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Original Article

Investigation on Clusters of Infection with Carbapenem-Resistant *Klebsiella pneumoniae* in Hospitals in 2011

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Abstract

The issue of healthcare-associated infections caused by multidrug resistant bacteria is becoming a major concern globally in both healthcare and public health sectors. In order to strengthen the surveillance of the relevant infections in this country, the Centers for Disease Control in Taiwan (Taiwan CDC) has collected carbapenem-resistant Enterobacteriaceae (CRE) strains from regional hospitals and medical centers through the implementation of research program. Following the identification of the KPC-producing (*Klebsiella pneumoniae* carbapenemase-producing) Enterobacteriaceae by the Taiwan CDC's laboratory, an epidemiological investigation was launched, which found two clusters of infection have occurred and all the cases involved were inpatients in the hospitals located in northern Taiwan. Based on the experiences obtained from the investigation, we explore how the hospitals involving cluster infections of KPC-positive patients rapidly collect data on laboratory test, prescribed drugs, and progression of disease during hospital stay, how they work together with health authorities to determine the areas at high risk of infections and to perform essential infection control measures and general control procedures to prevent the spreading of infections. In addition, we have examined the effectiveness of the MDR bacteria surveillance system and the relevant infection control measures in the hospitals.

Keywords: surveillance of multidrug-resistant bacteria, test of antibiotic resistance gene, epidemiological investigation of infection clusters

Introduction

The World Health Organization (WHO) indicated in the Report on the Global Burden of Health Care-Associated Infection (HCAI) published in 2011 that health care-associated infection will not only increase the cost of medical treatment for patients and the number of days in hospital but also can cause long-term disability and raise the possibility of developing the antibiotic-resistant bacteria. In addition, once a severe patient admitted to intensive care unit (ICU) is infected with multidrug-resistant (MDR) bacteria, the problem in medical treatment for the patient will probably become more troublesome and also the chance of the patient being fatal will be increased [1].

The MDR bacterial infections have become the issue of being the most worthy of paying more attention by healthcare and public health personnel among various issues related to health care-associated infections [2-5]. Since the antibiotics were clinically used for infection treatment in 1940's, the bacteria have developed resistance to them because of imprudent usage of the antibiotics and selective pressure of the bacteria. This has been the major reason resulted in the gradual increase in number of infections caused by antibiotic-resistant bacteria. Other factors contributing to the development of antibiotic resistance include abuse of non-prescribed antibiotics and use of inappropriate dosages and routes [6-7]. Furthermore, because of the development and promotion of medical technologies, some more active treatments (such as use of invasive medical device) were frequently applied to severe patients to maintain their lives. Inevitably, the occurrence of infections through hands of healthcare personnel during the treatment and care process will therefore be increased [8-9]. This also indicates that the control of the MDR bacterial infection has become more difficult.

Based on data from the European Union and the United States, an estimated of 25,000 people (around 5.1 per 100,000 people) from 29 countries in Europe have died from infections of MDR bacteria annually and 12,000 people (around 4.0 per 100,000 people) in the USA[10]. On medical expenditure, it is estimated that around 20 to 30 billion US dollars have spent for treatment of infections caused by antibiotic resistant bacteria yearly in the USA, with an average of around 18,588 to 29,069 US dollars per patient [11]. The data from the EU show that the MDR bacterial infections have led to additional 2.5 million person-days of hospital stay and 25,000 deaths annually, and the medical expenditure, therefore, increased around additional 9 million euros [12]. Except making the medical expenditure increase, MDR bacterial infections will also push medical institutions to take more infection control activities and, thus, add extra work to the workload of healthcare personnel. The most important is that the selection of antibiotics for clinical use will be limited due to antibiotic resistance and the kinds of novel antibiotics developed have been gradually decreasing in number [13-14]. Especially, for coping with MDR bacterial infections, the last-line antibiotics, such as carbapenems, have been used in clinical treatment. Therefore, to monitor the emergence of antibiotic-resistant strains and to prevent the spread of infections by these strains have been an important issue for countries of the world [5, 15-16].

Although antibiotics are the most appropriate drug prescribed for treatment of bacterial infections, they could not kill all of the bacteria. Therefore, in clinical practice, the development of drug-resistant strains become unavoidable and has occurred not just today. As a result, the biggest threats of it to medical section are that healthcare personnel will face the quandary of no effective antibiotics being available. This is the reason why the WHO repeatedly emphasized the meaning of the slogan "no action today, no cure tomorrow" throughout the global activities initiated for combating antibiotic resistance on the 2011 World Health Day [17]. Moreover, the WHO also issued an alert on the issue of antibiotic resistance and called on countries in the world to strengthen the four strategies for combating the problems of it. These strategies are to establish surveillance system for antibiotic resistance, to educate people about the rational antibiotic use (including healthcare workers and public), to formulate legislation related to stopping the selling of antibiotics without prescription, and to enforce the infection prevention and control measures (such as hand-washing measures) in healthcare facilities [18]. Therefore, each country should strengthen the implementation of rational antibiotic use and infection control measures, i.e. the enforcement of antimicrobial stewardship program (ASP), to delay the development of antibiotic resistance [19].

