Original article

Medical Procedures and *Klebsella pneumoniae* Extended–Spectrum β–Lactamases Infection among Patients in Intensive Care Unit

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Abstract

Background : The bacterial infection caused from *K. pneumoniae* is a majority problem worldwide. These pathogens are frequently resistant to antibiotics. The antibiotic resistant these pathogens have become a serious problem and frequently found resistant to Extended-Spectrum β-lactamases.

Objective: To investigate the association between medical procedures and *Klebsella pneumoniae* Extended-Spectrum β - Lactamases (KPESBL) infection among patients who were admitted in the intensive care unit.

Material and Methods: A hospital based case control study (Case: Controls =1:2) and data were collected from medical records. All patients were admitted in the intensive care unit (ICU) of Roi Et hospital, Roi Et province between January 1, 2014 to October 30, 2015. Data analyses were used descriptive statistics, univariable analysis and multivariable analysis by multiple logistic regressions.

Results: All 40 cases were with KPESBL infected, most of them were male 57.5 percent mean age 65.1 years and 80 controls were without KPESBL infected, most of them were male 51.3 percent mean age 52.5 years. The multivariable analysis showed the risk factors of KPESBL infection among patients in ICU were patients age more than 60 years old ($OR_{Adj.}$ = 2.9 :95%IC; 1.30-6.35), admitted more than 7 days($OR_{Adj.}$ =3.6 :95%IC; 1.34-9.42), blood receive ($OR_{Adj.}$ = 2.5 :95%IC; 1.11-5.66) and cardio-pulmonary resuscitation ($OR_{Adj.}$ = 3.9:95%IC; 1.14-13.94). The invasive medical procedures were statistically significant with patients underwent with surgeries ($OR_{Adj.}$ = 3.2:95%IC; 1.32-8.16), urinary catheterization ($OR_{Adj.}$ =3.0:95%IC; 1.26-7.24), central line ($OR_{Adj.}$ =3.9:95%IC; 1.09-13.77), endotracheal tube ($OR_{Adj.}$ =5.1:95%IC; 1.76-14.72), ventilator ($OR_{Adj.}$ =5.8:95%IC; 2.00-16.62), cut down ($OR_{Adj.}$ =6.2:95%IC; 1.75-61.62) and tracheostomy ($OR_{Adj.}$ =2.8:95%IC; 1.16-7.07).

Conclusion: The medical procedures were the factors, which were associated with KPESBL infections among patients were admitted in the intensive care unit. All patients who have long time admitted and underwent with invasive medical devices should have special guideline for them.

Keywords: Intensive care unit, Medical procedure, *Klebsella pneumonia*, Extended-Spectrum β-Lactamases

นิพนธ์ต้นฉบับ

การสอดใส่อุปกรณ์ทางการแพทย์และการติดเชื้อ *Klebsella pneumoniae* Extended–Spectrum β–Lactamases ในผู้ป่วยที่หอผู้ป่วยวิกฤติ

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บทคัดย่อ

ที่มาและความสำคัญ : โรคติดเชื้อแบคทีเรียที่เกิดจากเชื้อ *K. pneumoniae* เป็นปัญหาสำคัญในประเทศต่างๆ ทั่วโลก ซึ่งเชื้อแบคทีเรียชนิดนี้มีอัตราการดื้อยาต้านจุลชีพเพิ่มสูงขึ้น การดื้อยาต้านจุลชีพของเชื้อ *K. pneumoniae* ที่เป็นปัญหาสำคัญและพบได้บ่อยคือ การดื้อต่อยาต้านจุลชีพในกลุ่ม Extended-Spectrum β-lactamases

วัตถุประสงค์ : เพื่อศึกษาความสัมพันธ์ระหว่างการสอดใส่อุปกรณ์ทางการแพทย์และการติดเชื้อ *Klebsella pneumoniae* Extended-Spectrum β-Lactamases ในผู้ป่วยที่เข้ารับการรักษาที่หอผู้ป่วยวิกฤติ

