In-Hospital Mortality Due To Infectious Disease In An Internal Medicine Ward Of An University-Affiliated Hospital In The Tangerang District, Banten Province, Indonesia

N Lugito, A Kurniawan, Cucunawangsih

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Abstract

Infectious diseases are the causes of up to 30% of all admissions in the internal medicine ward. Data from the World Health Organization (WHO) and in Indonesia showed infectious diseases are the main cause of mortality. In-hospital mortality is an indicator of the healthcare quality and its analysis is important for planning healthcare management. The aim of this study is to describe the in-hospital mortality due to infectious diseases in the Internal Medicine Ward of an University-Affiliated Hospital in the Tangerang District, Banten Province, Indonesia. Epidemiological and clinical data of all in-hospital mortalities of patients aged above 18 year-old in 2014 were collected retrospectively from medical records and associated factors were evaluated. Out of 237 mortalities, 57.8% were due infectious diseases. Diagnosis of infectious diseases was 58.3%. The main causes of mortality were community acquired pneumonia (CAP) sepsis 18.6%, hospital acquired pneumonia (HAP) sepsis 10.9%, and pulmonary tuberculosis (TB) 9.7%. In patients who died due to infectious diseases: males were more frequent, median age was 53 year-old, and 32.1% were aged above 60 year-old. Co-morbidities such as chronic kidney disease (CKD), chronic liver disease (CLD), and non hemorrhagic cerebrovascular disease (NH CVD) were risk factors for in-hospital mortality due to infectious diseases.

INTRODUCTION

Infectious diseases are the causes of up to 30% of all admissions in the internal medicine ward (Nicolle L, et al., 1999; García, et al., 2005). Although advances in etiological and supportive treatment were reported, recent epidemiological data showed increased morbidity and mortality caused by infectious diseases (Armstrong , et al., 1999; Gómez, et al., 2009; Rebelo , et al., 2011). In-hospital mortality is an indicator of the healthcare quality and its analysis is important for planning healthcare management (Pac, et al., 2013; Al-Qurainy, et al., 2009; Sonnenblick M, et al., 2007). Data from the World Health Organization (WHO) showed infectious diseases are the main cause of mortality worldwide annually (27.5% of all mortalities) (WHO, 2008). In Indonesia, infectious diseases are also the leading cause of mortality. Indonesian and global data showed that infectious diseases including pneumonia and TB are leading causes of mortality (National Population and Family Planning Board, 2013; WHO, 2008), in contrast to studies in developed countries where infectious diseases including pneumonia and urinary infections are the second-highest cause of mortality (Zapatero, et al.,2010; Rebelo , et al., 2011). Data from WHO showed that vital statistics including cause of mortality and cause-specific mortality data in Asia, including Indonesia is minimal. Data are usually gathered from health care facilities such as hospitals or health surveys (WHO, 2011). The aim of this study is to describe the in-hospital mortality due to infectious diseases and associated risk factors in the internal medicine ward in the Tangerang District, Banten Province, Indonesia. The result of this study would also add data on cause-spesific mortality in Asia and compared to global data.

MATERIALS AND METHODS

Data of all in-hospital mortalities of patients aged above 18 year-old in 2014 were collected retrospectively from the Internal Medicine Ward of the Pelita Harapan University-Affiliated Hospital in the Tangerang District, Banten Province, Indonesia. Epidemiological data, clinical data and

associated factors for in-hospital mortality due to infectious diseases were obtained from medical records. .

The variables collected were epidemiological and clinical data. Epidemiological data include age and sex. Age is classified as young (below 60 year-old) and old (above 60 year-old). Clinical data included comorbidities, diagnosis at admission, length of stay, cause of mortality, and early mortality (within 48 hours after admission). Co-morbidities consisted of diabetes mellitus (DM), arterial hypertension (HT), chronic kidney disease (CKD), chronic heart failure (CHF), chronic liver disease (CLD), hemorrhagic (H), non hemorrhagic (NH) cerebrovascular disease (CVD), and solid tumors or leukemia, lymphoma. Complementary data included microbiological samples (blood, urine, faeces, cerebrospinal and sputum cultures), and the use of empiric antibiotic treatment. The characteristics of the study sample were described as mean (standard deviation), and median (range) for continuous variables such as age and hospital stay, frequencies and percentages for categorical variables such as sex, age above 60 year-old, co-morbidities, and early mortality.

