

## Incidence of nosocomial pneumonia and causative bacteria among chronically ill patients admitted in a general hospital<sup>a</sup>

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**Background** : *Nosocomial pneumonia (NP) is ranked high among all health care associated infections. The incidence and causative bacteria may be different from studied hospital to the others.*

**Objective** : *To investigate incidence of NP and its causative bacteria among chronically ill patients who were admitted at a general hospital in the central region of Thailand.*

**Methods** : *A prospective study, which was carried out in department of medicine of a general hospital in the central region of Thailand from April to September 2016. A total of 330 chronically ill patients who were admitted to the department of Medicine. NP is defined as pneumonia with onset no less than 48 hours after hospital admission and NP diagnosed by doctors. The causative bacteria were cultured from sputum of NP patients. Identification was carried out by standard biochemical profile and to test the multi-drug resistance of the bacteria from the microbiological laboratory of the study hospital. The descriptive statistics were used to analyze data.*

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- Results** : Among 330 chronically ill patients, 50% were female, and 58.2% were over 60 years of age. The incidence of NP was 16.4% (54/330) or 17.0 per 1,000 patient-days. The incidence of ventilator associated pneumonia (VAP) was 43.5% (40/92) or 32.7 per 1,000 ventilator days and the incidence of hospital-acquired pneumonia (HAP) was 5.9% (14/238) or 8.0 per 1,000 patient-days. Female patients, with age > 60 years, with underlying diseases such as cardiovascular and metabolic syndrome, patients with subconscious and unconscious, those with total dependence, those with long admission days, and those with medical instrument uses had relatively higher incidence of NP. The most predominant causative bacteria was *A. baumannii* (34.3%). Among sputum with *A. baumannii*, 79.2% were multiple-drug resistance *A. baumannii* (MDR - *A. baumannii*).
- Conclusion** : Chronically ill patients admitted at the hospital, especially, those with long duration of admission and/or receiving medical instrument had relatively higher incidence of NP. Among them, the predominant causative bacteria was *A. baumannii* with multiple-drug resistance.
- Keywords** : Nosocomial pneumonia, chronically ill patients, Incidence, *A. baumannii*.

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อักเสบจากการติดเชื้อในโรงพยาบาลและแบคทีเรียที่เป็นสาเหตุในผู้ป่วยโรคเรื้อรังใน  
โรงพยาบาลทั่วไปแห่งหนึ่ง. จุฬาลงกรณ์เวชสาร 2560 ก.ย. - ต.ค.;61(5): 563 - 76

**เหตุผลของการทำวิจัย** : การเกิดปอดอักเสบจากการติดเชื้อในโรงพยาบาลจัดว่าเป็นการติด  
เชื้อลำดับต้น ๆ ของการติดเชื้อในโรงพยาบาล อาจมีความแตกต่าง  
ของอุบัติการณ์การเกิดปอดอักเสบจากการติดเชื้อในโรงพยาบาล  
และแบคทีเรียที่เป็นสาเหตุในโรงพยาบาลแต่ละระดับ

**วัตถุประสงค์** : เพื่อศึกษาอุบัติการณ์การเกิดปอดอักเสบจากการติดเชื้อใน  
โรงพยาบาล และแบคทีเรียที่เป็นสาเหตุในผู้ป่วยที่เจ็บป่วยด้วย  
โรคเรื้อรังในโรงพยาบาลทั่วไปแห่งหนึ่งที่ตั้งอยู่ภาคกลางของ  
ประเทศไทย

**วิธีการทำวิจัย** : การศึกษาแบบติดตามไปข้างหน้าในผู้ป่วยที่เจ็บป่วยด้วยโรคเรื้อรัง  
จำนวน 330 ราย ที่พักรักษาในแผนกอายุรกรรมโรงพยาบาล  
ทั่วไปแห่งหนึ่งที่ตั้งอยู่ภาคกลางของประเทศไทย ตั้งแต่เดือนเมษายน  
ถึง กันยายน พ.ศ. 2559 โดยปอดอักเสบจากการติดเชื้อในโรงพยาบาล  
เป็นการเกิดปอดอักเสบที่เกิดขึ้นหลังจากเข้าพักรักษาในโรงพยาบาลหลัง  
48 ชั่วโมงเป็นต้นไป การวินิจฉัยโดยแพทย์ ส่วนแบคทีเรียที่เป็น  
สาเหตุได้จากผลการตรวจเสมหะของผู้ป่วยด้วยวิธีเพาะเชื้อ วิธีทดสอบ  
ทางชีวเคมีและทดสอบเชื้อดื้อยาโดยห้องปฏิบัติการทางจุลชีววิทยา  
ของโรงพยาบาลที่ศึกษา วิเคราะห์และนำเสนอผลการวิจัยโดยใช้  
สถิติเชิงพรรณนา