In addition, surveillance on changes of antibiotic resistance patterns is also very important. In order to understand the trend in antibiotic resistance, the Taiwan CDC has established the Taiwan Nosocomial Infections Surveillance System (TNISS). Starting in 2007, hospitals were required to provide data of cases meeting the case definition for surveillance of nosocomial infections through the TNISS for routine analysis. Furthermore, in response to the isolation of antibiotic resistant strain with New Delhi metallo-β-lactamase 1 (NDM-1) gene in 2101 [20]. Taiwan CDC promptly added the enteric infections caused by strain of NDM-1 Enterobacteriaceae to the list of category 4 communicable diseases in the same year. For some suspicious cases not totally meeting surveillance case definition, hospitals are also asked to report them to the National Notifiable Disease Surveillance System (NNDSS) and send isolates to laboratory at Taiwan CDC for confirmation. In 2011, Taiwan CDC launched two research programs to conduct surveillance on antibiotics resistance strain of Gram-negative Enterobacteriaceae and determine changes of their resistance gene. Project-1 is the Collection and Epidemiological Analysis of Data on Genetic Variation and Clinical Information of MDR Bacteria in Taiwan, and Project-2 is Epidemiology and Mechanism of Resistance of Enteric Bacteria to Carbapenem in Taiwan.

In these projects, the *Klebsiella pneumoniae* carbapenemase (KPC) has been included as one of the items tested for detection of antibiotic resistance genes. The KPC, a type of β-lactamase [21] is classified as class A β-lactamase, based on Amber molecular structure classification, which contain a serine amino acid at its active site, and group 2f β-lactamase, based on its function [22-23]. The bacteria genetically containing β-lactamase is commonly found in strains of Enterobacteriaceae, the gram-negative bacteria. Although the bacteria

with extended-spectrum β-lactamase (ESBL) have developed resistance to the third generation and part of the fourth generation cephalosporins, but they are still sensitive to carbapenem, the last-line antibiotics for treatment of cases suffered from severe infections [24]. The KPC has attracted global attention since it was detected in 2001 for the characteristics of being able to rapidly spread through its plasmid and having developed resistance to carbapenem. Between December 2002 and February 2003, infections caused by KPC-producing bacteria were spreading in several hospitals in New York City. In Taiwan, the National Taiwan University Hospital has reported in 2010 about an imported case from Zhejiang Province, China [26]. In 2010, two other cases positive for KPC were detected in a hospital in Taiwan. One of them was suspected to be transmitted by another one, an imported case, while they were staying in the same ICU at the same time [27].

This study describes the investigation and control of clusters caused by KPC-producing bacteria in hospitals detected through the implementation of Project-1 by Taiwan CDC. The existing strategies and measures for nosocomial infection control were reviewed, and relevant operation procedures are provided as a guideline for medical institutions in dealing with the similar infections.

Materials and Methods

A. Collection of bacterial strains

The bacterial strain, carbapenem-resistant Enterobacteriaceae (CRE), was collected from inpatients in 13 regional hospitals or medical centers during the Project-1 implementation period from June 2011, the start time of the Project-1, to 31 December 2011 (strains were collected during June and October). In principle, a maximum of one resistant strain was required for a single patient. For patients with multiple sites of infection, the priority was given to the strains isolated from blood specimens. While the number of CRE strains detected by a hospital was less than the quota assigned by the Project-1, the hospital can either give the quota to other hospitals or send another Gram-negative strain, *Acinetobacter baumannii* (AB strains), which is also a carbepenem-resistant strain (CRAB strain). A total of 500 resistant strains were expected to be collected through the Project-1. The resistant strains were first collected by the responsible hospital on a periodic basis, and then sent to the laboratory at Taiwan CDC for genetic test and determining of antibiotic resistance.

In order to understand the epidemiological characteristics of the patients infected with the bacteria resistant to antibiotics, and for the purposes of that infection control intervention measures could be timely taken when strains containing unique resistance gene (such as NDM-1 or KPC) were detected or cluster of patients infected with resistant strains occurred, the hospitals participating in the Project-1 were required to provide data on the patients. These data include medical record numbers, gender, date of birth, address of residence, name of disease, sites of infection, antibiotics prescribed, duration of taking

antibiotics, invasive treatment administered, date of admission, date of discharge, date of death, date of strain collected, and Acute Physiology and Chronic Health Evaluation (APACHE) Ⅱ.

B. Antibiotic susceptibility testing and antibiotic resistance gene typing

a. Antibiotic susceptibility testing:

An automated identification system, BD Phoenix, was used to run the bacterial strain differentiation and antibiotic susceptibility testing. A NMIC/ID panel with serial two-fold dilutions was applied to perform antibiotic susceptibility testing to obtain the values of minimal inhibitory concentration (MIC) for each antibiotic. The MIC values for Tigecycline were determined by using commercial kits (E-test strips).

b. Genetic typing of antibiotic-resistant strains and analysis on clusters of infection:

The polymerase chain reaction (PCR) test was performed to determine type of currently known carbapenemase genes, including KPC gene of class A β-lactamase; NDM-1, VIM, IMP, SPM, and GIM genes of class B β-lactamase; and OXA gene of class D β-lactamase.

Results

A total of 16 cases infected with KPC-producing strain were identified during the study period, including two clusters of infection occurred in hospital I and L with six and seven cases, respectively. The other three cases were reported from two other hospitals. All of the hospitals having KPC-positive cases are located at Taipei City or New Taipei City

In response to the occurrence of the clusters, Taiwan CDC actively conducted a KPC survey for 91 CRE strains identified from specimens sent by hospitals in 2011 through routine surveillance of cases infected with strain of NDM-1 Enterobacteriaceae. The survey shows that KPC gene was found in five strains from three hospitals, including one located in southern Taiwan and two at new Taipei City.