วิธีการศึกษา : รูปแบบการศึกษาแบบกลุ่มศึกษาและกลุ่มควบคุม (อัตราส่วน 1: 2) โดยใช้ฐานข้อมูลจากโรงพยาบาล ซึ่งดำเนินการเก็บข้อมูลประวัติการรักษาผู้ป่วยย้อนหลังจากเวชระเบียนของผู้ป่วยที่เข้ารับการรักษาในโรงพยาบาลร้อยเอ็ดระหว่างวันที่ 1 มกราคม 2557 ถึง วันที่ 31 ตุลาคม 2558 โดยสถิติที่ใช้ในการวิเคราะห์ข้อมูลได้แก่ สถิติเชิงพรรณนา การวิเคราะห์ตัวแปรเชิงเดี่ยว และการวิเคราะห์ ตัวแปรเชิงพหุ

ผลการศึกษา: กลุ่มศึกษาเป็นผู้ป่วยที่ติดเชื้อ KPESBL จำนวน 40 ราย ส่วนมากเป็นเพศชายร้อยละ 57.5 อายุเฉลี่ย 65.1 ปี กลุ่มควบคุมซึ่งเป็นผู้ป่วยที่ไม่ติดเชื้อ KPESBL จำนวน 80 ราย ส่วนมากเป็นเพศชายร้อยละ 51.3 อายุเฉลี่ย 52.5 ปี ผลการวิเคราะห์ข้อมูลโดยใช้สถิติพหุถดถอย พบปัจจัยที่มีความสัมพันธ์ต่อการติดเชื้อได้แก่ ผู้ป่วยมีอายุมากกว่า 60 ปี ($OR_{Adj.}$ = 2.9 :95%IC; 1.30-6.35) ผู้ป่วยที่นอนในหอผู้ป่วยวิกฤตินานมากกว่า 7 วัน ($OR_{Adj.}$=3.6 :95%IC; 1.34-9.42) ผู้ป่วยที่มีประวัติการได้รับเลือด ($OR_{Adj.}$= 2.5 :95%IC; 1.11-5.66) ผู้ป่วยที่ได้รับการปฏิบัติการช่วยฟื้นคืนชีพ ($OR_{Adj.}$=3.9:95%IC; 1.14-13.94) ส่วนปัจจัยเสี่ยงด้านการทำหัตถการและสอดใส่อุปการณ์ทางการแพทย์เข้าสู่ร่างกายได้แก่ ผู้ป่วยที่ได้รับการผ่าตัด ($OR_{Adj.}$=3.2:95%IC; 1.32-8.16) การใส่สายสวนปัสสาวะ ($OR_{Adj.}$=3.0:95%IC; 1.26-7.24) การใส่สายสวนหลอดเลือดดำส่วนกลาง ($OR_{Adj.}$=3.9:95%IC; 1.09-13.77) การใส่ท่อช่วยหายใจ ($OR_{Adj.}$=5.1:95%IC; 1.76-14.72) การใส่เครื่องช่วยหายใจ ($OR_{Adj.}$=5.8:95% IC; 2.00-16.62) การทำ cut down ($OR_{Adj.}$=6.2:95%IC; 1.75-61.62) และการเจาะคอ ($OROR_{Adj.}$=2.8:95%IC; 1.16-7.07)

สรุป: ผู้ป่วยที่เข้ารับการรักษาที่หอผู้ป่วยวิกฤติเป็นเวลานานและได้รับการรักษาด้วยการสอดใส่อุปกรณ์ทางการแพทย์ต่างๆเข้าสู่ร่างกายจะมีความเสี่ยงต่อการติดเชื้อ KPESBL ซึ่งผู้ป่วยกลุ่มนี้ควรที่จะมีมาตรการเฝ้าระวังเป็นพิเศษเพื่อป้องกันการติดเชื้อ