**ผลการศึกษา** : ผู้ป่วยด้วยโรคเรื้อรังที่ทำการศึกษามีจำนวน 330 ราย เป็นเพศหญิง  
ร้อยละ 50 อายุมากกว่า 60 ปี ร้อยละ 58.2 อุบัติการณ์การเกิด  
ปอดอักเสบจากการติดเชื้อในโรงพยาบาลคิดเป็นร้อยละ 16.4 (54/  
330) หรือ 17 ครั้งต่อ 1,000 patient - days โดยที่อุบัติการณ์  
การเกิดปอดอักเสบจากการใช้เครื่องช่วยหายใจ คิดเป็นร้อยละ 43.5  
(40/92) หรือ 32.7ต่อ 1,000 ventilator days และอุบัติการณ์ของ  
ปอดอักเสบที่ไม่ได้ใส่เครื่องช่วยหายใจ คิดเป็นร้อยละ 5.9 (14/238)  
หรือ 8.0 ต่อ 1,000 patient-days ผู้ป่วยเพศหญิง, อายุมากกว่า  
60 ปี, มีประวัติการเจ็บป่วยด้วยโรคหัวใจและหลอดเลือดและกลุ่ม  
อาการทางเมแทบอลิก, ผู้ป่วยที่มีระดับความรู้สึกตัวเปลี่ยนแปลง,

สรุป

:

ผู้ป่วยที่ช่วยเหลือตนเองไม่ได้, ผู้ป่วยที่พักรักษาในโรงพยาบาลเป็นเวลานาน และผู้ป่วยที่ได้รับการรักษาด้วยอุปกรณ์ทางการแพทย์ รวมถึงเครื่องช่วยหายใจ มีอุบัติการณ์ค่อนข้างสูงกว่า สำหรับแบคทีเรียที่เป็นสาเหตุส่วนใหญ่ที่พบร้อยละ 34.3 ได้แก่ *A. baumannii* โดยเชื้อ *A. baumannii* ที่พบร้อยละ 79.2 เป็นเชื้อดื้อยาหลายชนิด ผู้ป่วยที่เจ็บป่วยด้วยโรคเรื้อรังที่พักรักษาในโรงพยาบาล โดยเฉพาะอย่างยิ่งผู้ป่วยที่พักรักษาในโรงพยาบาลนาน และ/หรือ ผู้ป่วยที่ได้รับการรักษาด้วยเครื่องมือแพทย์มีอุบัติการณ์การเกิดปอดอักเสบจากการติดเชื้อในโรงพยาบาลที่สูง แบคทีเรียที่เป็นสาเหตุของการติดเชื้อที่พบส่วนใหญ่เป็นเชื้อ *A. baumannii* ดื้อยา

คำสำคัญ

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ปอดอักเสบจากการติดเชื้อในโรงพยาบาล, ผู้ป่วยด้วยโรคเรื้อรัง, อุตบัติการณ์, *A. baumannii*.