An active surveillance was continued in the two hospitals with cluster of infections, which CRE strains isolated by the hospitals after the cluster events were sent to the laboratory at Taiwan CDC for further analysis. The outcome shows that three KPC-positive strains were identified from I Hospital and L Hospital, respectively. Two of them were detected from strains isolated from patients through active surveillance while they were referred to B hospital. The other four strains were isolated from patients who have admitted to the hospitals for more than 72 hours.

In 2011, a total of 27 KPC-positive strains were identified through various surveillance methods, including implementation of research program, active surveillance in hospital with cluster event of infection, and routine surveillance of the NNDSS. All of the 27 KPC-positive strains belong to the strain of Klebsiella pneumonia (KP strain). Detailed information on distribution of antibiotic-resistant strains and KPC-positive strains is shown in Table 1.

Table1. Number of antibiotic-resistant strains* collected through research projects and routine surveillance system

Collection Routes	ıospitals	*E. coli*	*K.pneumoniae*	**Other Enterobacteriaceae	ا. *baumannii*	*P. aeruginosa*	Total	
	A				50		50	
	B	31	93(2) *	2	2		128	(2)
	C	1			8		9	
	D						0	
	E	4	9	1			14	
	F	4	12	4	36	1	57	
Project-1	G	1	15	1			17	
	H	7	25				32	
	I***	10	35(6)				45	(6)
	J0	1	39(1)	1			41	(1)
	K	11	9	14			34	
	L***	9	35(7)	1			45	(7)
	M	2	9	9	20		40	
Sub-total		81	281(16)	33	116	1	512	(16)
Project-2		53	122				175	
NNDSS		23	64(5)	13			100	(5)
Active surveillance	9		15(3)				15	(3)
	12		11(3)				11	(3)
Total		157	493(27)	46	116	1	813	(27)

Note: #: Strain isolations were conducted by hospitals, but KPC gene identifications were performed by Taiwan CDC Strains from Project-1 were performed by the National Health Research Institute. The calculations of the number of strains were done on the basis of the date of specimen collection.

*: The values in the parentheses are number of KPC-positive strains.

**: These include C. *koseri*, En. *Aerogenes*, E. *cloacae*, S. *marcescens*, K. *oxytoca*, etc.

***: The hospitals occurred clusters of KPC-producing strain infections.

The further analysis on the 27 cases infected with KPC-positive strains shows that 59.3% are male and 40.7% are female. The age group of over 80 years old has the highest percentage, around 59.3%, followed by the group of 61-80 years of age, around 25.9%, and the group of under 60 years of age records the lowest percentage, only 14.8%. The majority of the strains was isolated from sputum specimen (51.9%), followed by blood and urine, accounting for 18.5% and 14.8%, respectively. The analysis on the time interval from the date of admission to the date of specimen collection shows that most of strains were isolated from specimens collected during 4 to 30 days after admission to hospitals, accounting for about 63.0%, followed by 0 to three days, accounting for 18.5%. Two of the five KPC-positive cases from whom the specimens were collected within three days after being admitted to hospitals were identified through the screen test of the active surveillance initiated immediately after the occurrence of cluster events in the hospitals. Based on the active surveillance, all patients newly admitted to the hospitals would receive screening test for KPC-producing strains. This fact supports that the emergency response administered by Taiwan CDC and hospitals occurring cluster event of infections with KPC-producing bacteria has been working effectively, which the CRE surveillance was strengthened by enforcing active screening test for patients newly admitted to or suspected in the hospitals. The analysis on characteristics of cases infected with KPC-producing bacteria is presented in Table 2.

Figure 1 shows that the bacterial strains were collected during the period between June and October for Project-1. For the two hospitals cluster events, the specimens that the isolates were detected with KPC gene were collected during June to August (I Hospital) and July to October (L Hospital). To future explore the cluster, Taiwan CDC in cooperation with the involving hospitals initiated this investigation. Moreover, the hospitals also implemented essential infection control measures and performed active surveillance.

Table2. Analysis on number of KPC-positive cases in 2011

characteristics		N=27	%
Sex	Male	16	59.3
	Female	11	40.7
Age	Under 20	0	0
	21-40	2	7.4
	41-60	2	7.4
	61-80	7	25.9
	Over 81	16	59.3
Current situations of the cases *	Hospitalization	7	25.9
	Discharge	6	22.2
	Death	14	51.9
Types of specimens	Sputum	14	51.9
	Blood	5	18.5
	Urine	4	14.8
	Woud	1	3.7
	End of intubation	1	3.7
	Pus	1	3.7
	Ascetic fluid	1	3.7
Days from the date of admission to the date of sampling	0-3	15	18.5
	4-30	17	63.0
	31-90	4	14.8
	91-180	1	3.7

*:The situations of the cases were determined when the investigations were conducted after they were identified as KPC-positive cases.

