First report on antibiotic use and resistance in Vietnam hospitals in 2008-2009

A report from the Ministry of Health of the Socialist Republic of Vietnam in collaboration with the Global Antibiotic Resistance Partnership and Oxford University Clinical Research Unit.

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ABBREVIATION

ATC: Anatomical Therapeutic Chemical Classification System

CLSI: Clinical and Laboratory Standards Institute

DDD: Defined Daily Dosage

GARP: Global Antibiotic Resistance Partnership

HTD: Hospital for Tropical Diseases

MoH: Ministry of Health

NHTD: National Hospital for Tropical Diseases

OUCRU: Oxford University Clinical Research Unit

TB Hospital: National Tuberculosis Hospital (National Lung Hospital)

SUMMARY

The problem of antimicrobial resistance has received relatively little attention in many developing countries and has remained hidden because of lack of proper resistance surveillance. In Vietnam, a national resistance surveillance program existed until 2005, but was stopped due to lack of donor funding. As antibiotic use is an important driver of antimicrobial resistance, it is essential to do surveillance for both antibiotic use and resistance and report on this to the medical community, scientific community and policy makers. The Global Antibiotic Resistance Partnership (GARP) is a new initiative of Resources for the Future (RFF), a nonprofit organization that conducts independent research. The program aims to address the challenge of antibiotic resistance by developing actionable policy proposals in five low- and middle-income countries: China, India, Kenya, South Africa and Vietnam. GARP-Vietnam and the University of Oxford collaborated with the Vietnamese Ministry of Health (MoH) to set up new surveillance program for both antibiotic consumption and resistance[1].

A cross-sectional study was performed to collect antibiotic resistance and purchasing data from 15 participating hospitals since 2009. Only data from the following specimens were analyzed: blood, CSF, urine, sputum, and pus. Antibiotic consumption was assessed using drug purchasing data submitted by hospital pharmacies and data on number of hospital beds and bed occupancy rate to calculate the defined daily dose (DDD)/100 beddays.

Results on antibiotic use showed that the mean antibiotic consumption was 274.7 DDD per 100 bed days, significantly higher than corresponding figure reported in Netherlands in the same year with only 58.1 DDD per 100 bed-days [2] and median total antibiotic use reported from 139 hospitals in 30 European countries with 49.6 DDD per 100 bed-days in 2001[3]. In pediatrics hospitals, with average of 65 DDD per 100 beddays, overall antibiotics consumption in Vietnam was slightly higher than the figure in 5 children's hospitals in China in 2006 which was recorded in 49.9 DDD/100 bed-days [4]. 2nd and 3rd generation cephalosporins (J01DC, J01DD) are the most common used antibiotics at all hospitals, followed by broad spectrum penicillins (J01CA), fluoroquinolones (J01MA) and macrolides (J01FA). Expenditure of carbapenems has contributed a remarkable part in the treatment budget (12.3%) indicated that this group is been increasingly used in treatment in all hospitals. Older antibiotics such as phenicols, betalactamase sensitive penicillins, lincosamides are used little in treatment. Vancomycin consumption is very low in all hospitals. Since polymyxins (e.g. colistin) are not made available to hospital pharmacies, the consumption of this agent could not be assessed.

Corresponding to relatively high antibiotic consumption to other countries, an alarming high level of antibiotic resistance was shown in all hospitals. Currently, all laboratories base their testing on CLSI guidelines. On site assessments revealed that most labs perform too many resistance tests, for instance for antibiotics that would not be used for treatment or for several antibiotics in the same class. A positive development is that quality assurance is increasingly in place, but does need further improvement. Participating in an internationally recognized external quality assurance scheme is highly recommended.

Resistance was common in Gram-negative bacteria, including: *Acinetobacter sp., Pseudomonas, E. coli* and *Klebsiella* species. In general, about 30-70% of the gram negative bacteria are resistant to 3rd and 4th generation cephalosporins, approximately 40-60% to aminoglycosides and

fluoroquinolones. Up to 40% of *Acinetobacter* species showed decreased susceptibility to imipenem. The correlation between antibiotic use and resistance was seen clearly as the highest resistance rate of Gram negative bacteria to 4th generation cephalosporin was found in the north where there is higher consumption of this agents.