Nosocomial pneumonia (NP) is the first or second of nosocomial infection ranked among all health care associated infections.<sup>(1,2)</sup> It is defined as pneumonia that has the onset no less than 48 hours after hospital admission.<sup>(3)</sup> NP is common in those who receive mechanical ventilation but it can also develop in non-ventilated patients. Previous studies have identified NP in general wards and found that an incidence ranged from 2.45 to 4.5 per 1,000 patient-days.<sup>(4,5)</sup> The international Nosocomial Infection Control Consortium (INICC) reported the overall rate of ventilator-associated pneumonia (VAP) was 0.9 to 13.1 per 1,000 ventilator days.<sup>(1)</sup> In Thailand, the incidence rate of NP was 21.8 per 1,000 patient-days and VAP was 28.3 per 1,000 ventilator days.<sup>(6)</sup> A causative bacterial pathogen of NP included 60% of gram-negative bacilli, representing most frequently identified pathogens: *Pseudomonas aeruginosa*, *Enterobacteriaceae*, *Klebsiella* spp., *Escherichia coli* and *Acinetobacter* spp.<sup>(7,8)</sup> Many studies on NP have been performed in Intensive Care Units, but few have focused on patients in general wards including Thailand. Additionally, the incidence and causative bacteria may vary by the studied hospitals depending on the hospital environments and health care worker practices. Most studies demonstrated that NP was associated with the risk factors of respiratory tract colonization and patient-related conditions due to impairments in host defensive function.<sup>(3)</sup> The conditions included chronic diseases, coma, malnutrition, hypotension, metabolic acidosis, cigarette smoking, and the presence of a number of comorbid illness, such as central nervous system (CNS) dysfunction, diabetes mellitus and alcoholism.<sup>(9)</sup> Chronic diseases are defined as long-term diseases that develop slowly over time, often progressing in

severity, and can often be controlled, but rarely cured.<sup>(10)</sup> Accordingly, this study focuses on finding out the incidence of NP and its causative bacteria in admitted chronically ill patients in a general hospital, in the central area of Thailand.

## Materials and Methods

### Study design, subjects, sample size calculation

A prospective study was conducted on chronically ill patients admitted to male and female medical wards and sub-intensive care unit (sub-ICU) from April to September, 2016. As for the male and female medical wards and sub-ICU, these wards were the place to support the whole medical patients included chronically ill patients. The most of patients in sub-ICU received mechanical ventilator and no coma. Additionally, the environments and arrangement of three units were similarly condition such as open air unit, no air condition, and arrangement in units. Moreover, total of 330 studied patients were all patients who met the inclusion criteria and were admitted in the three units in the period of studied time. Quantitative data from surveillance form and patient's records were included. The causative bacteria were investigated from patient's sputum and reported from laboratory unit of studied hospital. Totally, 330 chronically ill patients were included due to the sample size calculated from the formula:<sup>(11)</sup>

$$n = \frac{Z^2_{\alpha/2} PQ}{d^2}$$

Where:  $Z_{\alpha/2}$  = alpha error at alpha 0.05 = 1.96

P = proportion of incidence of NP from a previous study = 0.28<sup>(6)</sup>

Q = 1-P

d = allow able error 0.05

Patients who voluntarily participated were included. The inclusion criteria were patients with chronic diseases, both sex, aged  $\geq 18$  years, and admitted in 3 studied units (male, female medical wards and sub-ICU) within 48 hours. Consequently, patients with NP before 48 hours after admitted in studied wards were excluded. These studied only patients who were full consciousness and able to sign their informed consent forms. However, for those who were not full consciousness and/or patients who could not read or write, the consent form was signed by a family member after receiving study information. After signing informed consents, these patients were followed-up and observed. Studied patients and their family members were interviewed using a surveillance form including socio-demographic characteristics. The patients' health status, medical instrument use, respiratory secretion specimens from patients with NP and NP diagnosis by doctors were recorded. All studied patients were observed until discharge or dead or referred to other units. As for patients who were referred to other units, a 48-hours follow-up was done to observe whether or not the patient develop NP. NP is defined as an infection of lung parenchyma that is neither present nor incubation at the time of hospital admission and which develops after 48 hours of hospital admission. Additionally, VAP is defined as pneumonia that occurs after 48 hours of endotracheal intubation and initiation of mechanical ventilation or within 48 hours after endotracheal tube removal.<sup>(3)</sup> NP and VAP were diagnosed by doctors.

## Research tools

### Surveillance form and record forms

A surveillance form and record forms were followed Augsornsri C. (2014)<sup>(12)</sup>, however, the content

validity of the forms was re-checked by 3 experts on infectious diseases prevention and epidemiology. These involve patients' health status and medical instrument use such as: sex, age, body weight, height, history of underlying diseases, level of consciousness, functional status, duration of admission, receiving mechanical ventilator, receiving nasogastric tube, aerosol therapy, antibiotic use before NP and steroid use. Sputum specimens were collected from all observed patients to culture the causative bacteria and to test the multi-drug resistant bacteria at microbiological laboratory of the study hospital.