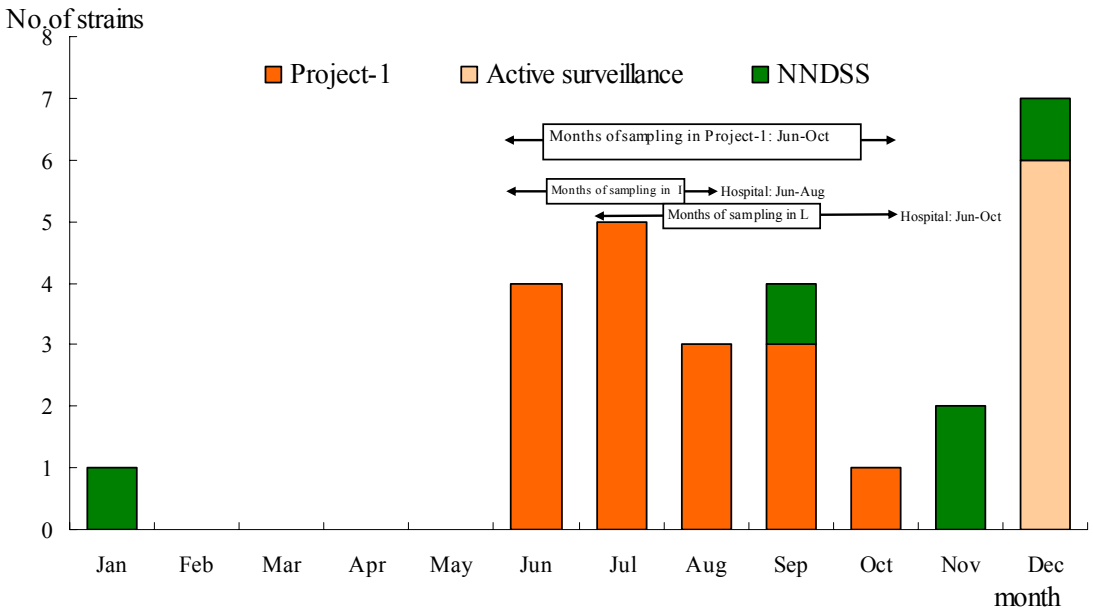

Figure1. Number of KPC-positive strains, by month of specimen collection and surveillance routes.

Either during or after the period of investigation of the clusters, once KPC genes were detected from the CRE strains isolated from specimens collected through active or routine surveillance, the hospitals would have to provide data on the antibiotic resistance testing results of the strains, as shown in Table 3. This table indicates that all strains have developed resistance to almost all of the antibiotics except amikacin, gentamicin, sulfamethoxazole/ trimethoprim, and tigecycline.

Besides resistance analysis, an epidemiological analysis of the KPC-positive cases based on the data offered by the hospitals, including data of hospitalization duration, ward bed/record of between-beds movement, and specimen collection date. In order to identify the wards at high risk of infection so that the hospitals could strengthen the implementation of environment disinfection, perform active surveillance, and enforce infection control measures, the information on wards that the KPC-positive cases have stayed during the period before the specimens were collected was analyzed to determine the overlapping periods or temporal associations with each other of the cases occurred in the same wards.

The analysis of temporal association with each other of KPC-positive cases occurred in I Hospital and L Hospital based on data of the duration of hospitalization, date of specimen collection, and record of between-beds movement is shown in Figure 2. The shortest time interval between the date of admission to hospital and the date of specimen collection of the 16 cases was equal to or less than 24 hours (case L-6) and the longest time interval was 64 days (case I-4). In Figure 2, different colors have been used to represent different wards. Taking the I Hospital as an example, all the cases besides case I-5 have stayed in ICU room 5C before the date of specimen collection, but the I-5 case has stayed in ward room 8B before specimen collection, which is partially overlapping with the period for I-3 case who has stayed in the same room during 16-22 August, 2011. From an epidemiological point of view, we consider

Table3. The data on antibiotic resistance testing of CRE strains with KPC-producing gene in 2011

Antibiotics	No. of tested strains	No. of resistant strains	Percentage of resistant strains (%)
Ampicillin	25	25	100.0
Ampicillin/Sulbactam	24	24	100.0
Cefazolin	26	26	100.0
Cefepime	16	16	100.0
Cefmetazloe	12	12	100.0
Cefuroxime	12	12	100.0
Ceftriaxone	20	20	100.0
Ciprofloxacin	23	23	100.0
Levofloxacin	7	7	100.0
Amikacin	19	4	21.1
Gentamicin	26	5	19.2
Ertapenem	25	25	100.0
Imipenem	16	16	100.0
Piperacillin/Tazobactam	20	20	100.0
Sulfamethoxazole/Trimethoprim	17	11*	64.7
Tigecycline	5	0	0.0

*: Including two intermediate resistant strains.

