and efforts to address it, population-based epidemiological data on incidence and prevalence of respiratory infections are not routinely or systematically available in Indonesia, or for most of the high burden areas of Asia and Africa. As part of an effort to better understand the impact of Hib vaccination in Indonesia, a population-based study was conducted in Lombok, Indonesia in the late 1990s[6]. The study, which focused on the target population for vaccination, young children under the age of 2 years, identified 21 episodes per 100 child-years of observation for simple pneumonia, 8.3 per 100 child years for severe pneumonia, and 5.3 per 100 child-years for hospitalized pneumonia similar to studies in Bangladesh recently[7]. ARI-specific mortality rate among children under 2 years of age was 33 per 1,000 live births.

**Pathogens associated with severe acute respiratory infections:**

Determining the etiology of severe acute respiratory infections and pneumonia is challenging even with well-resourced lab capabilities, much less with situations where there is lack of access to rapid and accurate microbiological diagnosis[8,9], much less molecular diagnostics. In any case, identification of an underlying pathogen occurs in only about 25-50% of cases[10]. The more accessible upper tract presents a diagnostic challenge

for bacterial diagnosis as pathogen must be distinguished from commensal or colonizing organisms that are not causing disease. Direct sterile specimens (i.e. pleural effusion) are not always present and may present a technical challenge. Indirect methods, such as blood cultures are also used but often the yield rates of detection are low.

Confidently distinguishing between viral and bacterial aetiologies from clinical presentation alone is often difficult and this is thought to lead to inappropriate prescription of antibiotics[11]. Traditional methods such as viral culture, antigen detection or serology is either too slow or too insensitive to aid clinical diagnosis[12]. Over the recent years, as a result of emerging threats such as SARS, avian and pandemic influenza, the focus on severe acute respiratory infections has intensified, with a high emphasis being placed on the need to detect and identify novel threats and influenza viruses of pandemic potential. The advancement of molecular techniques has also contributed to the increased emphasis on virological diagnosis.

The intense focus on influenza diagnostics in recent years have pushed the development and utilization of more reliable, specific and sensitive PCR methods across laboratories globally. Traditional PCR[13], real-time PCR[14] or PCR combined with Luminex liquid chip hybridization and identification[15] are broadly promoted, particularly those that can detect a large number of viral agents, but the relatively high costs of these assays, challenges in access to reagents and maintenance as well as lack of trained personnel hamper the full application and usefulness of these methods, particularly as an aid to clinical diagnosis. In a recent study, a multiplex real-time PCR was evaluated for the ability and cost of detecting respiratory pathogens in a virology lab of a university hospital in Sweden serving a catchment area of 600,000 inhabitants[16]. The assay, which analyzed for the presence of 10 pathogens detected a pathogen in 457 (48%) out of the 954 specimens analyzed. The following agents were detected (*n, % positives*): Influenza A (n= 114, 25%), Rhinovirus (n=93, 20%), human metapneumovirus (n=46, 10%), RSV (n=41, 9%); adenoviruses OC43 (n=33, 7%), Ad (n=33, 7%), NL63 (n=26, 6%), parainfluenza viruses (n=19, 4%), influenza B (n=4, 1%), enterovirus (n=1) and M. pneumoniae (n=44, 10%). *C. pneumoniae* was found only in 2 specimens. Although the authors argued that the streamlining of procedures allowed for assay runs to be organized and managed so as to keep costs low, the customer price of 33 Euro [divided on reagents for nucleic acid extraction (3 Euro), reagents for real-time PCR (11 Euro), personnel (8 Euro), laboratory space (3 Euro),

instrument cost (1 Euro), and overhead (5 euro)] is out of reach for many developing health systems, including Indonesia.

Figure 5 lists pathogens that are associated with community-acquired pneumonia in children and adults[17 18]. The majority of identified cases in children are bacterial, some related to an underlying viral process such as measles or RSV [17]. Other factors such as malnutrition and immune-compromised states also increase the risk of severe pneumonias. *Streptococcus pneumoniae* and *Haemophilus influenza type b*, are estimated to be responsible for about half of deaths attributed to pneumonia [19 20]. This, along with some evidence that bacterial pneumonias are associated with greater severity and higher case-fatality rates have driven case management initiatives of childhood pneumonias to try to ensure rapid and accurate clinical assessment and access to antibiotic treatment [1].

In recent years, attention has turned towards viral causes of acute lower respiratory infections, most particularly towards influenza viruses. Recently, particularly for developing countries, respiratory syncytial virus (RSV), the causal agent for bronchiolitis, is increasingly recognized as a major cause of morbidity and mortality. A recent systematic review estimated it as the most common cause of acute lower respiratory infections and a major cause of hospital admissions and mortality for children under five years, with almost all deaths estimated to occur in developing countries[21]. These and other viruses also have the potential to cause severe disease in the elderly and patients with an underlying chronic respiratory or cardiac condition.

*Streptococcus pneumonia**
*Haemophilus influenzae* type b (Hib)**
*Staphylococcus aureus*
*Mycoplasma pneumonia*
*Chlamydia pneumonia*
*Legionella pneumophilla*

*Respiratory syncytial virus*
*Rhinovirus*
*Influenza* A, B and C*
*Adenovirus*
*Parainfluenza viruses*
*Human metapneumovirus*
*Enteroviruses*
*Coronaviruses*
*Varicella-zaster viruses**
*Measles**
*Cytomegalovirus*
*Hantavirus*
*Human herpesvirus 6 and 7*
*Herpes simplex virus*
*Mimivirus*
*Bocavirus*
*Parechoviruses*

**Licensed vaccines are available against these organisms*

Figure 11 **Pathogens associated with community-acquired pneumonia in children and adults**

In the recent years, technical assistance and collaboration with various international entities following SARS in 2003 and the threat of pandemic due to a potential human to human

transmission of A/H5N1 influenza virus since end of 2003, have increased efforts for laboratory surveillance targeting primarily influenza viruses. Although such efforts are critical for establishing and strengthening lab capacity, the overwhelming emphasis on influenza has not yielded particularly helpful information for health planners and policy makers locally or internationally. For example, surveillance of nasal and throat swabs collected from patients admitted for SARI in 8 hospitals in 8 provinces in Indonesia over a one year period from April 2008 to March 2009, including Tangerang Hospital to detect influenza A (A/H1N1, A/H3N2 and A/H5N1) and Influenza B, detected influenza in only 6% of the specimens, the most common being A/H3N2[22]. Such studies illustrate the need to make these efforts more relevant to both medical and public health care in order to understand the extent and the relative contribution of not just major pathogens underlying SARI in Indonesia, but also the impact of medical care and risk factors on morbidity and mortality patient outcomes.

*"to scale up essential activities to implement pneumonia prevention and management at all level by:*

- *strengthening case management;*
- *setting up hospital sentinel site to collect information on etiology;*
- *intensifying risk factor surveillance;*
- *routine coordination meeting to link risk factors and the disease."*

**Figure 12 Excerpt from the "Report on Situational Analysis of Acute Respiratory Infections in children in Indonesia, *WHO Indonesia 2009"***

Lack of such information has an impact on the ability of hospital and health care system planners and policy makers to implement evidence-based policies to address the major problems causing significant morbidity and mortality in its populations. For example, lack of such information could act as one of the factors that delay immunization policy decisions for the introduction and deployment of conjugate pneumococcal and Hib vaccines, already decades in routine immunization programs of developed countries.

Before the rise in prominence of influenza on the global health agenda, the persistent burden of acute lower respiratory infections, particularly in children has long been recognized and efforts have been made to try to address it. It has driven the development of initiatives such as Integrated Management of Childhood Illnesses[23] to try to strengthen the ability of primary health care workers to appropriately recognize conditions such as severe pneumonia or dehydration in order that relatively inexpensive yet life-saving measures could be immediately taken. Indonesia in particular presents a potential intersection of many such initiatives. Faced both with the threat of avian and pandemic influenza as well as contributing significantly to the global

burden of pneumonia, Indonesia has been working with numerous global health initiatives to implement measures that address these threats and it faces tremendous challenges in doing so.

The global burden of pneumonia drove WHO to convene major stakeholders to develop a Global Action Plan for the Prevention of Pneumonia (GAPP) in 2008. In many countries, there were attempts to translate this into national plans and as part of this effort, WHO Indonesia commissioned a review of the situation in Indonesia, published in 2009 as the "Report on Situational Analysis of Acute Respiratory Infections in children in Indonesia". Among the major recommendations of the report, which described the ARI burden in Indonesia, were " *to scale up essential activities to implement pneumonia prevention and management at all level by: strengthening case management; setting up hospital sentinel site to collect information on etiology; intensifying risk factor surveillance; routine coordination meeting to link risk factors and the disease.*"

The study rationale is founded on these recommendations, which are based on addressing the burden posed by acute respiratory infections. The rationale recognizes the opportunity to forge a more integrated approach towards managing infectious diseases, where clinical, laboratory and epidemiological components are coordinated in order to ultimately impact health outcomes.