Associations between variables were analyzed using the Chi-square and Fischer's test for categorical variables, independent t-test for continuous variables. Statistical analyses were performed using SPSS Statistics 19th version (SPSS Inc, 2010). Level of statistical significance was established as $p < 0.05$.

RESULTS

In 2014, there were 496 mortalities of patients aged above 18 year-old in the University-Affiliated Hospital, of which 47.8% (N=237) were from the Internal Medicine Ward. Of these, 57.8% (N=137) were identified as mortality due infectious diseases and 42.2% (N=100) as mortality due to non-infectious causes.

Infectious diseases as the main diagnosis at admission was 71.6% (N=169), with the leading diagnosis of CAP (23.2%), HAP (13.1%), and pulmonary disease (TB 9.7%). The most common co-morbidities were DM (77.6%) and CKD (72.2%). Other data on diagnosis at admission of patients who died in the internal medicine ward can be seen on table 1.

Infectious diseases as the causes of mortality were CAP sepsis (18.6%), HAP sepsis (10.9%), and pulmonary TB (9.7%). Non infectious diseases as the cause of mortality were CHF (9.3%), H CVD (8.0%), and respiratory failure (6.8%). Other causes of mortality can be seen on table 2.

Of patients who died due to infectious diseases group compared to non-infectious diseases group, male were more frequent (56.9% vs. 51.0%, $p = 0.219$). Median age of infectious diseases group compared to non-infectious diseases group was 53 year-old (range 19-85) and 54 year-old (range 19-87) consecutively ($p = 0.240$), and in both groups only 32.1% were aged above 60 year-old. Patients who had 2 or more co-morbidities in infectious diseases group compared to non-infectious diseases group were lower (67.2% vs. 82.0%, $p = 0.07$). Median hospital stay was significantly longer in infectious diseases group compared to non-infectious diseases group was 5 days (range 1-36) and 3 days (range 1-24) consecutively ($p = 0.006$). Early mortality in the infectious diseases group compared to the non-infectious diseases group was significantly lower (23.4% vs. 35.0%, $p = 0.035$). Mortalities due to infectious diseases compared to non-infectious diseases were more frequent in patients with CKD (74.5% vs. 69.0%, $p = 0.218$), CLD (3.6% vs. 2.0%, $p = 0.371$), NH CVD (13.9% vs. 11.0%, $p = 0.326$), but not in patients with other comorbidities such as DM, HT, CHF, H CVD, solid tumor of any grade, leukemia and lymphoma. Sex and age were not associated with mortality due to infectious diseases. Other data are shown in Table 3.

Microbiological samples were collected in only 3.4% (N=8) of the patients and consisted of Staphylococcus aureus, Pseudomonas aeruginosa from sputum, Enterobacter aerogenes from urin, and Escherichia coli and Klebsiella pneumonia from pus and blood cultures. Empirical antibiotic therapy was given to 78.5% (N=186) of the patients and anti tuberculosis drugs to 18.1% (N=43).

Mortality due to cumulative infectious diseases were significantly lower in patients with history of CHF and H CVD compared to patients without the history (61.7% vs. 36.1%, $p = 0.004$ and 61.6% vs. 26.9%, $p = 0.001$ consecutively). Mortality due to HAP were significantly more frequent in patients with history compared to patients with no history of NH CVD (23.3% vs. 9.2%, $p = 0.02$), mortality due to urinary tract sepsis were significantly more frequent in patients above 60 year-old compared to patients below 60 year-old (9.2% vs. 2.5%, $p = 0.028$), mortality due to gastroenterological sepsis were more frequent in patients with CLD compared to no CLD (28.6% vs. 2.2%, $p = 0.015$). Datas on mortalities due to infectious diseases, co-

morbidities and other risk factors are shown on Table 4.