### Statistical analysis

Data were analyzed using descriptive statistics with SPSS program version 18.

### Ethical approval

The research protocol was approved by the Ethics Committee for Human Research, Faculty of Public Health, Mahidol University (COA. No. MUPH 2016-027) and the Ethics Committee of the studied hospital (Reference No. 2/2559) before data collection.

### Results:

#### Socio-demographic characteristics of studied chronically ill patients

Among 330 chronically ill patients, 50% were female. Approximately, 40.9% were admitted in a male medical unit, 38.2% were admitted in a female medical unit and 20.9% were admitted in sub-ICU. The majority of studied chronically ill patients aged over 60 years, had normal body mass index (BMI) 18.5 - 24.9, and finished their primary school and had no income. (Table 1)

**Table 1.** Characteristics of studied chronically ill patients admitted at studied general hospital.  
(n = 330 patients)

Characteristics	No.	%
<b>Sex</b>		
Female	165	50.0
Male	165	50.0
<b>Age (years)</b>		
≤ 60	138	41.8
>60	192	58.2
(Mean = 63.30, S.D.= 16.38, Range = 19 - 93)		
<b>Body Mass Index (BMI)*</b>		
< 18.5 (under weight)	60	18.2
18.5 - 24.9 (healthy)	164	49.7
25.0 - 29.9 (over weight)	81	24.5
≥ 30 (obese)	25	7.6
(Mean = 23.06, S.D. = 4.67, Range = 12.40 - 40.0)		
<b>Education level</b>		
Primary school	200	60.6
Secondary school and higher	53	16.1
Illiterate	77	23.3
<b>Income per month (Baht)</b>		
No income	185	56.1
<10,000	105	31.8
≥10,000	40	12.1

\*Classified by WHO 2004 <sup>(13)</sup>

#### **Incidence of NP classified by some socio-demographic characteristics**

The incidence rate of NP was 16.4% (54/330) or 17.0 per 1,000 patient - days. When the incidence was classified by some socio-demographic characteristics, it showed that the incidence of NP in female, that in age group > 60 years and that in BMI ≥ 30 was relatively higher than that in male, that in age group ≤ 60 years and with BMI < 30, respectively. (Table 2)

#### **Incidence of NP classified by patient's health and medical instruments use**

When the incidence was classified by patient's health and medical instruments use, it showed that the incidence of NP in patients with cerebrovascular and metabolic syndrome was relatively higher than those with other diseases. The incidence of NP in patients with subconscious or unconscious, those with total dependence, and were admitted to hospital >20 days, and those who received

mechanical ventilator or received nasogastric tube and others were relatively higher than that those with consciousness, those with partial dependence or complete independence, and those admitted to

hospital  $\leq$  20 days, those without mechanical ventilator or nasogastric tube, and others, respectively. (Table 3)

**Table 2.** Incidence of NP among studied chronically ill patients classified by some socio-demographic characteristics and admitted units.

Socio-demographic characteristics and admitted units	No. of studied patients	Incidence of NP	
		No.	%
<b>Sex</b>			
Female	165	32	19.4
Male	165	22	13.3
<b>Age (years)</b>			
> 60	192	39	20.3
$\leq$ 60	138	15	10.9
<b>Body Mass Index (BMI, kg/m<sup>2</sup>)</b>			
$\geq$ 30 (obese)	25	5	20.0
25.0 - 29.9 (overweight)	81	15	18.5
18.5 - 24.9 (healthy)	164	24	14.6
< 18.5 (underweight)	60	10	16.7
<b>Admitted units</b>			
Male medical ward	135	10	7.4
Female medical ward	126	10	7.9
Sub-ICU	69	34	49.3

**Table 3.** Incidence of NP among studied chronically ill patients classified by patients' health and medical instrument use.

Patients' health status	No. of studied patients (n = 330)	Incidence of NP	
		No.	%
<b>History of underlying diseases</b>			
Cerebrovascular and metabolic syndrome	236	50	21.2
Other diseases	94	4	4.3
<b>Level of consciousness</b>			
Subconscious and unconscious	84	29	34.5
Consciousness	246	25	10.2



**Table 3.** (Cont.) Incidence of NP among studied chronically ill patients classified by patients' health and medical instrument use.