This study is intended to build and expand on previous and ongoing collaborations to strengthen the capacity of the Tangerang District Hospital as the referral hospital for the district and to be ensure its readiness to respond to future epidemics and pandemic situations. An ultimate goal of the investigators is to ensure that its clinical management practices and its diagnostic capacity are ready to respond to the needs of the district, and this study will collect critical information as well as establish essential diagnostic capacities that will contribute to the knowledge needed to achieve this goal. Clinical management practices for treatment of SARI can be compared to the standard operating procedures and recommendations of the hospital and to national and international guidelines for care and treatment of acute respiratory infections[24 25 26].

Data from this study will help to better understand the scope and extent of the problem. This will in turn contribute to identify and develop strategies and potential interventions, as

well as inform the feasibility and the design of subsequent studies to implement and evaluate these strategies in the future.

It is expected that coordinating and communicating hospital data on children and adults who require hospitalization due to severe acute respiratory infections in this study will help to inform future interventions and strategies for prevention and control of pneumonia in this and similar situations in Indonesia and other developing countries.

### *a. Study Setting and Partners*

Since the emergence of avian influenza in Indonesia, there has been intense national and international efforts to control and manage the problem, particularly in areas where there have been human cases. Tangerang District Hospital is located in Banten Province on the west side of Jakarta, which has seen among the highest number of cases and fatalities in the country[27]. It serves as the main Influenza referral hospital for a catchment area comprising 6 million people. More than 40 public and private hospitals and public health clinics in the Province refer patients to the hospital for primary and tertiary care. Strengthening capacity for diagnosis and treatment of avian influenza at the hospital has been a priority of the Trilateral (Indonesia, Singapore & USA) *Pilot Project for Control of Avian Influenza in Tangerang.*

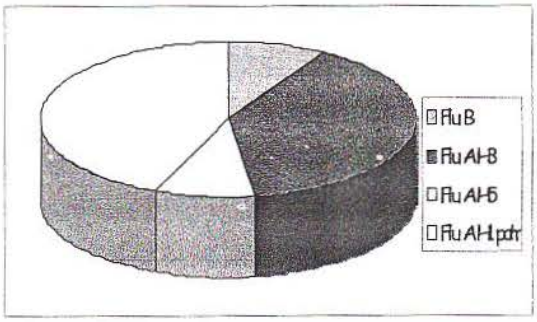


**Figure 7 Distribution of influenza viruses (%) from SARI study at Tangerang Hospital 2008 - 2009**

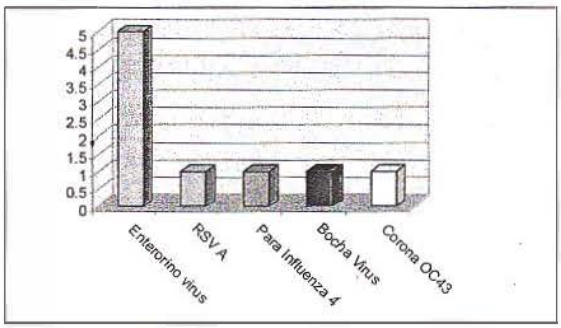


**Figure 8 Distribution of influenza viruses (%) from SARI study at Tangerang Hospital 2008 - 2009**

The Hospital has an Airborne Infectious Disease Team to conduct surveillance and research on acute respiratory diseases and other infectious disease of public health concern. With support from US CDC and WHO the hospital initiated SARI surveillance in 2008 as part of a multi-center study in Indonesia. From December 2008 to December 2009 Tangerang District Hospital enrolled 128 SARI patients. Influenza A/B viruses were

detected in 17 percent and non-influenza viruses in 7 percent of the cases (Figure 6 and 7). Influenza viruses included H5N1, the 2009 pandemic HINI, H3N2 and Influenza B. Bacterial infections were detected in 21 percent of the cases and the distribution of organisms detected is illustrated in Figure 8. However, the study was unable to identify the causative agents in 55% of SARI cases using the available detection methods.

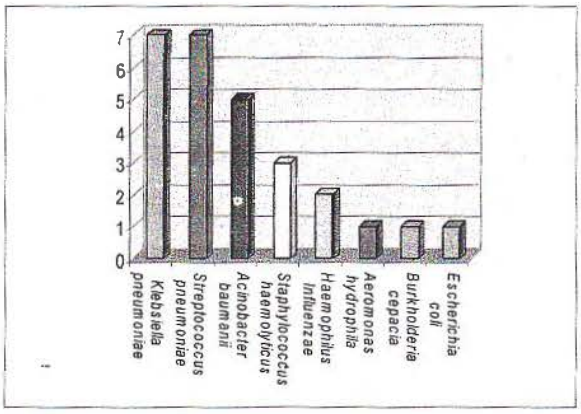


**Figure 9 Distribution of bacterial pathogens from SARI study at Tangerang Hospital 2008 -2009**

REDI Center and Tan Tock Seng Hospital have been collaborating with the team by providing training and technical assistance and resources to develop and implement this project. REDI Center and Singapore MOH have supported training for influenza case management and infection prevention and control for the hospital's doctors and nurses. More intensive training has been provided to the clinical and laboratory staff of the hospital's Airborne Infectious Disease Unit that was dedicated in May 2010. Singapore MOH, REDI Center and the WHO Country Office have provided the Unit with respiratory ventilation and monitoring equipment, laboratory equipment and reagents, and personal protective equipment. The Unit has both laboratory and patient isolation rooms, consisting of both regular and intensive care treatment rooms. With these enhanced capacities the hospital has been increasingly better prepared to respond to challenges of treating severe cases, for example the severe cases of influenza that were admitted during the 2009 HINI pandemic.

## III. OBJECTIVES

1. To describe the etiologies and clinical features of children and adults hospitalized for severe acute respiratory infections in Tangerang Hospital
2. To describe clinical management and outcomes for children and adults hospitalized for severe acute respiratory infections in Tangerang Hospital
3. To assess and compare clinical case management practices for SARI with current available hospital, national and professional recommendations.
4. To detect unusual trends in severe morbidity and mortality, including those that may be caused by unknown, emerging and reemerging bacterial and viral infections that have the potential for large scale epidemics or pandemics
5. To investigate possible risk factors for severe acute respiratory infections through additional epidemiological investigations in the community
6. To determine the extent of antibiotic resistance of the main respiratory pathogens isolated from the study population

## IV. METHODS

### 1. STUDY DESIGN

The study is an observational, non-interventional, prospective study, designed to capture etiological and clinical information about children and adults hospitalized for severe acute respiratory infections in Tangerang Hospital.

### 2. STUDY HOSPITAL, POPULATION AND SAMPLE

#### *a. Study hospital*

Tangerang District Hospital, is located in Banten Province on the west side of Jakarta, which has seen among the highest number of cases and fatalities of avian influenza in the country[28]. It serves as the main Influenza referral hospital for a catchment area comprising 6 million people. More than 40 public and private hospitals and public health clinics in the Province refer patients to the hospital for primary and tertiary care. In the Indonesian hospital system, Tangerang hospital is categorized as a "Type B" hospital with 437 beds. The hospital has 88 beds in general adult ward and 48 beds in the pediatric wards. It also has 8 beds in the ICU for either adult or pediatric patients. The hospital has an airborne infection disease isolation unit with negative pressure and HEPA filter, consisting of 3 ICU beds and 4 regular ward beds.

*b. Inclusion and exclusion Criteria*

All children and adults who fulfill the following criteria were considered eligible for enrollment:

- Inclusion criteria:
  - Hospitalized less than 48 hours
  - Meet the study case definitions for severe acute respiratory infection (Table 4)
  - Patient (or parents in the case of children) agrees to participate in the study

The study has not included the following patients:

- Exclusion criteria:
  - Age one month or less
  - Any circumstances when specimen collection is not possible
  - Patients known with confirmed active pulmonary tuberculosis
  - Patients known as HIV infected
  - Patients receiving steroid treatment or other immunosuppressive therapy
  - Patients with malignancies and other similar conditions

*c. Case definitions*

The study investigators derived the case definitions from on-going SARI surveillance studies which base their case definitions on those of the WHO and US CDC for influenza surveillance.[29] For the study, patients who are eligible will be assessed if they meet the following case definitions in order to be enrolled. Case definition criteria differ between different age groups in children, and between children and adults.