Table 1

Diagnosis at admission of patients who died in the internal medicine ward of university-affiliated hospital

Diagnosis	N	%
CAP	55	23.2
HAP	31	13.1
NH CVD	30	12.7
H CVD	26	11.0
Pulmonary TB	23	9.7
Extrapulmonary TB	15	6.3
UTI	21	8.9
SSTI	15	6.3
GE	9	3.8
IAI	8	3.4
Solid tumors	31	13.1
Leukemia, lymphoma	6	2.5
DM	184	77.6
HT	36	15.2
CKD	171	72.2
CLD	7	3.0
CHF	36	15.2
ACS	6	2.5
UGIB	13	5.5

CAP: community acquired pneumonia, HAP: hospital acquired pneumonia, NH CVD: non hemorrhagic cerebrovascular disease, H CVD: hemorrhagic cerebrovascular disease, TB: tuberculosis , UTI: urinary tract infection, SSTI: skin and soft tissue infection, GE: gastroenteritis, IAI: intra abdominal infection, DM: diabetes mellitus, HT: arterial hypertension, CKD: chronic kidney disease, CLD: chronic liver disease, , CHF: chronic heart failure, ACS: acute coronary syndrome, UGIB: upper gastrointestinal bleeding.

Table 2

Causes of mortality in the internal medicine ward of university-affiliated hospital.

Causes of mortality	N	%
CAP sepsis	44	18.6
HAP sepsis	26	10.9
Pulmonary TB	23	9.7
CHF	22	9.3
H CVD	19	8.0
Respiratory failure	16	6.8
Urinary tract sepsis	11	4.6
NH CVD	10	4.2
CKD	9	3.7
Skin and soft tissue sepsis	8	3.4
Intra-abdominal sepsis	8	3.4
Extra-pulmonary TB	8	3.4
Gastroenterological sepsis	7	3.1
Hemorrhage	7	3.1
CLD	6	2.8
Others	7	3.1

CAP: community acquired pneumonia, HAP: hospital acquired pneumonia, CKD: chronic kidney disease, CHF: chronic heart failure, CLD: chronic liver disease, H CVD: hemorrhagic cerebrovascular disease, NH CVD: non hemorrhagic cerebrovascular disease, TB: tuberculosis

Table 3

Epidemiological and clinical characteristics of patients died due to infectious diseases and non-infectious diseases in the internal medicine ward of university-affiliated hospital.

	Mortality due to infectious diseases N=137 (%)	Mortality due to non-infectious diseases N=100 (%)	*p*-value
Male	56.9%	51.0%	0.219
Median age (range), year-old	53 (19-87)	54 (19-85)	0.240
Age above 60 year-old	32.1%	32.1%	0.550
Co-morbidities			
DM	74.5%	82.0%	0.111
HT	11.7%	20.0%	0.058
CHF	9.5%	21.0%	0.004
CKD	74.5%	69.0%	0.218
CLD	3.6%	2.0%	0.371
NH CVD	13.9%	11.0%	0.326
H CVD	5.1%	19.0%	0.001
Leukemia	0.7%	2.0%	0.383
Lymphoma	0.0%	3.0%	0.074
Solid tumor	8.8%	19.0%	0.021
High co-morbidities (≥ 2)	67.2%	82.0%	0.070
Hospital stay (range) (days)	5 (1-36)	3 (1-24)	0.006
Early mortality	23.4%	35.0%	0.035

DM: diabetes mellitus, HT: hypertension, CHF: chronic heart failure, CKD: chronic kidney disease, CLD: chronic liver disease, NH CVD: non hemorrhagic cerebrovascular disease, H CVD: hemorrhagic cerebrovascular disease

Table 4

Mortalities due to cumulative infectious diseases and to each infectious disease compared to comorbidities and risk factors