คำสำคัญ: หอผู้ป่วยวิกฤติ, อุปกรณ์ทางการแพทย์, Klebsella pneumonia, Extended-Spectrum β-Lactamases

Introduction

The bacterial infection cause from *K. pneumoniae* is a majority problem in worldwide.[1,2,3] These pathogens frequently infected in the urinary tract, respiratory tract and blood stream infection. The antibiotic resistant of *K. pneumoniae* was difficult to treat has become a serious problem and leads to treatment failure. The antibiotic resistant of *K. Pneumonia* frequently found to Extended-Spectrum β-lactamases and Cabapenams.[2,4,5]

Previous study done in Japan, which they found out the risk of *E. coli, K. oxytoca, K. pneumoniae, P. mirabilis* infection were patients underwent cerebrovascular disease, intubation/tracheostomy, major surgery within 60 days, antimicrobial usage more than 4 days during preceding 60 days especially aminoglycoside, oxazolidinone, trimethoprim/sulfamethoxazole tetracycline, fluoroquinolone and second- and fourth-generation cephalosporin.[6] In China, they found out that the risk factors of sepsis patients caused from multidrug-resistant *K. pneumoniae* were prolonged duration of mechanical ventilation before infection, a larger total number of days of mechanical ventilation, more days of antibiotic use before infection, more types of antibiotics used and use of third-generation cephalosporin and carbapenems.[7]

In Thailand, the incident of *K. pneumoniae* in the northeast region was 13.9%.[8] In 2015, the incident of *K. Pneumoniae* in Roi Et hospital were 1,566 isolations and has Extended-Spectrum β-Lactamases (ESBL) 702 isolations and *Klebsella pneumoniae* Extended-Spectrum β-Lactamases (KPESBL) infections among patients in ICU were 86 isolations. Although have many studies reported on the area of risk factors, epidemiology, genetic and incident of KPESBL infection but it is rarely reported in Thailand especially the study about the association between invasive procedure and KPESBL infection among admitted patients in ICU. The aimed of this study was to investigate the association between medical procedure and KPESBL Infection among patients admitted in ICU.

Material and Methods

This research design was a cases controls study and data used for this study were from hospital data bases. The populations of study were patients who admitted in the intensive care unit in Roi Et hospital, Roi Et province, Thailand between 1 January 2014 to 31 October 2015 and all data were retrieved from medical records. The definitions and criteria of KPESBL infection in this study were followed from the standard guideline from department of infectious controls of Roi ET hospital. The document for data collection was approved by one doctor and two nurses who responsible for infectious controls in the hospital. The data collections of cases and controls were by nurses and before data

collection were submitted all the documents to the director of the hospital and to the ethical committee of Roi ET hospital to approve and allowed for this study.

The study subjects in cases group, In the duration of study (during 1 January 2014 to 31 October 2015) the total numbers of KPESBL infection in ICU ward were 86 isolations from 58 patients, which 45 cases confirm of infection. In 45 cases were 3 cases age under 15 years old were not included to this study and 2 cases were can't access to medical records. The total numbers of cases was included to this study were 40 cases.

The criteria of cases: All 40 cases were patients admitted in ICU and have KPESBL infection. The confirmations of infection of cases came from the summery of medical recorded by doctors. All of cases were has the resulted for culture and sensitivity test, admitted more than 48 hours and age more than 15 years old were included to study. The exclusion criteria of cases were patients age under 15 years old, admitted in the ICU less than 48 hours, didn't have the doctor's summaries and culture and sensitivity test reported.

The criteria of controls: All 80 controls were without KPESBL infected and were randomization from patients who has admitted at the ICU and admitted same day with cases, admitted more than 48 hours and age more than 15 years old.

The variables of interested included the general characteristic of patients, day of admitted, history of blood receive, surgery and cardio-pulmonary resuscitation. The variables of invasive medical procedure were included ventilator, cut down, urinary catheterization, nasogastric tube feeding, central line, endotracheal tube and tracheostomy all variables were categorize in two group (No/Yes).