In adults, a case of SARI refers to an acute respiratory illness with onset during the previous 7 days requiring overnight hospitalization that includes history of fever OR measured fever $\geq 38^{\circ}C$ AND cough AND shortness of breath OR difficulty breathing.

In children aged 5-14 years, a case of SARI refers to an acute respiratory illness with onset during the previous 7 days requiring overnight hospitalization that includes history of fever OR measured fever $\geq 38^{\circ}$ C, with or without cough AND shortness of breath (i.e. Head bobbing, Nasal flaring, Chest indrawing/retraction) or difficulty breathing as manifested by any of the following:-

- tachypnea (defined as respiratory rate ≥60 /minute for age < 2 months; ≥50 /minute for age 2 – 12 months; ≥40 /minute age > 1-5 years old)
- grunting, crackles/ronchi, decreased vesicular breath sound, bronchial breath sound AND a positive CXR.

In children aged 1 month to less than 5 years, a case of SARI refers to an acute respiratory illness with onset during the previous 7 days requiring overnight hospitalization with or without cough AND shortness of breath (i.e. Head bobbing, Nasal flaring, Chest indrawing/retraction) or difficulty breathing as manifested by any of the following:-

- tachypnea (defined as respiratory rate ≥60 /minute for age < 2 months; ≥50 /minute for age 2 – 12 months; ≥40 /minute age > 1-5 years old)
- grunting, crackles/ronchi, decreased vesicular breath sound, bronchial breath sound AND a positive CXR.

Table 2 summarizes the case definitions for the study.

Table 2 Study case definitions (Adapted from WHO and US CDC[30])

| Age Categories | Study case definitions |
|---|---|
| < 5 Years Old | Children aged 1 month to 5 years admitted the pediatric ward or ICU:<br>1. With OR without cough<br>2. AND Shortness of breath *(defined as having at least one of the following signs: Head bobbing, Nasal flaring, Chest indrawing/retraction)*<br>3. With OR without any of the following:<br>a. tachypnea (defined as respiratory rate ≥60 /minute for age < 2 months; ≥50 /minute for age 2 – 12 months; ≥40 /minute age > 1-5 years old)<br>*b.* grunting, crackles/ronchi, decreased vesicular breath sound, bronchial breath sound<br>4. Chest x-ray : Consistent with SARI/Pneumonia as diagnosed by Radiologist<br>5. Onset of symptoms less than 7 days |
| Children ages 5-14 years (WHO/CDC combines this category into the >5 years age group) | Children admitted the pediatric ward or ICU<br>1. History of fever or measured fever ≥ 38° C on admission<br>2. With OR without cough<br>3. AND Shortness of breath *(defined as having at least one of the following signs: Head bobbing, Nasal flaring, Chest indrawing/retraction)*<br>4. With OR without any of the following:<br>a. tachypnea (defined as respiratory rate ≥30 /minute for age > 5 years old)<br>*b.* grunting, crackles/ronchi, decreased vesicular breath sound, bronchial breath sound<br>5. Chest x-ray : Consistent with SARI/Pneumonia as diagnosed by radiologist<br>6. Onset of symptoms less than 7 days |
| Adult ≥ 15 years | Adults admitted to the ward or ICU with<br>- History of fever or measured fever ≥ 38° C on admission<br>- Cough, AND<br>- Shortness of breath or difficulty breathing<br>- Onset of symptoms less than 7 days |

*d. Enrollment procedures and sample size*

All hospital admissions, whether they originate from hospital outpatient clinics or are referrals by other hospitals, were processed through the emergency department. The staff of the emergency department were sensitized to the study and made aware of the need to identify eligible patients. "Eligibility cards" has created which had the study inclusion/exclusion criteria printed on them, and was used as reminders and chart covers. These were specially prepared and made available to the physician or nurse who first managed and admitted the patient, to facilitate ease of screening and tracking potential study participants from the emergency department to the ward. The study team ensured that information posters regarding the study, patient eligibility criteria and case definitions are strategically placed in the emergency, outpatient and relevant in-patient areas as easy reminders to hospital staff.

The inclusion cards helped remind the ward nurse or doctor who received the patient for admission to flag the patient for notification to members of the study team to follow-up on the ward. Study nurses and physicians reviewed the charts to ensure eligibility criteria and clinical features were consistent with a suspect case of SARI and therefore enroll eligible patients from the inpatient pediatric and adult wards and ICUs. Eligible patients were enrolled after explaining the study procedures and giving written informed consent by a study physician. A standardized Case Reporting Form (CRF) was filled for each eligible patient. The following on-site investigations has been performed: chest x-ray, sputum smear (for Acid Fast Bacilli detection) and basic blood tests (Complete Blood Count, glucose, ureum, creatinine and transaminases (ALT and AST))

The following information has been collected in the CRF: socio-demographic characteristics (age, gender and area of residence), medical history (including vaccination status), relevant epidemiological history related to risk factors (smoking, exposure to poultry, asthma etc.), clinical findings (including co-existing illnesses, symptoms, examination signs, antibiotics therapy during hospitalization, diagnostic at discharge, follow-up status), and results of the on-site investigations. Based on the reports of previous years, it was estimated that approximately 50 patients were recruited each month. It was then targeted to include 500 patients for the duration of the project (March 2012 – December 2012)

## 3. STUDY PROCEDURES AND EVALUATIONS

- ***Clinical assessment and management***

This assessment and observational stage would not involve any systematic changes or interventions to care and treatment practices used by hospital physician and nurses to determine admission or other routine clinical management. Hospital physicians made clinical assessment and management decisions on severity, treatment, diagnosis and admission according to their routine practice. As guidance, the study investigators distributed reminders regarding the availability of hospital case management recommendations for the management of pneumonia in adults and children (Appendices 4 and 5: Hospital Pneumonia SOP adult and pediatric). The study physicians were not directly involved in the routine admission and case management of patients on a systematic basis.

The ward nurse or physician has screened ward admissions for eligibility and criteria meeting case definition and alert the study physician. The study physician approached eligible patients (and parents for children) to explain and inform them about the study. If after being informed of the study objectives, procedures, potential risks and benefits, the patient or parents agree to take part, written informed consent were obtained by the study physician.

The study nurse and physician interviewed the patient and collected demographic information and medical history, and conducted a physical examination, all according a study questionnaire. The study nurse was ensure that standard request forms for the conduct of study investigations and tests, such as specimen collection for sputum, blood for hematology and biochemistry, blood culture and chest x-ray (if these have not been done prior to enrollment) were completed and liaise with the nursing staff on the ward and follow-up on the conduct and results of these tests. During the hospital admission, study physicians reviewed daily the patient's clinical state and evolution as well as treatment and management practices and document findings in a standard case-report form.

All demographic information as well as information on vaccination status, medical history including illness duration as well as treatment prior to admission, clinical feature at presentation and admission, admitting diagnosis, and all treatment provided at admission

and while hospitalized, duration of hospital stay, and outcome has recorded using a standard case-report form for all enrolled patients

- ***Laboratory evaluations***

Laboratory evaluations included:

- Complete blood count;
- Serum chemistries for glucose, ureum, creatinine, ALT, and AST;
- Sputum from adults for AFB and bacterial culture, blood from children for bacterial culture. Positive cultures were evaluated for antibiotic sensitivity using a standard impregnated disk inhibition method.
- Throat and nasal swabs or nasopharyngeal swabs were obtained for Influenza A and B virus by PCR assays . For other respiratory viruses and some bacterial will be detected by multiplex.
- Detection for other respiratory viruses and some bacterial were done at NIHRD using the Multiplex.
- Influenza virus isolation and serology for influenza A H5 has conducted in conjunction with an ongoing laboratory surveillance study by NIHRD and the US-CDC.

- ***Radiological assessment***

Chest X ray is a criteria of the study case definition. Radiographic findings and diagnosis has been confirmed by the study radiologist. For children,. the CXR will include the posteroanterior (PA) and lateral views. For adult, the CXR only include the posteroanterior (PA)

## 4. *MANAGEMENT OF SAMPLES AND SPECIMENS, INCLUDING STORAGE AND UTILIZATION*

### *1. Sample and specimen collection*

Sample and specimen collection follow hospital standard operating procedures (SOP).

***Adults :***

- Two throat and 2 nasal or nasopharyngeal swabs were taken and put into 6 ml VTM / Hanks transfer media in 1 (one) sterile Falcon tube. The VTM were aliquoted into several sterile cryotubes, 1 tube to be sent to NIHRD (cold chain) for RT-PCR, multiplex (viral) and Influenza viral isolation. All specimens were be kept in -20 °C prior to the lab tests. The remaining tubes were sent to Tangerang hospital laboratory for RT-PCR and keep in -20 °C.