Patients' health status	No. of studied patients (n = 330)	Incidence of NP	
		No.	%
<b>Functional status</b>			
Total dependence	125	42	33.6
Partial dependence	82	8	9.8
Complete independence	123	4	3.3
<b>Duration of admission (days)</b> (Mean = 9.61, S.D. = 11.9, Range = 2-145)			
≤10	242	16	6.6
11 - 20	59	17	28.8
> 20	29	21	72.4
<b>Receiving mechanical ventilator</b>			
Yes	92	40	43.5
No	238	14	5.9
<b>Receiving nasogastric tube</b>			
Yes	113	47	41.6
No	217	7	3.2
<b>Aerosol therapy</b>			
Yes	77	41	53.2
No	253	13	5.1
<b>Antibiotic use before NP</b>			
Yes	186	53	28.5
No	144	1	0.7

### Causative bacteria isolated from chronically ill patients with NP

Totally, 70 sputum specimens were collected from 54 patients with NP to identify causative bacteria. The most predominant causative bacteria of NP were *Acinetobacter baumannii* 34.3%, *Pseudomonas aeruginosa* 24.3%, *Klebsiella pneumoniae* 14.3%,

normal flora 14.3%, *Escherichia coli* 4.3% and *Staphylococcus aureus* 4.3%. Additionally, some NP patients were infected with more than one types of microorganisms and most of *A. baumannii* isolated from NP patients (79.2%) were multiple-drug resistance. (Table 4)

**Table 4.** Causative bacteria isolated from sputum of NP patients.

Causative pathogens	NP (n = 70 specimens)	
	HAP (n, %)	VAP (n, %)
<i>Acinetobacter baumannii</i>	6 (8.6%)	18 (25.7%)
<i>Pseudomonas aeruginosa</i>	3 (4.3%)	14 (20.0%)
Normal flora	3 (4.3%)	7 (10.0%)
<i>Klebsiella pneumoniae</i>	3 (4.3%)	7 (10.0%)
<i>Escherichia coli</i>		3 (4.3%)
<i>Staphylococci Aureus</i>	1(1.4%)	2 (2.9%)
Non-fermentative Gram negative bacilli	1 (1.4%)	1 (1.4%)
<i>Staphylococcus spp.</i>		1(1.4%)

n = number of sputum of NP patients

Some patients with NP had more than 1 pathogens due to more than 1 specimen collection.

**Remark:** 79.2% of *A. baumannii* positive were MDR (19/24)

47.1% of *P. aeruginosa* positive were MDR (8/17)

33.3% of *E. coli* positive were MDR (1/3)

20.0% of *K. pneumoniae* positive were MDR (2/10)

## Discussion

In this study, incidence of NP among chronically ill patients was 16.4% or 17.0 per 1,000 patient-days. The incidence is higher than that of a previous study done in the United Kingdom which showed 10.9% of NP or 5.2 per 1,000 patient-days.<sup>(14)</sup> However, the incidence of NP in this study was lower than a study in Asia which reported the NP incidence of 28.3% or 21.8 per 1,000 patient-days in Thai patients.<sup>(6)</sup> All NP cases were divided into 2 groups: 40 patients with mechanical ventilator associated pneumonia from 92 observed patients (incidence rate = 43.5% or 32.7 per 1,000 ventilator day) and 14 NP patients who did not receive mechanical ventilator from 238 observed patients (incidence rate = 5.9% or 8.0 per 1,000 patient-days). The peak incidence was in those over 60 years old (20.3%) similar to studies

of Burton LA, *et al.*, (2016).<sup>(14)</sup> It might be due to the fact that older patients with several physiological and immunological changes are inherent to aging process. Moreover, most of them often spend a long time in hospital, they have relative immune compromise and are commonly exposed to multiple courses of antibiotics. This evidence occurred in the present study which demonstrated that patients with longer duration of admission or receiving the antibiotics having higher incidence of NP. Furthermore, older patients are more likely to have swallowing dysfunction leading to aspiration.<sup>(15,16)</sup> A previous study found that factors reducing host defense function predispose patients to colonization and development of pneumonia related to patients who presence of chronic diseases.<sup>(17)</sup> Likewise, the present study also found higher NP incidence in those with chronic