Statistical analysis: The statistic were used to analysis including descriptive statistics, univariable analysis which is to present crude odds ratio (Crude OR) and 95% CI, multivariable analysis were used to adjusted odds ratio by multiple logistic regression to present adjusted odds ratio (Adjusted OR) 95% CI and p-value. The statistical significantly was set at p-value <0.05. All analysis was used STATA version 12.0.

The ethic consideration: This research was approved by the ethical committee Roi Et hospital, Roi Et province. The reference number is 004/2559.

Results

The total numbers of cases were 40 patients with KPESBL infection. Most of them were male 57.5 percenr, mean age 65.1 years. In control group were 80 patients without KPESBL infection. Most of them were male 51.3 percent, mean age 52.5 years. In both groups most of them were agriculture, non-cigarettes smoking and non-alcohol drinking. Data show in Table1.

Table1 The general characteristic of cases and controls

Variables	Cases		Controls	
	Number (n=40)	Percent (%)	Number (n=80)	Percent (%)
Gender				
Male	23	57.5	41	51.3
Female	17	42.5	39	48.7
Age (years)				
≤60	25	36.5	30	37.5
>60	15	37.5	50	62.5
Mean±SD	65.1±15.2		52.5±17.9	
Occupational				
Agriculture	28	70.0	46	57.5
Government officer	1	2.5	5	6.3
Business owner	1	2.5	3	3.7
Company worker	2	5.0	10	12.5
Other	8	20.0	16	20.0
Cigarettes smoking				
No	30	75.0	55	68.7
Yes	10	25.0	25	31.3
Alcohol drinking				
No	31	77.5	57	71.3
Yes	9	22.5	23	28.7

The multivariable analysis of factors association with KPESBL infection were found out that patients age more than 60 years old ($OR_{Adj.}$ = 2.9 :95%IC; 1.30-6.35), patients who prolong admitted more than 7 days ($OR_{Adj.}$=3.6 :95%IC; 1.34-9.42), patients who has history of blood receive ($OR_{Adj.}$ = 2.5:95%IC; 1.11-5.66) and patients who has been underwent by cardio-pulmonary resuscitation ($OR_{Adj.}$= 3.9:95%IC; 1.14-13.94) were risked of KPESBL infection. Data show in Table 2.

Table 2 Show the factors associated with KPESBL infection among patients in intensive care unit.

Variables	Cases	Controls	OR_C(95%CI)	OR_A (95%CI)	p-value
	n(%)	n(%)			
Gender					0.382
Male	23(57.5)	41(51.3)	1	1	
Female	17(45.5)	39(48.7)	0.8 (0.36-1.67)	0.7(0.32-1.55)	
Age (years)					0.009**
≤60	25(36.5)	30(37.5)	1	1	
>60	15(37.5)	50(62.5)	2.8(1.27-6.08)	2.9(1.30-6.35)	
Day of admitted					0.011**
≤ 7 days	7(17.5)	32(40.0)	1	1	
>7 days	33(82.5)	48(60.0)	3.1(1.24-7.97)	3.6(1.34-9.42)	
Blood receive					0.027**
No	16(40.0)	46(57.5)	1	1	
Yes	24(60.0)	34(42.5)	1.8(1.02-4.39)	2.5(1.11-5.66)	
Surgery					0.011**
No	24(60.0)	62(77.5)	1	1	
Yes	16(40.0)	18(22.5)	2.3(1.09-5.22)	3.2(1.32-8.16)	
Cardio-Pulmonary Resuscitation					0.031**
No	33(82.5)	74(92.5)	1	1	
Yes	7(17.5)	6(7.5)	2.6(1.81-8.39)	3.9(1.14-13.94)	

OR_C= Crude Odds ratio; OR_A= Adjusted Odds ratio were adjusted for gender and age; 95%CI: 95% confident interval; p-value from multiple logistic regressions.