- Sputum, which was taken with nebulizer/expectorant or spontaneously, was put in a sterile container. One sputum specimen was collected in the morning for three consecutive days. Specimen collected on the first day were aliquoted into 2 sterile containers: one for ZN stain/AFB, bacterial culture and antibiotics sensitivity test, and the other has been sent to NIHRD for multiplex assay (for bacteria). Sputa from the second and third day are only for ZN stain.

- Five cc blood was collected, 2 cc placed in EDTA tube and 3 cc placed in plain tube. Blood in EDTA tube was for Complete Blood Count, 1.5 cc serum from plain tube was for glucose, transaminase, ureum and creatinine tests.The remaining serum has been sent to NIHRD for influenza serology test.

***Children:***

- Two throat and 2 nasal or nasopharyngeal swabs were taken and put into 6 ml VTM / Hanks transfer media in 1 (one) sterile Falcon tube. The VTM was aliquoted into several sterile cryotubes, 1 tube was sent to NIHRD (cold chain) for RT-PCR, multiplex (viral and bacterial) and Influenza viral isolation. All specimens were kept in - 20 °C prior to the lab tests. The remaining tube had been sent to Tangerang hospital laboratory for RT-PCR and kept in - 20 °C

- Three cc blood was collected, 0.5 cc placed in EDTA micro tube, 1 cc in plain tube and 1.5 cc in medium culture for bacteria (BacTalert bottle). Blood in EDTA micro tubes was for Complete Blood Count. 750 uL serum from plain tube was for glucose, transaminase, ureum and creatinine tests, the rest of 250 uL for influenza serology test conducted at NIHRD. Blood in BacTalert bottle was for bacterial culture and antibiotics sensitivity test (was put in incubator).
- CBC, glucose, transaminase, ureum, creatinine tests, bacterial cultures and antibiotics sensitivity tests had been conducted in the hospital laboratory, while serology test for influenza A H5 had been conducted at NIHRD.

2. ***Microbiological testing***

Gram stain, AFB/ZN stain and bacterial culture were performed according to Tangerang hospital laboratory SOP. First, the sputum had been assessed for potential contamination (through the assessment of the ratio of WBC to epithelial cells). Gram stain was performed on a sputum sample for the rapid identification of pathogens. A series of stains were applied to the sample and examined under microscope) checking the color, size and shape of potential organisms

For the culture, conventional microbiology techniques were conducted to isolate and detect bacteria causing SARI (e.g. *Streptococcus pneumoniae, Haemophilus influenza*, Enteric Gram negative i.e. *E. coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Bulkholderia pseudomallei, Bulkholderia cepacea,etc*)

Antibiotics susceptibility tests were systematically performed on positive cultures using discs for a series of antibiotics such as Penicillin, Amoxicillin, Amoxcillin- Clavulamic acid, Ceftriaxone, Cefotaxime, Ceftazidime, Azytromycin, Ciprofloxacin, Levofloxacin and Meropenem

Approximate number of specimens for culture sputum and antibiotics sensitivity tests : 10 (month) X 30 (adult specimen) = 300

In adults, Ziehl Neelsen staining was applied on sputum smears for the detection of Acid Fast Bacilli such as *Mycobacterium tuberculosis.*

Approximate number of specimens for ZN staining : 10 (month) X 3 (test) x 30 (adult specimen) = 900

In children, Blood culture had performed using the BacTalert system for the detection of bacteria causing SARI ( e.g. *Streptococcus pneumoniae, Haemophilus influenza*, Enteric Gram negative i.e. *E. coli, Klebsiella pneumoniae, Pseudomona aeruginosa, Acinetobacter baumannii, Burkholderia pseudomalleietc*).

Antibiotics susceptibility assessment were systematically performed using discs on positive cultures only for a series of antibiotics such as Penicillin, amoxicillin, Amoxcillin-Clavulamic acid Ceftriaxone,Cefotaxime, Ceftazidime, Meropenem, Amicacyn, Cefixime and Gentamicyn

Approximate number of specimens for blood culture and antibiotics sensitivity tests: 10 (months) X 20 (children specimens): 200

### 3. *Molecular diagnostic testing*

RT-PCR was performed on throat, nasal or pharyngeal (adult and children) swab, according to the SOP from NIHRD. If a specimen was negative for H5N1, but positive for Influenza A and B, specimens were cultured and identified in NIHRD laboratory.

Approximate number of specimens for PCR: 10 (months) X 50 (adult and children specimens) = 500

Approximate number of specimens for culture for influenza: 100

Multiplex assay has been performed on throat, nasal, or nasopharyngeal (adult and children) swabs at NIHRD Jakarta, for detection of Corona virus, influenza A, B, H1, H3, H5, Adenovirus, Human-metapneumo virus, RSV A, B and Para influenza virus 1,2,3 and 4.

Approximate number of specimens : 10 (months) X 50 (adult and children specimens) = 500

Multiplex assay has been performed on throat, nasal, or nasopharyngeal (children) swabs and sputa (adult) at NIHRD Jakarta, for detection of *Mycoplasma pneumoniae, Chlamydia pneumoniae, Legionella, Streptococcus pneumoniae, Neisseria meningitidis, Haemophillus influenzae.*

Approximate number of specimens: 10 (months) X 50 (adult specimens) = 500

*4. Serology assay for H5 antibody*

Serum was examined using modified Hemagglutination Inhibition test according to WHO's SOP and will be conducted in NIHRD Lab.

Approximate number of specimens: 10(months) X 50 (adult and children specimens) = 500

*5. Hematology: Complete Blood Count*

CBC was done for EDTA blood, based on the hematology's standard operating procedure, using the automatic hematology analyzer Sysmex XT-18001, XT-2000 or Mindray BC-5200.

Approximate number of specimens: 10 (months) X 50 (adult and children specimens) = 500

*6. Blood chemistry testing*

Chemical tests for glucose, ureum, creatinine, transaminase (ALT and AST) from sera specimens were done based on SOP using the automatic chemical analyzer PENTRA-400.

Approximate number for each test: 10 (months) X 50 (adult and children specimens) = 500

Note: The monthly average number of pneumonia patient in 2010 at Tangerang hospital was 50 (30 adults and 20 children)

## 7. STORAGE AND UTILIZATION, INCLUDING OF LEFTOVER SPECIMENS

Specimens were stored according hospital lab SOP. Leftover samples and specimens were stored in the Tangerang Hospital Laboratory at -20 °C until the Multiplex test was completed for all specimens.

## 8. RECORD-KEEPING, DATA HANDLING AND MANAGEMENT

Data hasbeen recorded in the patient's chart, which served as the main source docu ment for the study. Study data captured daily on standard case report forms (CRF s). Charts were reviewed daily along with the CRFs and frequent, systematic data verification with the support of study monitors.

Data were entered and managed at Tangerang hospital, using STATA data entry software and data analysis was conducted using STATA version 10. A check program

has been developed in order to optimize the consistency, the coherence and the completeness of database.

## V. ACTIVITY REPORT, STUDY RESULTS AND DISCUSSION

Following the development of SARI protocol, in March 2012, Tangerang hospital has conducted introduction of the SARI activity to the hospital directors. The other activity was in house training for case finding, case management, questionnaire completion, specimens collection – handling– shipping and data entry. During the in house training, Tangerang hospital team with REDI and NIHRD team also conducted socialization of SARI surveillance. The in house training agenda was case finding simulation and practice on how to fill up the questionnaire. The participants of the case finding simulation and practice on how to fill up the questionnaire questionnaire were 17 general practitioners and nurses. The participants for speeimens collection and handling were 20 laboratory staffs.

Following the in house training, Tangerang hospital team conducted routine technical review meeting from April until now (December 2012). Hospital SARI team conducted clinical assessment and management, collect the result of chest X-Ray and specimen from SARI patient and conduct certain laboratory testing within hospital sites (Complete blood count, blood glucose, SGOT/SGPT, ureum, creatinin, blood culture/ sputum culture & sensitivity antibiotics test, ZN stain test for sputum). The result of laboratory tests was recorded in the Tangerang hospital reporting system. The laboratory staff is responsible to pack and ship the specimens to NIHRD for PCR multiplex test, HI test, specimen isolation, and sequencing test. The print out of SARI reporting, labels, informed consent form have been done and delivered to Tangerang hospital.

The Tangerang hospital activities for specimen collection were conducted since 18 April until 31 December 2012 and already collected 117 SARI cases (71 children and 46 adults). For children, the male:female ratio is 1:0.77, while for adults, the male : female ratio is 1:1.35 . For children, age is ranging from 1 month to 13 years (median 10 months, IQR 40 months); as for adults, age is ranging from 18 to 71 years old (mean age 40 ± 14.2 years old).