Antibiotic consumption and susceptibility data indicate that the resistance rates are high, driving the use of more expensive last resort antibiotics, resulting in worsening of resistance.

Currently, all the clinical laboratories test of 15 participating hospitals according to CLSI criteria. Site assessment (in 2011) noted that most laboratories test bacteria against more antibiotics than recommended by CLSI. On site assessments revealed that most labs perform too many resistance tests, for instance for antibiotics that would not be used for treatment or for several antibiotics in the same class. A positive development is that quality assurance is being increasingly performed, but does need further improvement. Participating in an internationally recognized external quality assurance scheme is highly recommended.

INTRODUCTION

The global problem of antimicrobial resistance is particularly pressing in developing countries, where the infectious disease burden is high and costs constrain the replacement of older antibiotics with newer, more expensive ones. Gastrointestinal, respiratory, sexually transmitted, and nosocomial infections are leading causes of disease and death in the developing world, and management of all these conditions has been critically compromised by the appearance and rapid spread of resistance[1].

Vietnam already experiences high levels of antibiotic resistance. Within the Asian Network for Surveillance of Resistant Pathogens (ANSORP), Vietnam had the highest prevalence of penicillin resistance (71.4 percent) and erythromycin resistance (92.1 percent) [5]. Seventy-five percent of pneumococci are resistant to three or more classes of antibiotics[6]. Resistance is common among Gram-negative bacteria (enterobacteriaceae). A study published in 2009 reported that 42 percent of studied enterobacteriaceae were resistant to ceftazidime, 63 percent were resistant to gentamicin and 74 percent to nalidixic acid. These high resistance rates were also found in healthy individuals in community setting [7]. As a consequence of the high rates of resistance, many antibiotic regimens advised in current treatment guidelines are unlikely to be effective. Although very hard to quantify, the profile of antibiotic resistance observed in Vietnam undoubtedly causes negative health and economic impacts.

This is almost certainly a consequence of the high levels of antibiotic use in both humans and in agriculture, much of which is inappropriate. According to a community-based study undertaken in 1999, 78 percent of antibiotics were purchased in private pharmacies without prescriptions. 67 percent of the participants consulted the pharmacist while 11 percent decided themselves about antibiotic use. Only 27 percent of the pharmacy staff had correct knowledge about antibiotic use and resistance[8]. Despite the regulations and guidelines set for antibiotics, sales of most antibiotics without a prescription is a common practice in Vietnam[9]. Another community study in 2006 showed unnecessary antibiotic use for mild acute respiratory infections in children under five in rural Vietnam. 63% of the children with mild ARIs were treated with antibiotics[10]. Whilst antibiotic use in animals is widespread, the role this plays in resistance levels in human pathogens remains unclear in Vietnam and other countries.

A resistance surveillance project known as Antimicrobial Sensitivity Testing Study (ASTS) stopped in 2005 due to lack of donor funding. Since that time there has been no active nationwide antibiotic resistance surveillance program in Vietnam. As antibiotic pressure through human and animal use is one of the important drivers of resistance, it is essential to set up new surveillance program for both antibiotic consumption and resistance. We have undertaken study to present resistance data in the context of usage in hospital level. This report presents the results of antibiotic use and resistance in 15 hospitals spread throughout Vietnam. Surveillance data are crucial to create awareness and target potential interventions.

Surveillance objective

Program aims to assess the situation of antibiotics use and resistance in 15 hospitals in Vietnam.

Surveillance methodology

The antibiotic use and resistance surveillance program was conducted by the Ministry of Health (MoH) in collaboration with Global Antibiotic Resistance Partnership (GARP) program and the Oxford University Clinical Research Unit - Vietnam. The objective of the surveillance was to assess the total hospital consumption of antimicrobial agents and resistance rates in 15 hospitals in Vietnam.

Fifteen hospitals that annually submit both their Antibiotic Procurement data (see Appendix B: Antibiotic Procurement Report) and Antibiotic Resistance data (see Appendix B: Antibiotic Resistance Report Form) to the Ministry of Health were selected to participate in the national surveillance program. Part of the program also included a site visit to assess the pharmacy and microbiology department. Seven out of the eight northern hospitals are located in Hanoi, three in central Vietnam, and the remaining four are located in the south. Among them, there were nine national hospitals and six provincial. Eleven out of fifteen hospitals are general, and the four remaining are specialist hospitals, like tropical disease (Figure 1).