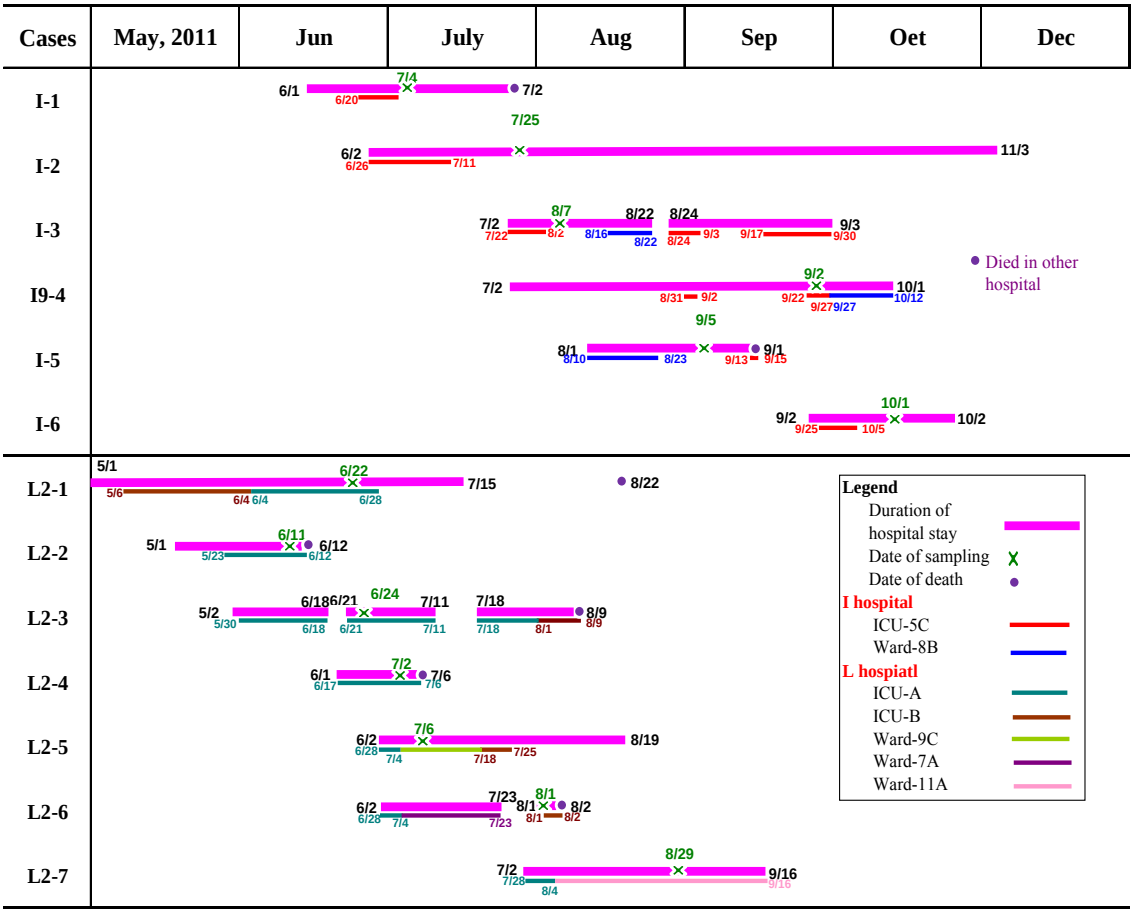

Figure2. Analysis on data of duration of hospital stay, date of specimen collection, and between-beds movements

that room 5C or 8B was at high risk of infection. Taking the L Hospital as another example, all the seven cases have stayed in ICU area A before the date of specimen collection. Three of them, case L-5, L-6, and L-7, specimens were collected after they have been moved from ICU area A to other ward rooms for 2, 27, and 25 days, respectively. Therefore, except ICU area A, other ward rooms, including room 9C, 7A, and 11A, were probably also at high risk of infection.

Discussions

The current data show that the first identified KP strain containing KPC-producing gene was originated from an imported case in 2010. Another KPC-positive KP strain identified in the same year was also an imported case. Unfortunately, the latter case has led to the infection of another patient while they were staying together in the coronary care unit. In any case, these incidents have sent two warning signals about the issue of antibiotic resistance infection. The first is that we should pay more attention on the surveillance of antibiotic resistant bacteria so that imported cases could be timely detected and effective response measures could be taken immediately. The second is that infection control measures for the patient infected with antibiotic resistant bacteria should be strengthened and enforced in order to avoid the occurrence of nosocomial infections or health care-associated infections.

The existing strategies for combating multidrug-resistant bacteria can be reviewed and improved from three aspects. These are that how hospitals and health authorities establish the measures for monitoring drug-resistant bacteria, the models for effectively responding to cluster events of drug-resistant bacterial infection, and the incentive payment system that can direct hospital to the way of strengthening their infection control measures.

A. Systematic surveillance of antibiotic resistant bacteria

To effectively prevent the occurrence of health care-associated infections and to minimize the probability of occurrence of the infections with antibiotic resistant bacteria, health care institutions will have to establish a hospital-wide surveillance system in ordinary time, conduct further analysis on antibiotic resistant genes through regional and inter-institutional cooperation, and to strengthen the implementation of infection control measures for patients at high risk population, so that the existing patient referral activities normally occurred among health care institutions will not be enough to become a risk factor that makes antibiotic resistant bacterial infection become a cross-institutional cluster event of infection.

The high risk population means elderly patients with chronic disease or requiring endotracheal intubation from long-term care institutions or respiratory care wards who either develop fever symptom at the time of admission to hospital or are diagnosed as a suspected case of bacterial infection by physician. If hospital can perform active screen test for patients meeting these conditions through surveillance system or treat them as the patient infected with antibiotic resistant bacteria at the time when they are admitted to the hospital, the probability of health care-associated infection will be reduced. In addition, if the medical information system within a hospital can link the database maintained by laboratory about the antibiotic resistant bacteria to the system of infection control room and provide retrieval and searching function for infection control personnel, the hospital will be able to timely isolate the patient infected with antibiotic resistant bacteria and strictly require health care workers to exactly follow relevant infection control measures, so as to prevent the spread of antibiotic resistant bacterial infection.