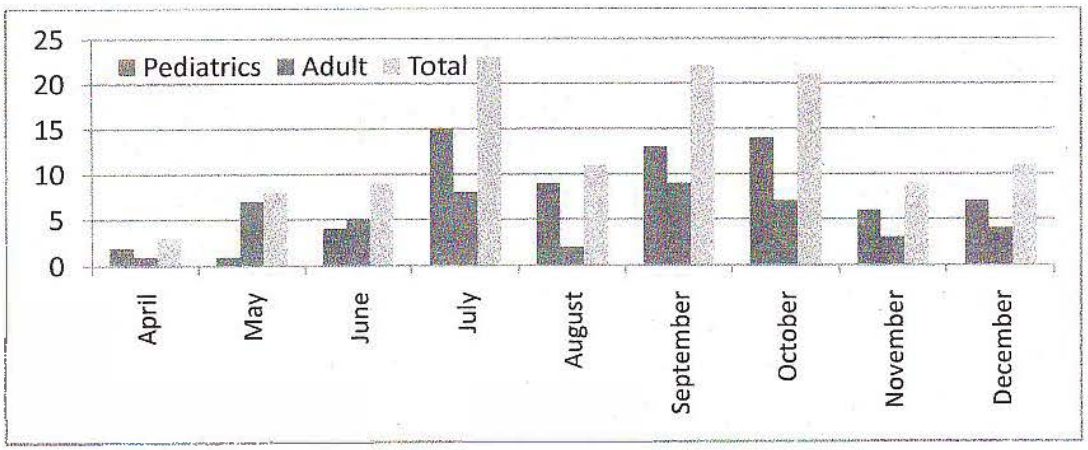


**Figure 10. Number of study participant by month**

**Table 3. Percent of patients enrolled**

| Month | # of study participants | # of Pneumonia Inpatients | % of eligible patients enrolled |
|---|---|---|---|
| April 2012 | 3 | 12 | 25.0 |
| May 2012 | 8 | 15 | 53.3 |
| June 2012 | 9 | 16 | 56.3 |
| July 2012 | 23 | 29 | 79.3 |
| Aug 2012 | 11 | 19 | 57.9 |
| Sept 2012 | 22 | 28 | 64.3 |
| Oct 2012 | 21 | 25 | 84% |
| Nov 2012 | 9 | 12 | 75% |
| Dec 2012 | 11 | 15 | 73% |
| Average | 117 | 171 | 68% |

**Table 4. Chief Complaint**

| Sign/Symptoms | # Adult | # Children |
|---|---|---|
| Cough + Fever + Shortness of Breath | 33 | 12 |
| Cough + Shortness of Breath | 13 | 6 |
| Cough + Fever | 0 | 18 |
| Shortness of Breath + Fever | 0 | 19 |
| Shortness of Breath only | 0 | 12 |
| Fever only | 0 | 2 |

**Table 5. Vital signs on Admission and on Discharge**

| | Adult On Admission | Adult On Discharge | Children On Admission | Children On Discharge |
|---|---|---|---|---|
| Temperature | 38.4 ± 0.8 | 37.7 ± 0.6 | 38.3 ± 1.1 | 37.2 ± 0.9 |
| RR/min | 42.7 ± 7.4 | 30.3 ± 11.9 | 50.8 ± 14.1 | 37.4 ± 11.8 |

**Table 6. CBC and Clinical Chemistry on Admission**

| | Adult (on admission) | Children (on admission) |
|---|---|---|
| Hb | 11.3 ± 1.8 | 10.7 ± 1.7 |
| Leukocyte | 16767.6 ± 10842.5 | 15349.3 ± 15452.5 |
| Thrombocyte | 262804.3 ± 158785.2 | 346977.1 ± 171091.1 |
| Glucose | 132.7 ± 52.4 | 93.9± 22.8 |
| SGOT | 53.2 ± 56.5 | 59.9 ± 58.8 |
| SGPT | 51.3 ± 66.9 | 38.5 ± 40 |
| Ureum | 40.5 ± 26.8 | 22.7 ± 11.2 |
| Creatinine | 1.7 ± 3.8 | 0.6 ± 0.1 |