diseases. Additionally, the present study showed higher incidence of NP in those with duration of admission > 20 days (72.4%). It was similar to a study of Karatas M, *et al.* (2016) which reported a greater risk of NP in patients who were admitted to hospitals with  $26.7 \pm 16.3$  days.<sup>(18)</sup> Our study found higher incidence of NP in female patients (19.4%) which was different from previous studies of Golia S, *et al.* (2013) and Zhang Z, *et al.* (2015) that reported a greater NP incidence in the male.<sup>(19,20)</sup> This may be the female cases in this study were underlying as cerebrovascular and metabolic syndrome (76.4%: 126/165), age > 60 years (61.8%: 102/165), loss of consciousness (29.7%: 49/165) and impaired functional status (64.9%: 107/165). Additionally, the present study revealed that higher incidence in patients receiving mechanical ventilator and longer duration of admission. It was similar to the study of Rodriguez MH, *et al.* (2016) which found that patients who have total duration of mechanical ventilator (days  $\pm$  SD)  $8.91 \pm 14.49$  can develop ventilator-associated pneumonia and have statistical significance ( $P < 0.001$ ).<sup>(21)</sup> The study of Lee JM. (2012) found that those who had been endotracheal tube intubated for 6 days or longer had a higher level of bacterial biofilm compared with those intubated for less than 6 days.<sup>(22)</sup> The reason of endotracheal-tube (ETT) intubation promotes the aspiration of colonized oropharyngeal secretions across the ETT cuff. It disrupts the cough reflex, promotes accumulation of tracheobroncheal secretions and mucus, and provides a direct of pathogenic microorganisms to reach the lower respiratory tract increasing the risk of respiratory infection.<sup>(23)</sup> Moreover, a previous study found that VAP was associated to colonization of the ventilator circuit from collecting and

contamination from patient's secretion.<sup>(24,25)</sup> Humidifier is also a device condensing steam into droplets accumulating in ventilator circuit. These droplets serve as a reservoir of bacteria particularly gram negative bacilli. The droplets may directly enter into the lungs.<sup>(26)</sup>

For aerosol therapy, the present study showed that the incidence in patients with receiving aerosol therapy (53.2%) were higher than those without aerosol therapy (5.1%). This was similar to a study of Sopena N, *et al.* (2014) which showed higher incidence in patients with aerosol therapy (39.1%). It might be reason of microbial organisms invading to the lower respiratory tract by major routes, such as inhalation of infected aerosol from contamination of medical therapy equipment as well as aerosol nebulizer.<sup>(27,28)</sup> Aerosol nebulizers are reservoirs of bacteria particularly gram negative bacilli, likely *A. baumannii* in this study, they can contaminate with high levels of microorganisms if used repeatedly in the same patient.<sup>(26)</sup> The isolated bacteria from NP patients in our study were similar to studies of Zhang Z, *et al.* (2015) and Walaszek M, *et al.* (2016) which showed *A. baumannii* was the most common isolated pathogen, and other common isolated pathogens were *P. aeruginosa*, *K. pneumoniae*, *S. aureus*, and *E. coli* but most drug-resistance bacteria were *Methicillin-Resistance Staphylococcus Aureus* (MRSA) only.<sup>(20,29)</sup> A study of Lagamayo EN. (2008) in 10 Asian countries found the most common pathogens causing NP and VAP were *Acinetobacter spp.*, *E. coli*, *Klebsiella spp.*, and *P. aeruginosa* which was similar to this study.<sup>(30)</sup>

In this study, incidence of NP in sub-ICU was quite high as compared with male and female medical

units it might be due to the most of patients in sub-ICU were received mechanical ventilator. Additionally, sub-ICU might be similar to ICU not medical wards.

### Conclusion

The present study demonstrates that 16.4% (54/330 patients) developed NP. Incidence rate was 17.0 per 1,000 patient-days. Female patients, patients with age > 60 years, patients with underlying disease such as cardiovascular and metabolic syndrome, those with subconscious and unconscious, those with total dependence, those with longer admission and those with medical instrument used had relatively higher incidence of NP. Totally, 70 sputum specimens were collected from 54 patients with NP to identify the causative bacteria. The most predominant causative bacteria of NP were 34.3% of *A. baumannii*, and most of isolated *A. baumannii* (79.2%) were multi-drug resistance.

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