The multivariable analysis between medical procedures and risk of KPESBL infection were found statistically significant with surgery ($OR_{Adj.}$= 3.2:95%IC;1.32-8.16) and patients who has underwent with urinary catheterization ($ORZ_{Adj.}$=3.0:95%IC; 1.26-7.24), central line ($OR_{Adj.}$=3.9:95%IC; 1.09-13.77), endotracheal tube ($OR_{Adj.}$= 5.1:95%IC;1.76-14.72), mechanical ventilator ($OR_{Adj.}$ =5.8:95%IC; 2.00-16.62), cut down ($OR_{Adj.}$ =6.2:95%IC; 1.75-61.62) and tracheostomy ($OR_{Adj.}$ =2.8:95%IC; 1.16-7.07). Data show in Table 3.

Table 3 Show the medical procedure factors associated with KPESBL infection among patients in intensive care unit

Variables	Cases n(%)	Controls n(%)	OR_C (95%CI)	OR_A(95% CI)	p-value
Urinary Catheterization					
No	10(25.)	39(48.7)	1	1	0.013**
Yes	30(75.0)	41(51.3)	2.8((1.23-6.01))	3.0(1.26-7.24)	
Nasogastric tube Feeding					
No	22(55.0)	47(58.7)	1	1	0.159
Yes	18(45.0)	33(41.3)	1.7(0.81-3.74)	1.8(0.80-8.98)	
Central line					0.035**
No	33(82.5)	76(92.5)	1	1	
Yes	7(17.5)	6(7.5)	2.6(0.82-8.39)	3.9(1.09-13.77)	
Endotracheal tube					0.003**
No	5(12.5)	34(42.5)	1	1	
Yes	35(87.5)	46(57.5)	5.2(1.83-14.58)	5.1(1.76-14.72)	
Ventilator					0.001**
No	9(12.5)	36(45.0)	1	1	
Yes	31(87.5)	44(55.0)	5.7(2.03-16.13)	5.8(2.00-16.62)	
Cut down					0.010 **
No	35(87.5)	78(97.5)	1	1	
Yes	5(12.5)	2(2.5)	5.6(1.03-30.02)	6.2(1.75-61.62)	
Tracheostomy					0.022**
No	33(57.5)	78(73.5)	1	1	
Yes	7(42.5)	12(25.5)	2.1(0.93-4.62)	2.8(1.16-7.07)	

OR_C= Crude Odds ratio; OR_A= Adjusted Odds ratio were adjusted for gender and age; 95%CI: 95% confident interval; p-value from multiple logistic regressions.

Discussion

This study found out that there were many factors associated with KPESBL infection among patients underwent with invasive medical procedures in the ICU. Our study showed that the duration of admitted was risked factor of KPESBL infection it is consistency with previous study they found out that the long time admitted in the hospital were a risked of infection from these pathogens.[7,9,10]

The cardio-pulmonary resuscitation, cut down and the history of blood receive were the risked of KPESBL infection but no previous study supported. The multivariable analyses on the invasive medical procedures were found among patients who had surgery and tracheostomy were the risked of KPESBL infection it has been consistency with previous studies which they found patients who has surgery and underwent with tracheostomy were the risked factors of infection.[6,11] The study among mechanical ventilation, endotracheal tube, urinary catheterization and central line insertion were a high risked of KPESBL infection, which were consistency with previous studies.[12,13,14] The invasive procedure by urinary catheterization previous study find out that it was the factor associated with bacteremia.[15] It is consistency with ours finding which were found out that patients in ICU were has urinary catheterization were risked of KPESBL infection but this study not show about the association of this devices as risk of bacteremia. The benefit of this research is use to be evidence bases to prevent and control KPESBL infection.

Conclusion

Ours study finding that invasive medical procedures were important risk factors for KPESBL infection. Patients who underwent in this condition should have special guideline for them to prevent KPESBL infection.

Acknowledgments

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