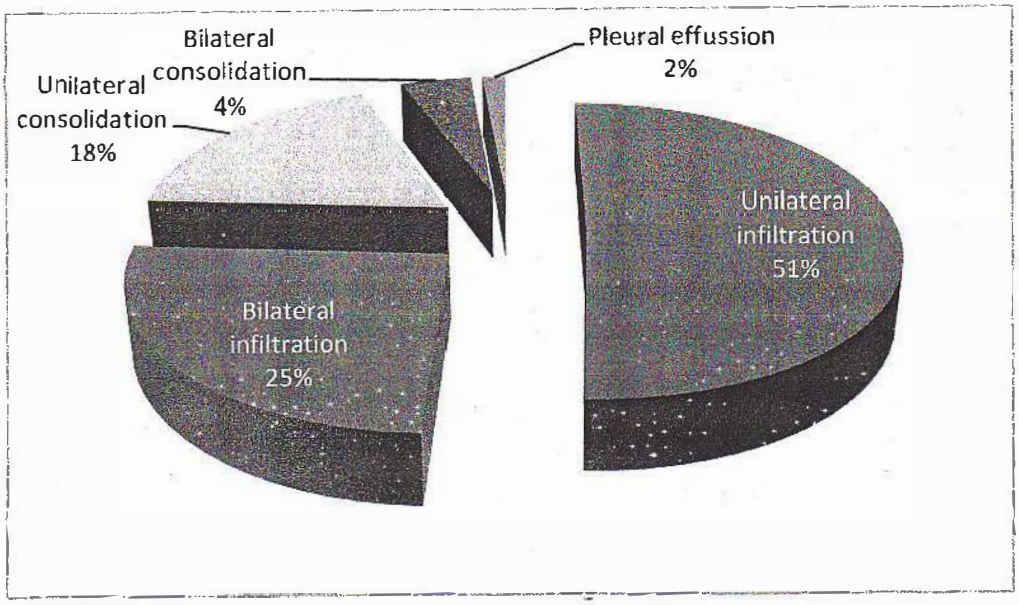


**Figure 11. Chest X-Ray in Pediatrics patients**

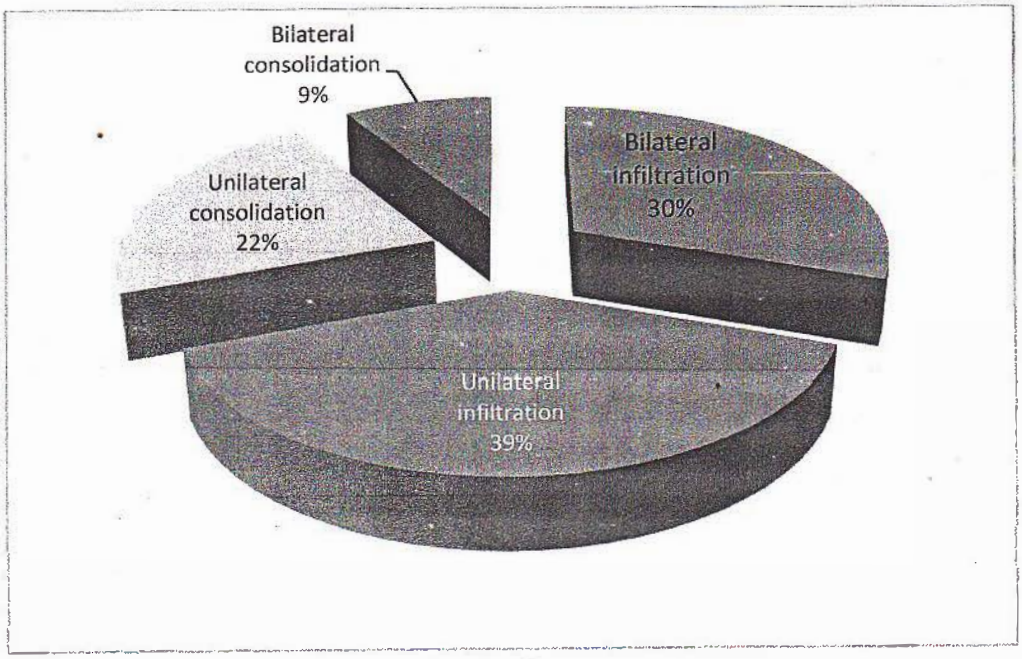


**Figure 12. Chest X-Ray in Adult patients**

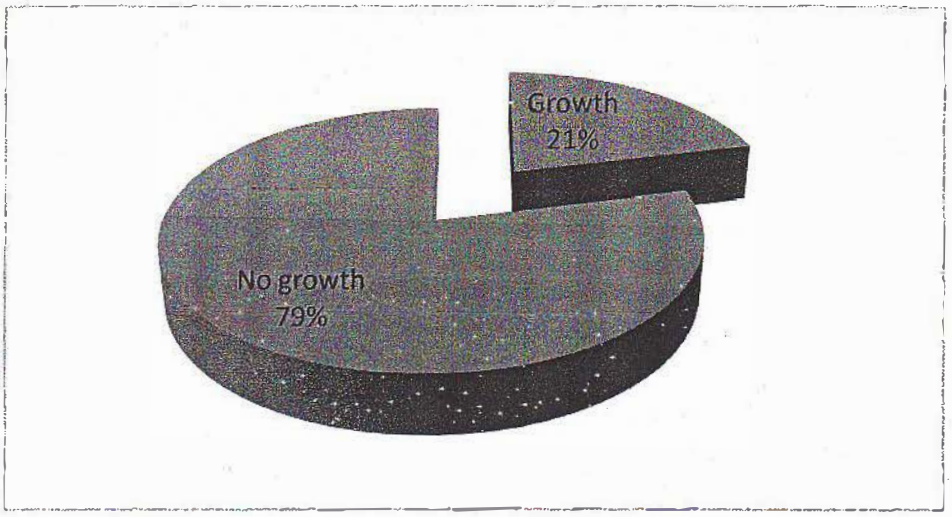


**Figure 13. Bacterial Culture in Pediatrics patients**

From 71 blood cultures, 15 (21%) were positive and the rest were negative.

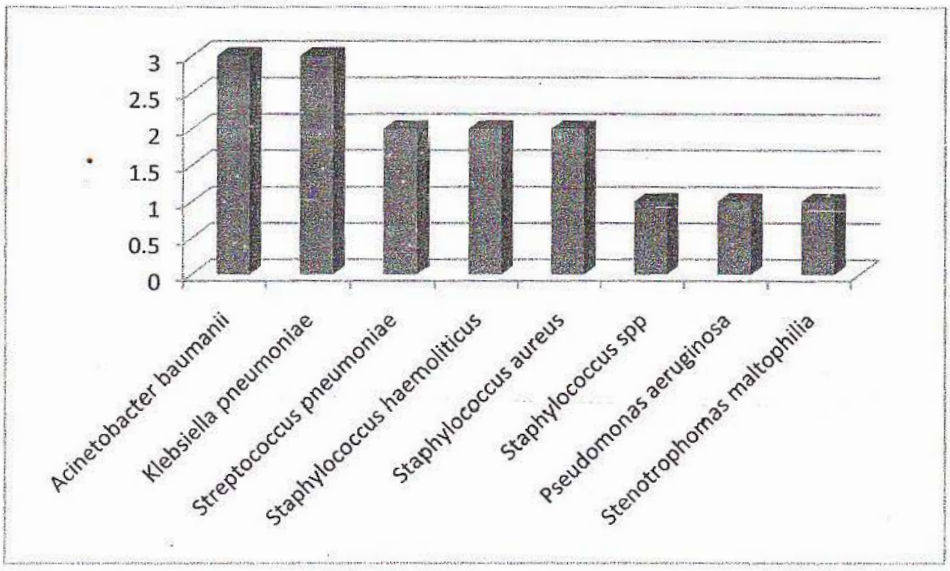


**Figure 14. Culture results in pediatrics study participant**

From 15 positive blood culture, *Acinetobacter baumannii* were found to be the highest followed by *Klebsiella pneumonia and Streptococcus pneumonia* respectively.

**Table 7. Antibiotics sensitivity results in pediatrics study participant**

| Bacterial | CN | AMC | SAM | MEM | OFL | CPO | CRO | CTX | CAZ | CIP | LEV | SXT | E | CFM |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | % | % | % | % | % | % | % | % | % | % | % | % | % | % |
| *K. pneumoniae* | 33.3 | 66.6 | 33.3 | 100 | * | 33.3 | 33.3 | 33.3 | 33.3 | 100 | 66.6 | 33.3 | 0 | 0 |
| *A. baumanii* | 66.6 | 66.6 | 66.6 | 66.6 | 0 | 66.6 | 66.6 | 66.6 | 66.6 | 0 | 66.6 | 66.6 | 66.6 | 0 |
| *S. pneumoniae* | 50 | 50 | 50 | 100 | * | 50 | 50 | 50 | 50 | 100 | 50 | 50 | 0 | * |
| *S. haemoliticus* | 0 | 50 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | * | 50 | 100 | * | 0 |
| *S. aureus* | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 50 | * | 100 | 100 | * | 0 |
| *P. aeruginosa* | 100 | 0 | 0 | 100 | * | 100 | 100 | 0 | 100 | * | 100 | 100 | 0 | 0 |
| *Staphylococcus spp* | 100 | 100 | 100 | 100 | * | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | * |
| *S. maltophilia* | 100 | 100 | 100 | 100 | * | 100 | 100 | 100 | 100 | * | 100 | 0 | 100 | 100 |

CN : Gentamycin
AMC : Amox-Clavulamic acid
SAM : Sulbactam ampicillin
MEM : Meropenem
OFL : Ofloxacin
CPO : Cepirom
CRO : Cefriaxone
CTX : Cefotaxime
CAZ : Ceftazidime
CIP : Ciprofloxacin
LEV : Levofloxacin
SXT : Sulfametoxazol Trimetroprim
E : Eritromycin
CFM : Cefixime

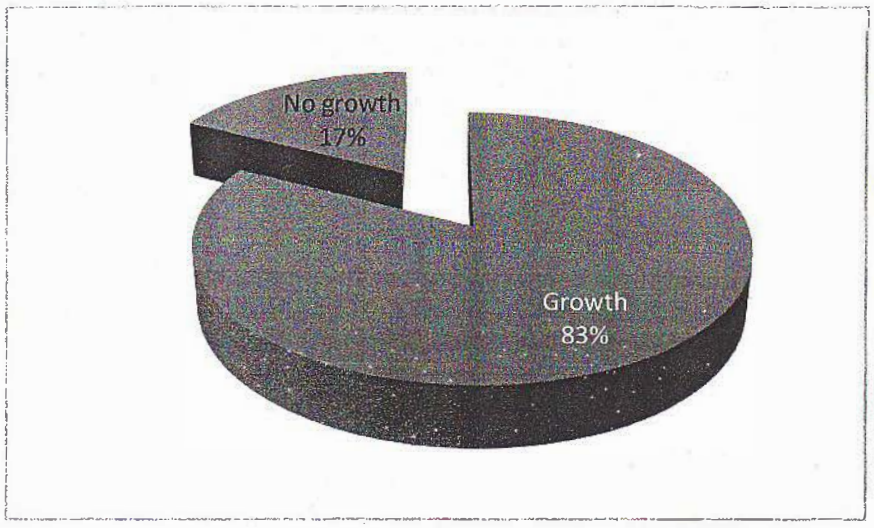


**Figure 15. Bacterial culture in Adult patients**

From 46 sputum cultures, 38 (81%) were positive and the rest were negative.

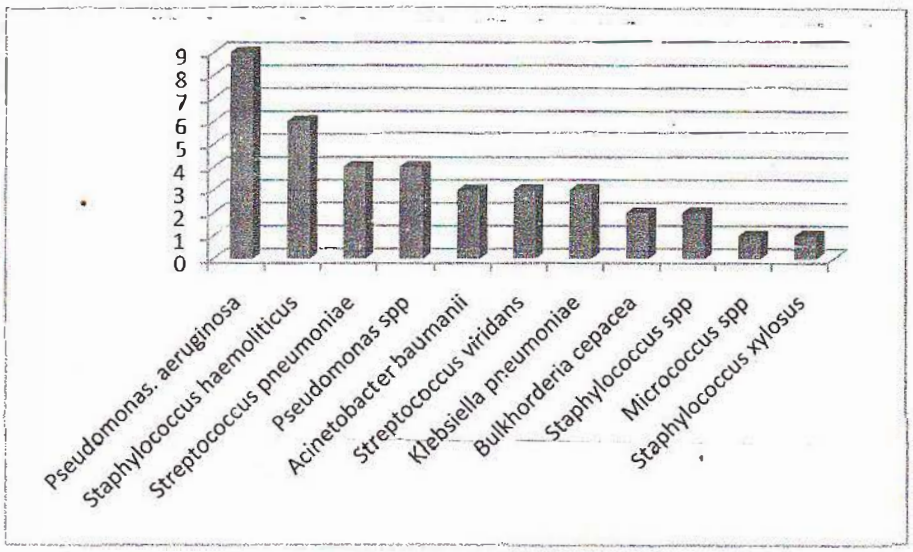


**Figure 16. Culture results in adult patients**

From 38 positive sputum culture, *Pseudomonas aeruginosa* were found to be the highest followed by *Staphylococcus haemoliticuc* and *Streptococcus pneumonia.* respectively.