		Cause of Mortality															
		Infectious Diseases		CAP		HAP		Pulmonary tuberculosis		Urinary tract sepsis		Skin and soft tissue sepsis		Gastro enterological sepsis		Extra pulmonary tuberculosis		Intra abdominal sepsis	
		%	p	%	p	%	p	%	p	%	p	%	p	%	p	%	p	%	p
Sex	Male	60.5	0.360	20.2	0.490	12.4	0.441	9.3	0.819	4.7	0.821	2.3	0.268	3.9	0.302	3.9	0.465	3.7	0.337
	Female	54.8		16.7		9.5		10.2		4.7		4.6		3.9		2.8		3.1	
Age	≥ 60 y.o	57.8	0.985	16.8	0.301	11.2	0.881	10.8	0.340	2.5	0.028	4.4	0.212	3.1	0.800	4.4	0.212	4.4	0.212
	< 60 y.o	57.9		22.4		10.5		7.9		9.2		1.3		2.6		1.3		1.3	
DM	No	60.0	0.368	24.5	0.205	11.3	0.928	9.4	0.889	9.4	0.060	0.0	0.327	3.9	0.931	3.8	0.987	5.7	0.255
	Yes	55.4		16.8		10.9		9.8		3.5		4.4		3.5		3.5		2.7	
HT	No	60.2	0.678	18.4	0.863	9.9	0.235	10.9	0.304	4.9	0.481	3.9	0.262	2.9	0.712	3.9	0.262	3.9	0.262
	Yes	44.4		19.4		16.7		2.8		2.8		0.0		2.8		0.0		0.0	
CKD	No	53.8	0.355	13.8	0.223	10.8	0.911	12.3	0.289	3.0	0.366	3.0	0.807	3.5	0.378	4.6	0.395	3.5	0.296
	Yes	59.8		20.4		11.1		8.8		3.5		3.5		3.5		2.9		4.1	
CLD	No	57.4	0.459	18.7	0.616	0.0	0.438	9.1	0.340	4.8	0.714	3.5	0.348	2.2	0.815	3.5	0.784	3.5	0.784
	Yes	71.4		14.2		11.3		28.6		0.0		0.0		28.6		0.0		0.0	
CHF	No	61.7	0.004	18.9	0.510	10.9	0.582	10.9	0.304	4.9	0.481	3.9	0.262	2.9	0.712	3.9	0.262	3.9	0.262
	Yes	36.1		16.8		11.1		2.8		2.8		0.0		2.8		0.0		0.0	
NH CVD	No	57.8	0.512	17.8	0.472	9.2	0.820	10.6	0.178	3.9	0.350	3.4	0.732	3.4	0.383	3.9	0.333	3.9	0.333
	Yes	63.3		23.3		23.3		3.3		10.0		3.3		0.0		0.0		0.0	
H CVD	No	61.8	0.001	19.4	0.247	10.9	0.365	10.9	0.060	4.7	0.035	3.8	0.389	3.3	0.438	3.8	0.389	3.8	0.389
	Yes	26.9		11.5		11.5		0.0		3.9		0.0		0.0		0.0		0.0	
Leukemia	No	58.1	0.388	18.3	0.462	11.1	0.305	9.8	0.735	4.7	0.867	3.4	0.902	2.9	0.914	3.4	0.902	3.4	0.902
	Yes	33.3		33.3		0.0		0.0		0.0		0.0		0.0		0.0		0.0	
Lymphoma	No	58.5	0.074	18.8	0.318	11.1	0.306	9.8	0.735	4.7	0.867	3.4	0.902	2.9	0.914	3.4	0.902	3.4	0.902
	Yes	0.0		0.0		0.0		0.0		0.0		0.0		0.0		0.0		0.0	
Solid tumor	No	60.7	0.021	19.2	0.278	11.2	0.549	11.2	0.033	4.9	0.585	3.4	0.719	2.9	0.830	3.4	0.719	3.4	0.719
	Yes	38.7		12.9		9.7		0.0		3.2		3.2		3.2		3.2		3.2	
High co-morbidities (≥ 2)	No	86.3	0.000	24.4	0.260	13.3	0.379	20.0	0.010	4.4	0.032	2.2	0.531	2.2	0.804	8.9	0.045	6.7	0.178
	Yes	51.8		17.2		10.4		7.5		4.7		3.7		3.1		2.1		2.0	

DM: diabetes mellitus, HT: hypertension, CHF: chronic heart failure, CKD: chronic kidney disease, CLD: chronic liver disease, NH CVD: non hemorrhagic cerebrovascular disease, H CVD: hemorrhagic cerebrovascular disease

DISCUSSION

In 2014, 496 patients aged above 18 year-old died, of which 47.8% (N=237) were from the Internal Medicine Ward of an University-Affiliated Hospital in the Tangerang District, Banten Province, Indonesia. Of these, 57.8% (N=137) were identified as mortality due to infectious diseases and 42.2% (N=100) as mortality due to non-infectious causes. The data were in contrast with the Indonesia's Basic Health Research 2007 which stated that only 28.1% of mortalities in Indonesia were due to infectious diseases (Basic Health Research, 2007). It was also in contrast to Global Burden of Disease Study 2013, which stated that 11.8 million (23.6%) mortalities were caused by infectious, maternal, neonatal, and nutritional disorders, compared to 38.3 (76.4%) million mortalities caused by non-infectious diseases (GBD, 2013).