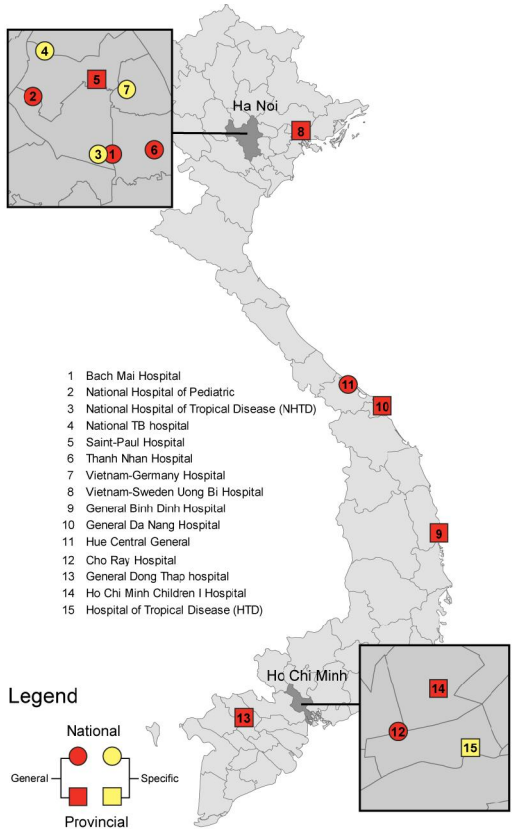

Figure 1. Location of participating hospitals

Antibiotic consumption surveillance

The antibiotic consumption for 2008 was calculated from the annual Antibiotic Procurement Report that each hospital submits to MoH every year (Appendix A). The Antibiotic Procurement Report form of Ministry of Heath is used to collect aggregated data of antibiotic consumption from hospital pharmacies. The participating hospital pharmacy departments were visited to verify the source of the data and to assess whether the Antibiotic Procurement Report reflects antibiotic use in these hospitals. The antibiotic consumption of the participating hospitals was expressed in defined daily dosages per 100 occupied bed days (DDD/100 BD) in 2008. To calculate the DDD/100 bed days we used data on number of hospital beds and bed occupancy rate for each hospital for 2008. The antibiotic procurement data were entered into a MS Access database with a built in DDD / 100 bed days calculator, based on the ABC calculator. The ABC calculator is a simple computer tool to measure antibiotic consumption in hospitals. It transforms aggregated data provided by hospital pharmacies (generally as a number of packages or vials) into meaningful antibiotic utilization rates. It was developed for the ESCMID Study Group on Antibiotic Policies (ESGAP) at the National Center for Antimicrobials and Infection Control, Statens Serum Institute (Copenhagen, Denmark), as part of the Danish Integrated Antimicrobial Resistance Monitoring and Research Programme (DANMAP, see: http://www.escmid.org/research_projects/study_groups/esgap/abc_calc)

NOTE: As there was no antibiotic procurement data available for whole of 2009 at time of the initiation of this project, we used the data for the whole of 2008.

Antibiotic resistance surveillance

Resistance data for 2009 were collected from the same 15 hospitals that provided the antibiotic consumption data for 2008. The hospital laboratory departments submit annually their resistance data using an Antibiotic Resistance Report Form developed by the Ministry of Health (Appendix B). This form collects data on more than 20 bacterial indicators from Blood, CSF, Feces, Pus, Sputum, Urine and and others. The received reports were appraised and checked for inconsistencies, unlikely resistance rates, and unlikely antibiograms. Resistance data were entered in MS Access database that was developed by OUCRU. Only data from following specimens were analyzed: blood, CSF, urine, sputum and pus. Furthermore, we only reported resistance rates on five common bacteria including *E. coli, Klebsiella* species*, Acinetobacter* species*, Pseudomonas aeruginosa and Staphylococcus aureus*. These bacteria were chosen as they are relatively simple to identify and test for resistance, hence increasing the reliability of the dataset. The participating laboratories were visited to assess the microbiological techniques used to culture, identify bacteria and antibiotic resistance tests, and the quality control systems they had in place.