There are also some weaknesses that need to be improved by central health authorities about the current strategies of nation-wide surveillance of antibiotic resistant bacteria. For example, the TNISS established for monitoring of antibiotic resistant bacterial infection is not connected to the systems working for transport of bacterial strain. Moreover, although the NNDSS that contains the function for notification of CRE strains also provides a channel that could serve a function for reminding hospitals of notifying the cases not totally meeting the notification definition of NDM-1 Enterobacteriaceae infection, it is not a mandatory process for hospitals. Therefore, except asking hospitals to send CRE strains to Taiwan CDC for further testing of antibiotic resistance gene, in order to expand surveillance activities, some significant antibiotic resistant strains commonly found in hospitals also collected currently through the implementation of research program, including the strains of vancomycin-resistant

Enterococcus (VRE), vancomycin-resistant *Staphylococcus aureus* (VRSA), vancomycin-intermediate *Staphylococcus aureus* (VISA), and carbapenem-resistant *Acinetobacter baumannii* (CRAB). In reference to the results of the research program, the next steps would be amendment of the regulations to mandatorily require hospitals send selected antibiotic resistant strains that are newly emerged and internationally important, or are natively important, to the Taiwan CDC for further testing. Hopefully, these procedures will be able to elevate the timeliness and completeness of the surveillance, to update the epidemiological information on changes of the antibiotic resistance genes, and to assist hospitals to conduct intervention, evaluation, and improvement activities in the clusters of nosocomial infection.

To take the clusters of infections in I Hospital and L Hospital as an example, if the Taiwan CDC had not launched active surveillance and epidemiological investigation activities to strengthen the surveillance and control of MDR bacteria through Project-1, even though the hospitals have detected antibiotic resistant strains and have taken infection control measures based on existing guideline, the reasons causing the clusters would have not been clarified and the infections might have not been prevented. Therefore, for both health care institutions and health authorities, the first priority in the implementation of control strategy for antibiotic resistant bacterial infection would be to plan and to establish effective surveillance activities so that the possible problems can be identified and solved timely.

B. Standardization of procedures for investigation of MDR bacterial infection

While infection clusters occur, hospitals and health authorities will have to take relevant control strategies, such as to block the route of spread and trace the possible infection source. In order to block the spread of infection, except that health care workers should more closely follow relevant infection control regulations and guideline in the process of caring patients infected with MDR bacteria, to track and determine the source of infection is also important. For example, the process of between-beds or between-wards movements on the date of specimen collection of the patients infected with antibiotic resistant bacteria in the I Hospital and L Hospital has made the determination of possible infection sources more complicated and will inevitably extend the geographical areas where the activities of blocking the spread of infections are supposed to be taken. Moreover, the infection clusters occurred in a hospital will add workload to the health care workers if no extra support staff is deployed. In order that the routine work can be operated normally, the effectiveness of infection control in the hospital will definitely be decreased. Therefore, the model for dealing with the infection clusters would be to combine the first-line clinical healthcare workers and infection control staff in the hospital and employee in health authorities to work together, so that the infection could be blocked within the shortest time.

After the hospitals were informed of the positive test report of the patients with suspected MDR bacterial infection, it is important for the hospital to collect complete data about the hospital stay records, antibiotics use, between-beds movement, and laboratory test reports of the patients (such as basic information of the patients, paper sheet on analysis of high risk areas,

and floor plan of the inpatient ward), and to analyze them as soon as possible, so that the infection source or high risk areas could be determined. In addition, to integrate manpower and resources of the infection control unit and clinical unit in the hospital and to perform effective intervention will be two of the key points that determine whether the infection clusters could be effectively controlled, as might be expected.

In some instances, the infections may originate from sources in long-term care institutions where the patients have resided before they were admitted to the hospital. For these cases, the investigation of infection sources and activities of infection control will have to be extended to those institutions through the assistance of local health authorities or Taiwan CDC. When MDR genes were detected, if the time interval from the date of specimen collection to the date of admission to hospital is less than 72 hours, we can define that the infections are acquired from community (i.e. possibly not a nosocomial infection). Under this situation, the staff in the Branch Office of the Taiwan CDC or local health authorities will intervene and participate in the investigation on the medical care that the patients have received before being admitted to the hospitals, the record of bacterial test having been done for the patients, and the identification of infection sources so as to effectively prevent spread of antibiotic resistant bacterial infections. In order to more efficiently handle similar infection clusters in the future, we have compiled the "Procedures for Control of MDR Bacterial Infection in Hospital " (Figure 3), based on the experience from treating the above described infection clusters and the contents of the "Procedures for Notification and Treatment of Patients infected with NDM-1 Enterobacteriaceae" designed in 2010.

Except to strengthen the internal infection control practices, the hospitals involving the events of infection clusters also conducted active surveillance for patients when they were admitted to the hospital from areas (such as respiratory care wards) at high risk of infections by performing laboratory screen test. As a result, two of the six KPC-positive cases identified through active surveillance activities were detected by the hospitals. Based on the identification of the cases, the hospitals, therefore, took necessary infection control measures to prevent another infection from occurring and made every effort to ensure the safety of patients. Their experiences have provided a good model to other hospitals for dealing with similar events.

C. To enforce infection control measure in hospitals by improving health insurance payment system

The factors associated with the occurrence of cluster infection with MDR bacteria in a hospital include enforcement of infection control practices (such as hand hygiene) and cleaning and disinfection procedures (including devices/instruments used in or in contact with a patient) in ordinary time, treatment and management of the MDR bacterial infection cases (such as isolation), and implementation of active screen test for patients at the time of admission to the hospitals when they were referred from areas potentially at high risk of MDR bacterial infections. However, the establishments or enforcements of the infection control measures will

largely increase the cost of operation in hospital, and whether hospitals are willing to spend more money on the infection control practices is inseparable from items eligible for reimbursement from the health insurance payment system.