The infectious diseases as cause of mortality in this study were CAP sepsis 18.6% (N=44), HAP sepsis 10.9% (N=26), pulmonary TB 9.7% (N=23), urinary tract sepsis 4.6% (N=11), skin and soft tissue sepsis 3.4% (N=8), intra-abdominal sepsis 3.4% (N=8), extra-pulmonary TB 3.4% (N=8) and gastroenterological sepsis 3.1% (N=7). Indonesia's Basic Health Research 2007 found infectious diseases as causes of all age group mortalities were TB 7.5%, CAP 3.8%, gastroenteritis 3.5%, typhoid fever 1.6%, malaria 1.3% and sepsis 0.2% (Basic Health Research, 2007). The Global Burden of Disease Study 2013 described that deaths caused by infectious diseases, 2.7 million (22.9%) were caused by lower respiratory infections, 1.3 million (11.0%) by TB, and 1.3 million (11.0%) by gastroenteritis (GBD, 2013). The infectious diseases as causes of mortality in this study were comparable to data in

Indonesia and global data, which found pneumonia and TB as leading causes. This is attributable to the WHO Global Report 2014 which described that 56% of 9 million TB cases in the world were in Southeast Asian and Western Pacific regions (Global Tuberculosis Report, 2014). A study in Spain found that infectious diseases were the second-highest cause of mortality (10.5%), including pneumonia (7.5%) and urinary infections, (1.7%) (Zapatero, et al.,2010). The difference between this study compared to similar studies in Europe is that TB was not prevalent thus not a leading causes of mortality. Mortality due to pneumonia in this study was higher than other studies assessing overall mortality (Briongos-Figuero,et al., 2015; Rodríguez, et al., 2006; Sanclement, et al., 2004) but was similar to other studies of mortality of cause-specific infections (Gao, et al., 2005; Vallejo, et al., 2003). Other studies have results contradictory to this study that found that the leading cause of mortality due to infection was urinary tract sepsis, followed by the respiratory tract sepsis (Zafrir, et al., 2010; Hernández-Roca, et al., 2013).

In this study, male patients died more frequently. Median age of the infectious diseases group compared to the non-infectious diseases group was 53 year-old and 54 year-old consecutively, and in both groups only 32.1% were aged above 60 year-old. Both sex and age were not associated with mortalities due to infectious disease.

A study in Israel in 2006 found that in nonagenarian patients hospitalized in Internal Medicines wards, acute infection was the most common reason for admission (82.4%). Older age and infections at admission, but not co-morbidities were associated with overall mortality (Zafrir, et al., 2010). Another study in Italy in 2008 found that overall mortality in Internal Medicine wards was 5%, with a mean age of patients of 79.4 year-old (SD 7.5), 46% were aged above 80 year-old, while age and co-morbidities were associated with hospital mortality (Nobili, et al., 2011). In the Southeast Asia countries, including Indonesia, the fertility decline has changed the population pyramid from high fertility to a high middle working age group (Jones, 2013). In 2010, the Indonesian population were characterized by the high percentage of the productive age group (National Population and Family Planning Board, 2013), shown in the patients' characteristics of this study. It is different to developed countries which have a high life expectancy with high prevalence of comorbidities (WHO, 2011; Basic Health Research, 2007) and also high mean age of the hospitalized patients in the Internal Medicine ward (Zafrir, et al., 2010; Nobili, et al., 2011).

Mortality due to infectious diseases compared to non-infectious diseases were more frequent in patients with CKD (59.6% vs. 53.0%, p = 0.355), CLD (71.4% vs. 57.4%, p = 0.459), NH CVD (63.3% vs. 57.0%, p = 0.512). A study showed that factors associated with in-hospital mortality due to infectious diseases were CKD, bacteraemia of unknown source of infection, severe cognitive impairment, hypoalbuminea, hypoxemia, and hypothermia (Rebelo M, et al., 2011). Patients with CLD have an increased risk of developing bacterial infection, sepsis, and mortality (Fernandez and Gustot, 2012). In patients with advanced CLD, high circulating levels of proinflammatory cytokines induced by infection contributes to the development of sepsis-related organ failures and mortality (Fernandez and Gustot, 2012). Hypoalbuminaemia which is prominent in CLD was the associated factor of increased mortality. Hypoalbuminaemia was a general indicator of low health status and immunologic competence, and also indicator of patient's low physiologic reserve for handling stresses such as infections and bacteraemias (Rebelo M, et al., 2011; Grabska, et al., 2011). A study on infections and NH CVD found that patients with coexistent CAP and UTI had an increased risk of poor short-term outcomes of death and long-term outcomes of death or dependency (Grabska, et al., 2011).