RESULTS

Antibiotic consumption

The number of beds and bed occupancy rates varies by hospital (Table 1). Most hospitals are overcrowded, often with more than one patient in a bed, especially in the larger general hospitals located in the big cities (Table 1). In several hospitals the bed occupancy rates reached >170% for 2008.

Table 1. List of 15 participating hospitals

No	Hospital	Location	Region	Level	Number of beds in 2008	Bed occupancy rate 2008,%
1	Bach Mai Hospital	Hanoi	North	National	1500	176.6
2	National Hospital of Pediatrics	Hanoi	North	National	650	180.0
3	National Hospital of Tropical Diseases	Hanoi	North	National	170	101.0
4	National TB hospital	Hanoi	North	National	448	92.5
5	Saint-Paul Hospital	Hanoi	North	Provincial	539	156.2
6	Thanh Nhan Hospital	Hanoi	North	National	673	96.0
7	Vietnam-Germany Hospital	Hanoi	North	National	763	106.0
8	Vietnam-Sweden Uong Bi Hospital	Quang Ninh	North	Provincial	583	100.8
9	General Binh Dinh hospital	Binh Dinh	Middle	Provincial	818	152.0
10	General Da Nang hospital	Da Nang	Middle	Provincial	852	186.0
11	Hue Central General	Hue	Middle	National	2006	106.6
12	Cho Ray Hospital	Ho Chi Minh city	South	National	1531	157.0
13	General Dong Thap hospital	Dong Thap	South	Provincial	824	99.2
14	Ho Chi Minh Children Hospital 1	Ho Chi Minh city	South	Provincial	969	139.0
15	Hospital of Tropical Disease (HTD)	Ho Chi Minh city	South	Provincial	500	107.5

The significant difference of the total antibiotic consumption were noted across 15 surveyed hospitals with the highest rate in Binh Dinh general hospital (466 DDD/100 bed-days) which is located in the middle region and lowest rate in Nation Pediatrics Hospital (28 DDD/100 bed-days)-northern hospital (Figure 2). The lowest average consumption of antibiotics was seen in southern hospitals with average 206.7 DDD/100 bed-days, moderate in the north (270 DDD/100 bed-days) and the highest consumption was found in middle region with 347 DDD/ 100 bed-days (Table 6, Appendix A).