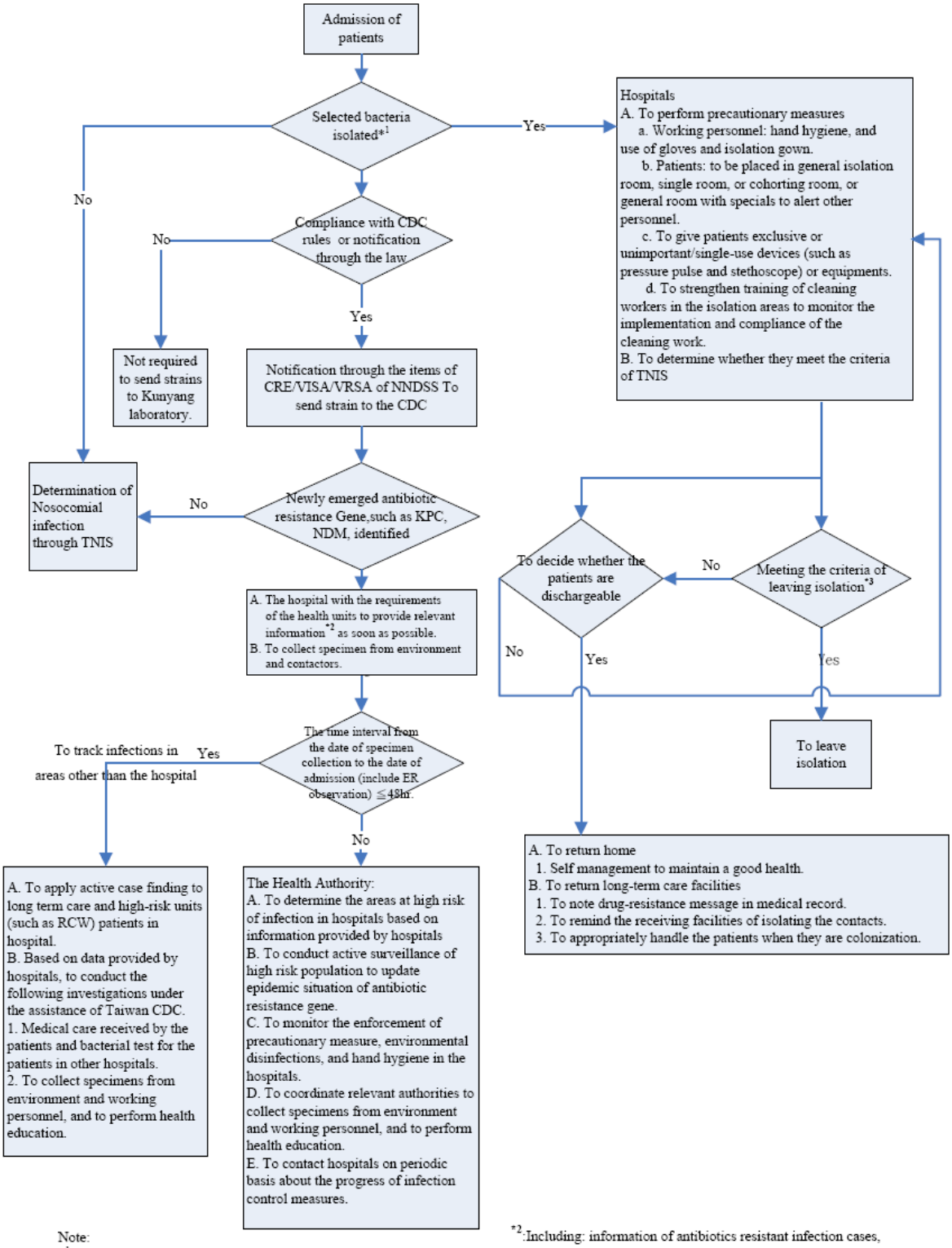

Figure3. Procedures for control of MDR bacterial infections in hospitals

Although health care institutions have the consensus that the medical expenditures for treatment of patients infected with antibiotic resistant bacteria will increase and, based on current regulations, the institutions can be reimbursed by the current health insurance payment system for the increasing expenses, the spending for improving and enforcing infection control measures is absorbed by hospitals or patients themselves. This development will inevitably discourage hospitals to push the implementation of infection control measures. Eventually, the medical expenses related to antibiotic resistant bacterial infections will affect the finance of health insurance.

If the costs spent for improving infection control activities (such as the difference of cost for isolation treatment, cost for active screening test of population at high risk, and the cost for elevating medical quality i.e. quality-based payment policy) in a hospital are covered by health insurance payment system but the expenses used for treatment of patients suffered from health care-associated infections are not reimbursable from health insurance budgets, the hospitals will have more motivations to push and improve infection control measures. The recommendations for improving infection control practices in hospitals are as follows:

a. reimbursement of expenditures for isolation treatment

The isolation treatment process itself is a health care activity that can not only remind of health care worker to cautiously perform infection control measures but also can prevent other patients in the same ward from getting infection, and, thus, stop the spread of antibiotic resistant bacteria. However, the current health insurance payment system did not cover the cost arising from isolation treatment of the patients infected with antibiotic resistant bacteria. This phenomenon has led the hospitals to be unable to generally enforce the isolation treatment for the patients infected with antibiotic resistant bacteria. Instead, they have mostly treated these patients in general wards along with patients having other diseases, increasing the risk of cross-infection between them.