**Table 8. Antibiotics sensitivity results in adults study participant**

| Bacterial | CN | AMC | SAM | MEM | OFL | CPO | CRO | CTX | CAZ | CIP | LEV | SXT | E | CFM |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | % | % | % | % | % | % | % | % | % | % | % | % | % | % |
| *P. aeruginosa* | 44.4 | 0 | 33.3 | 55.6 | * | 44.4 | 22.2 | 11.1 | 44.4 | 33.3 | 55.6 | 33.3 | 11.1 | * |
| *S. haemoliticus* | 33.3 | 50 | 50 | 50 | 25 | 50 | 33.3 | 33.3 | 33.3 | 0 | 0 | 33.3 | 100 | 100 |
| *S. pneumoniae* | 25 | 25 | 0 | 100 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| *Pseudomonas spp* | 75 | 25 | 75 | 75 | * | 0 | 0 | 0 | 25 | 25 | 66.7 | 75 | 25 | * |
| *A. baumanii* | 33.3 | 33.3 | 66.7 | 66.7 | 0 | 33.3 | 0 | 0 | 33.3 | 33.3 | 33.3 | 66.7 | 33.3 | * |
| *S. viridans* | 33.3 | 66.7 | 66.7 | 100 | 100 | 33.3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| *K. pneumoniae* | 66.7 | 66.7 | 66.7 | 66.7 | * | 66.7 | 33.3 | 66.7 | 66.7 | 66.7 | 100 | 66.7 | 33.3 | 0 |
| *B. cepacea* | 50 | 0 | 0 | 50 | * | 0 | 0 | 0 | 50 | 0 | 50 | 100 | 0 | * |
| *Staphylococcus spp* | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 0 | 50 | 50 | 100 | 0 | * |
| *Micrococcus spp* | 0 | 0 | 0 | 100 | * | 0 | 0 | 0 | 0 | 0 | 0 | 0 | * | * |
| *S. xylosus* | 0 | 0 | 100 | 100 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 100 | * | * |

CN : Gentamycin
AMC : Amox-Clavulamic acid
SAM : Sulbactam ampicillin
MEM : Meropenem
OFL : Ofloxacin
CPO : Cepirom
CRO : Cefriaxone
CTX : Cefotaxime
CAZ : Ceftazidime
CIP : Ciprofloxacin
LEV : Levofloxacin
SXT : Sulfametoxazol Trimetroprim
E : Eritromycin
CFM : Cefixime

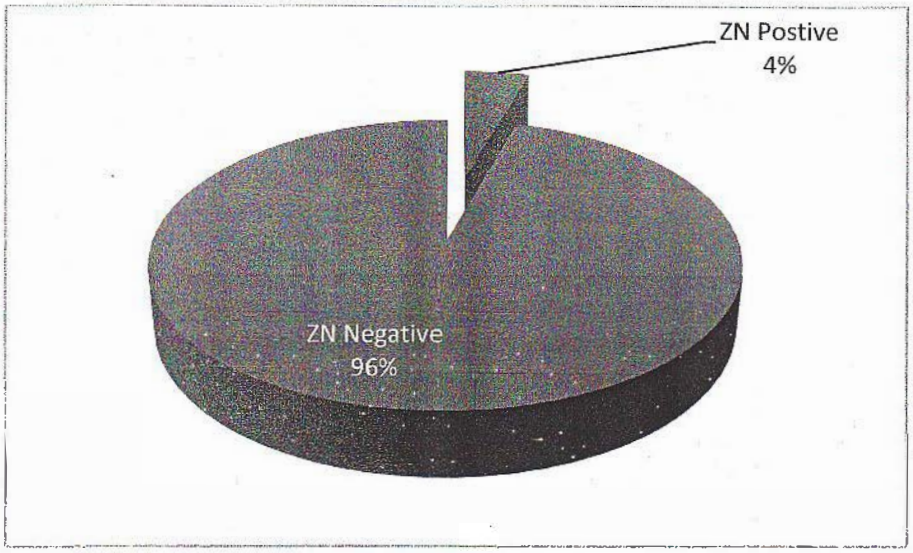


**Figure 17. ZN smear results**

From 46 ZN smears, 2(4%) were positive for acid fast bacilli and the rest were negative.

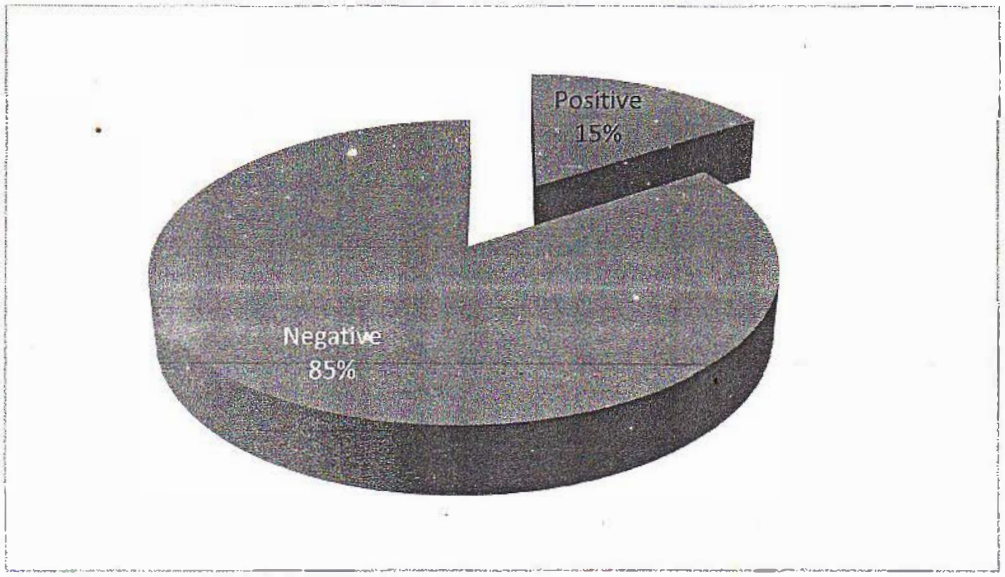


**Figure 18. PCR result for influenza (all)**

From 234 specimens (TS and NS), 22(15%) were positive for influenza.

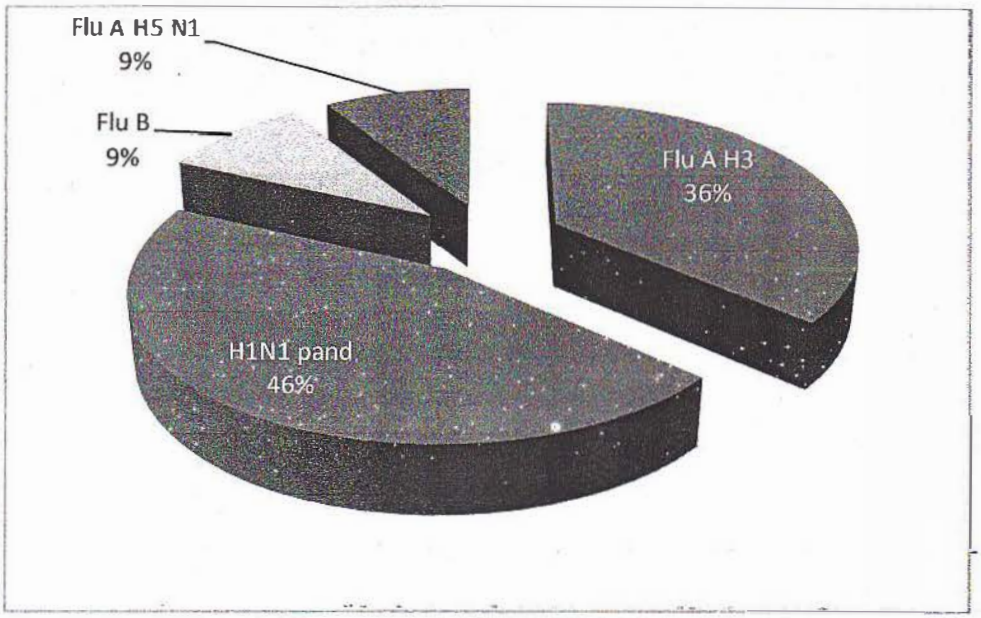


**Figure 19. Serotype results for influenza**

H1N1 pand was found to be the highest, followed by Flu A H3. Flu A H5 N1 was found among the SARI patients.