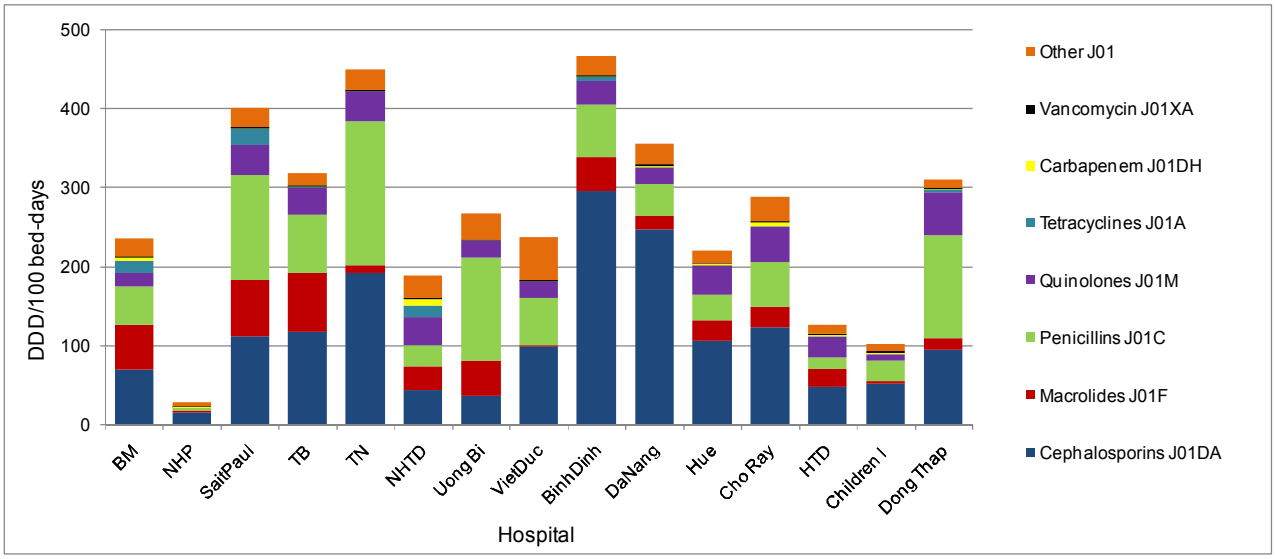

Figure 2. Total antibiotic consumption for systemic use (J01) by ATC class in 15 hospitals in Vietnam in 2008

In general, cephalosporins (J01DA) were the most common used antibiotics at all hospitals, followed by penicillins (J01C), macrolides (J01F) and quinolones (J01M). New generation antibiotics such as carbapenems and 4th generation cephalosporin accounted for a minor part of the total antimicrobial consumption (J01). Older antibiotics such as phenicols, betalactamase sensitive penicillins, lincosamides were also little used in treatment. The use of polymyxins (for example colistin) and vancomycin were rare in all hospitals. Since colistin it is not currently registered in Vietnam, it is not available to hospital pharmacies and is only available for purchase from private pharmacies at relative high prices. Therefore we could not access the consumption of colistin for this report. (See Figure 2).

Figure 3 shows the proportion of the four different types of penicillins: beta-lactamses resistance penicillins J01CF, combinations with beta-lactamase inhibitors J01 CR, broad spectrum penicillins J01CA and narrow spectrum penicillins J01CE. Overall, the use of narrow spectrum penicillins was negligible in all hospitals. Broad spectrum penicillins dominated, followed by combinations with beta-lactamase inhibitors. In the National TB hospital and VietDuc hospital the combinations were the most common choice among the four kinds of penicillins.

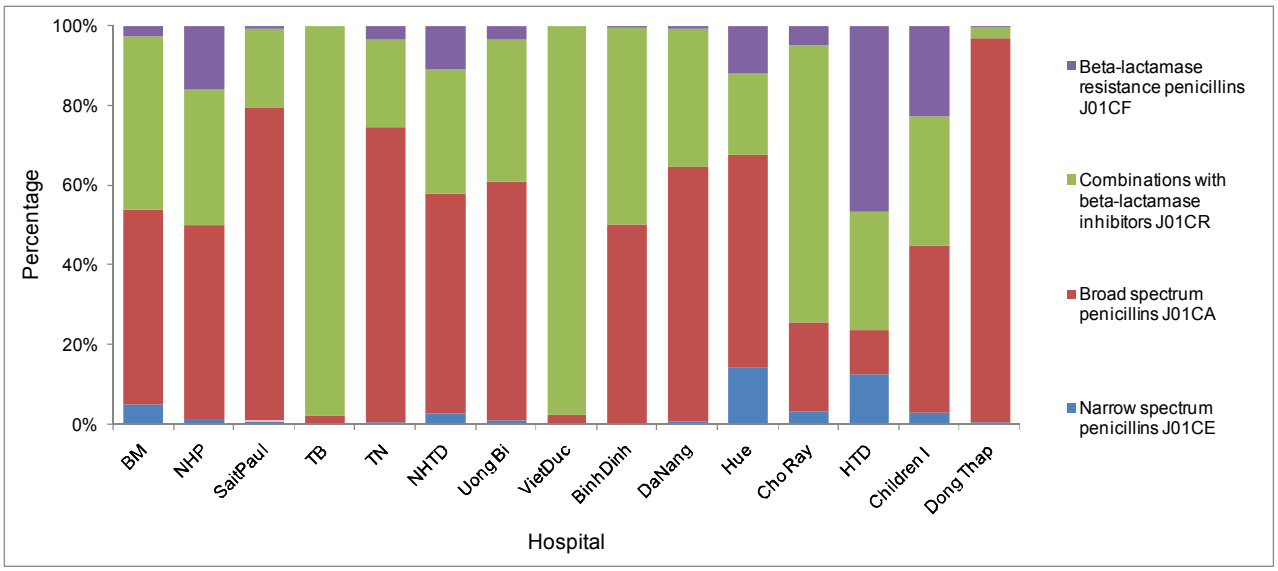

Figure 3. Consumption of penicillins in 15 hospitals in Vietnam in 2008

Similarly, the use of second and third generation cephalosporins was more common than the other generations (Figure 4). Several hospitals such as HTD, Viet Duc hospital did not use first generation cephalosporins in treatment anymore. Fourth generation cephalosporins only registered an unsubstantial part of total 4 generations cephalosporins.