Mortality due to infectious diseases compared to non-infectious diseases were less frequent in patients with history of HT (44.4% vs. 60.2, p = 0.078), CHF (55.4% vs. 66.0, p = 0.168), and DM (36.1% vs. 61.7, p = 0.004). History of cardiovascular involvement were inversely associated with mortality due to infectious disease as described in one study (Grabska, et al., 2011). Other studies found that HT, CHF, and DM were associated with mortality due to infectious disease (Hernández-Roca, et al., 2013; Nobili, et al., 2011). Diabetes mellitus and its complications due to microvascular and macrovascular diseases including cardiovascular involvement, and the cardiovascular diseases themselves render the patients susceptible to hypoxemia. Hypoxemia has been showed in a study as an independent risk factor for death. Hyperglycemia in DM impairs the humoral immunity and polymorphonuclear leucocyte and lymphocyte functions (Caterino, et al., 2009).

The high co-morbidities were also more frequent in patients who died due to non-infectious compared to infectious

diseases (86.7% vs. 51.0%, p = 0.000), possibly because patients with higher co-morbidities died due to the complications of their diseases before suffering infectious diseases. This is also the explanation for the higher rate of early mortality in the group of non-infectious diseases compared to infectious diseases (35.0% vs. 23.4%, p = 0.035).

Mortalities due to HAP were significantly more frequent in patients with history of NH CVD compared to patients with no history (23.3% vs. 9.2%, p = 0.02). This data is in accordance to a study that showed that patients died from neurological causes had more frequent nosocomial infections (Rodríguez, et al., 2006). Mortalities due to urinary tract sepsis were significantly more frequent in patients above 60 year-old compared to patients below 60 (9.2% vs. 2.5%, p = 0.028). A recent study showed that age and female sex were associated with risk of urinary tract infection (Hsiao, et al., 2014). Mortalities due to gastroenterological sepsis were more frequent in patients with CLD compared to no CLD (28.6% vs. 2.2%, p = 0.015). Gastroenteritis changed the microflora of the intestine, making CLD patient more prone to spontaneous bacterial peritonitis and gastroenterological sepsis (Fernandez and Gustot, 2012; Fernandez and Arroyo, 2013).

Studies found the importance of antibiotic therapy and its relationship with mortality (Hernández-Roca , et al., 2013; Martínez, et al., 2003, Magrini, et al., 2013). Empirical antibiotic therapy was given to 78.5% (N=186) patients and maintained to the end of treatment because microbiological samples were collected in only 3.4% of patients. The detection of microorganisms is very low, because culture of microorganisms could not be routinely done in the low resource settings area.

Major limitation of this study is the retrospective design, thus some datas were be incomplete in the medical records especially the microbiological data. Also this study was conducted in a single hospital, other hospitals and/or regions could have differed in the settings of patient's characteristics, co-morbidities and microbiological pattern.

CONCLUSIONS

This study describes the in-hospital mortality due to infectious diseases. The most common infectious diseases as cause of mortality in this study were CAP, HAP, and pulmonary TB. Co-morbidities such as CKD, CLD, NH CVD were risk factors for in-hospital mortality due to infectious disease. Mortality due to HAP was significantly more frequent in patients with history of NH CVD ,urinary tract sepsis was significantly more frequent in patients above 60 years, and gastroenterological sepsis was more frequent in patients with CLD.

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Author Information

Nata Pratama Hardjo Lugito
Department of Internal Medicine, Faculty of Medicine, Pelita Harapan University
Banten, Indonesia
nata.lugito@uph.edu

Andree Kurniawan
Department of Internal Medicine, Faculty of Medicine, Pelita Harapan University
Banten, Indonesia

Cucunawangsih
Department of Microbiology, Faculty of Medicine, Pelita Harapan University
Banten, Indonesia