The result of Multiplex assay for bacteria and virus are reported separately. Those results are reported on the SARI surveillance in 3hospitals report.

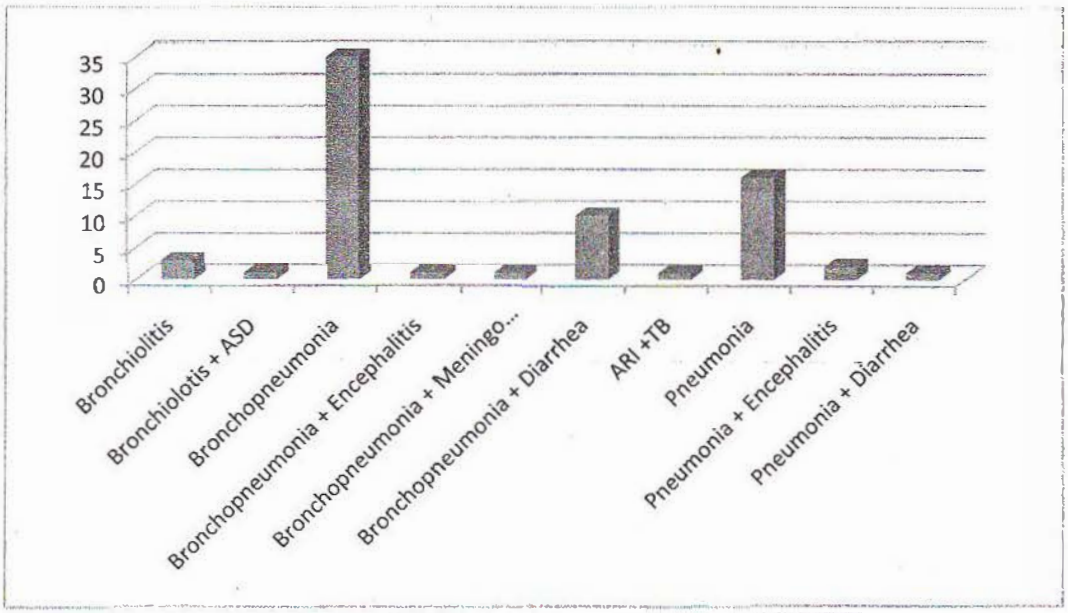


**Figure 20. Final diagnosis in pediatric patients**

Bronchopneumoniae was found to be the highest of final diagnosis in pediatric patients. Most of the patients experienced the co-morbidity.

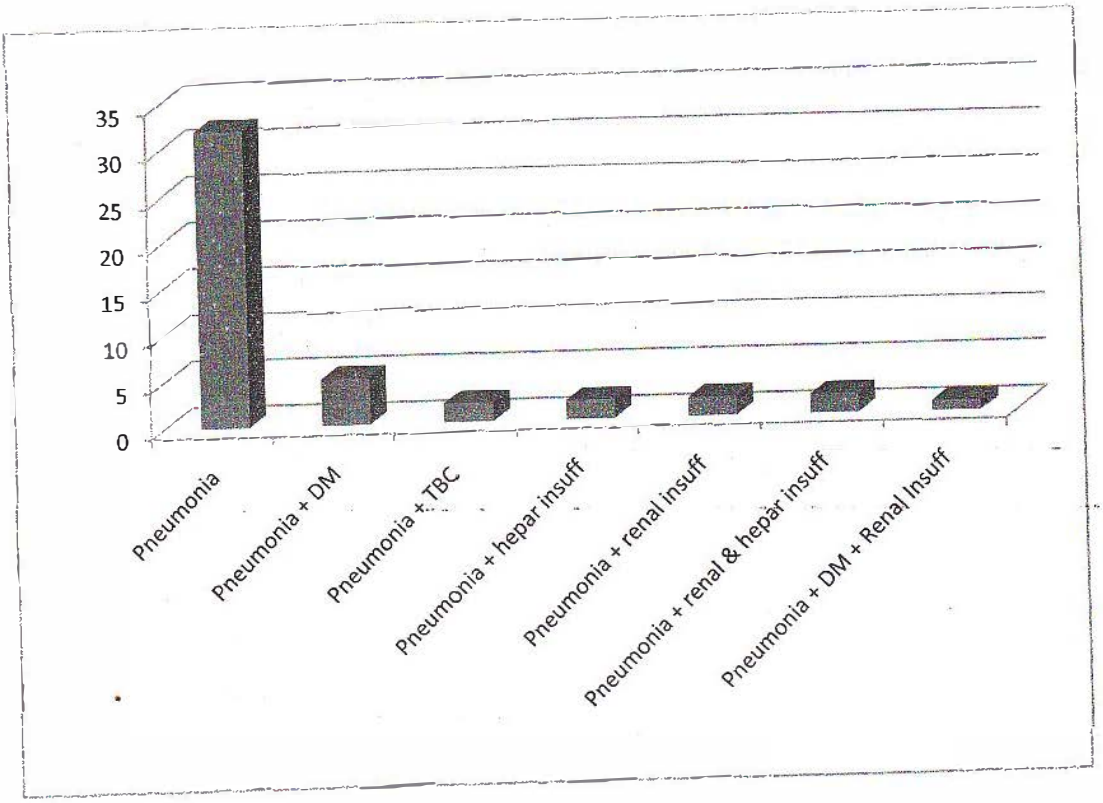


**Figure 21. Final diagnosis in adult patients**

Pneumoniae was found to be the highest of final diagnosis in adult patients. Most of the patients experienced the co-morbidity.

**Table 9. Treatment**

| | Adult | Children |
|---|---|---|
| Meropenem only | 12 | - |
| Meropenem + Azythromycin | 4 | - |
| Ceftriaxone only | 24 | 15 |
| Ceftriaxone + Azythromycin | 1 | - |
| Ceftriaxone + Levofloxacin | 4 | - |
| Ceftriaxone + Dexamethasone | - | 3 |
| Ceftriaxone + Oseltamivir | - | 2 |
| Levofloxacin + Azythromycin | 1 | - |
| Cefotaxime only | - | 40 |
| Cefotaxime + Ampicillin | - | 1 |
| Cefotaxime + Dexamethasone | - | 5 |
| Cefotaxime + Erythromycine | - | 1 |
| Cefotaxime + Oseltamivir | - | 1 |
| Ceftazidine | - | 1 |

The average time in the hospital among pediatrics was 7.1 ± 3.4 days (Range: 1 - 21 days), while among adult patients was 7.8 ± 2.8 days (Range: 4 -14 days).

The overall Case Fatality Rate (CFR) is 14.5 % (17/117). CFR in children 12.7% (9/71), while in adults is 17.4% (8/46). The number of patients recovered from the illness were 92 (78.6%); 57 (80.3%) among pediatrics and 35 (76.1%) among adult patients. There were 8 patients (6.8%) who were discharged without the doctor approval; 5 (7%) among pediatrics and 3 (6.5%) among adult patients.

## VI. CONCLUSION

1. All study participants were met the inclusion criteria of SARI.
2. The number of pediatric study participants were higher compared to the adult participants.
3. The number of study participants enrolled were not met the target number due to several reasons:
   a. Number of pneumonia patients in 2012 were lower than expected, based on 2011 data.
   b. Delay of patient recognition upon admission (more than 48 hours).
4. Bacterial patterns and antibiotic sensitivity tests, both in adults and pediatric patients were similar with the results of the previous Indonesian SARI surveillance.
5. The implementation of case management SOPs from the Indonesian Pediatric Association and Pulmonology Association is recommended.

# ETHICAL CLEARANCE

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## ETHICAL APPROVAL
## FOR THE USE OF HUMAN SUBJECTS

No. LE.01.06/KE/695/2012

The Committee on Health Research Ethics of the National Institute of Health Research and Development, Indonesia Ministry of Health, after conducting review on the research protocol entitled :

***"Hospital-Based Surveillance of Severe Acute Respiratory Infections at Tangerang District Hospital"***

submitted on : *June 5, 2012* by : *dr. Titin Mertiani, Sp.A.*

has hereby declared that the above protocol whereby human subjects will be used, has been approved for implementation in duration as stated in the protocol.

Please note that this *ethical approval* is for the period of 1 year since approved date.

Should there be any modification and/or extention of the study, the Principal Investigator is required to resubmit the protocol for approval. The progress and final summary reports should be submitted to NIHRD ethics committee.

Jakarta, 15 June 2012

Committee of Health Research Ethics,
Chairperson,

Prof. Dr. M. Sudomo

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