b. reimbursement of cost for active screening test of patients from high-risk population

If the hospitals could perform active screening test of MDR bacteria for patients from high-risk population, including those from long-term care institutions, respiratory care wards, ventilator dependent care units, or other units caring patients with serious illness (such as ICUs, burn centers, or oncology units) at the time when they are admitted to the hospitals and having one of the following conditions: fever, leucocytosis, elderly aged over 65 years and having chronic disease, or under intubation, they will be able to early perform isolation treatment for patients with a positive test result to avoid transmitting to other patients during hospital stay. Although these are effective strategies in reducing the infections of antibiotic resistant bacteria, the current health insurance payment system did not pay the cost incurred from the implementation of the strategies. Therefore, it is difficult to ask hospitals to enforce the active screening test in consideration of the spending.

c. quality-based incentive payment system

Although the Bureau of National Health Insurance (BNHI) has made contract with hospitals, which the medical expenditure was paid by maximum allowance budget system to contain the rapidly increasing health care cost, the hospitals still can submit application for refund of medical expenditure to the BNHI on the basis of the amount of expenses for medical services provided. However, these regulations did not bring enough incentive for hospital to pay more attention to the activities of control of antibiotic resistant bacterial infection because of cost consideration. If the effectiveness of quality improvement intervention, such as the rate of the appearance of antibiotic resistant bacteria in the hospital and the volume of antibiotics prescribed, can be used as a reference indicator for reimbursement of medical expenditure, the hospitals may have more incentives to improve infection control measures.

Conclusions

The surveillance of CRE through the implementation of Project-1 found that all the strains carrying the KPC resistance genes belong to the carbapenem-resistant *Klebsiella pneumoniae* (CRKP) bacteria. The areas at high risk of infection are the ICUs in each of hospitals involving clusters of infection. The health care institutions having KPC-positive cases are geographically concentrated in northern areas of Taiwan. We have to do our best to stop the spread of bacteria with KPC resistance genes as soon as possible.

Based on the data obtained from surveillance of antibiotic resistant bacteria in ICU of regional hospitals or medical centers in Taiwan conducted by Taiwan CDC [28], the percentage of CRKP bacteria increased from 1.2% of all KP bacteria in 2003 to 8.4% in 2010, representing a seven-fold growth during the eight-year period. The data from both investigation of infection cluster and ordinary surveillance shows that the burdens of medical expenditure incurred from MDR bacterial infections exhibited an increasing trend, which have generated threats to public health to the extent that should not be neglected. The key points for the control of the infection with MDR bacteria will return to the rational use of antibiotics and the enforcement of infection control measures by health care institutions.

Since the number of patients having a prolonged stay in health care institutions for various chronic disease and receiving invasive treatment and medical therapy is continually increasing, and the pattern of medical care-seeking behaviors of civilians in Taiwan is impossible to be changed within short period, to eradicate the patients with infections of antibiotic resistant bacteria is difficult. Hospitals should strengthen the analysis and discussion of data from various surveillance systems to find out the exact causes that lead to the infections of patients or clusters with MDR resistant bacteria, so that the right control measures can be performed and the quality of health care can be elevated. In addition, the health authorities should play a more active role in integrating regional

resources for pushing antibiotic management activities among health care institutions by creating a platform, so that the health care institutions in the region will cooperate more closely. These include, based on the type of antibiotic resistant bacteria in individual region, to establish guideline for rational use of antibiotics, to institute standard procedures for management of antibiotics, and to develop benchmarking activities and plan various motivation programs so that these guidelines and procedures could be smoothly enforced. Of course, in the long run, the most effective ways to thoroughly solve the problems associated with antibiotic resistance are to conduct fundamental review of the current health care payment system and to gradually establish regularized surveillance systems.

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Outbreak Investigation Express

An Amoebiasis Outbreak at A Psychiatric Sanatorium in Tainan City in February 2012

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Abstract

In February 2012, an amoebiasis outbreak occurred at a psychiatric sanatorium in Tainan City. A 54-year-old resident of the sanatorium was sent to a hospital for medical treatment due to symptoms of diarrhea, bloody stools and fever. The resident was notified as a suspected amoebiasis case by the hospital, and confirmed after laboratory examination by the Taiwan Centers for Disease Control (Taiwan CDC). To further gauge the infection extent, following the enzyme-linked immunosorbent assays (ELISA) screening and polymerase chain reaction (PCR) test for all residents, eight residents were confirmed. In the end, a total of nine amoebiasis cases were detected in the sanatorium (all were residents, no staff) with an attack rate of 6.7%. As the residents of the psychiatric sanatorium had poor daily care and sanitary habits, and amoebiasis was not included in the sanatorium's annual routine health examination, infection control was relatively not easy. The residents with psychiatric disabilities in institutions are usually difficult to manage their personal hygiene, so that latent infection of *Entamoeba histolytica* is not uncommon among residents. For institutions with high frequency of outbreak clusters, it is recommended to adopt the *Entamoeba histolytica* screening as a routine check item in the annual health examination for residents. The implementation of diarrhea monitoring, quarantine, advocacy of hand washing for staff and residents, strengthening environmental disinfection in institutions, and complete treatment for confirmed cases, are all the focal works for outbreak prevention.

Keyword: Amoebiasis

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