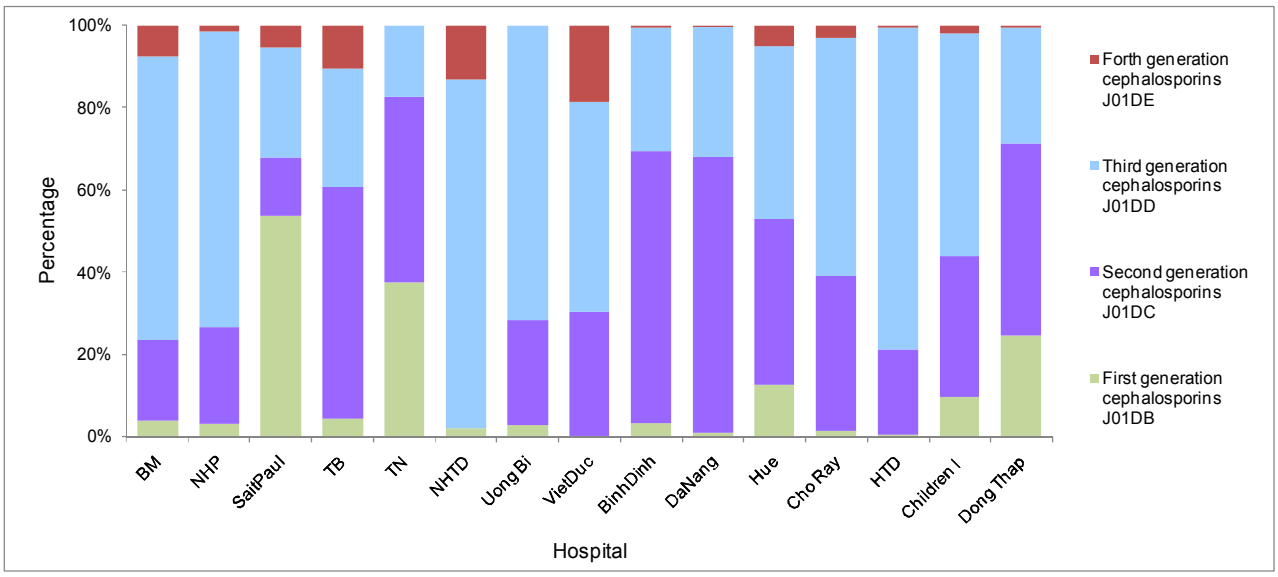

Figure 4. Consumption of cephalosporins in 15 hospitals in Vietnam in 2008

By value, the average antibiotic expenditure per hospital in 2008 was 1.75 million USD. The highest expenditure of antibiotics (6.74 million USD) was seen in Cho Ray hospital – the biggest one in the south with scale of 1500 beds, followed by another same scale hospital in the north-Bach Mai which was accounted for 5.5 million USD. Other smaller hospitals or specific ones such as pediatrics or

provincial hospitals showed relative low expenditure on antibiotics, consistent with the observed low antibiotic consumption, as well as tended to use older antibiotics more. (Figure 5).

It was observed that in all hospitals the third generation cephalosporin contributed a major part to the antibiotic expenditure (39.5%). Other antibiotic classes with a relatively high contribution to the total antibiotic expenditure are in decreasing order: carbapenems (12.3%), second generation cephalosporins (11.8%), combinations of penicillins with beta-lactamase inhibitors (6.7%) and fluoroquinolones (6.5%). Despite that carbapenems are used less in comparison to other drugs; their high price does lead to a significant high contributed to the hospital expenditure on antibiotics (Figure 5).

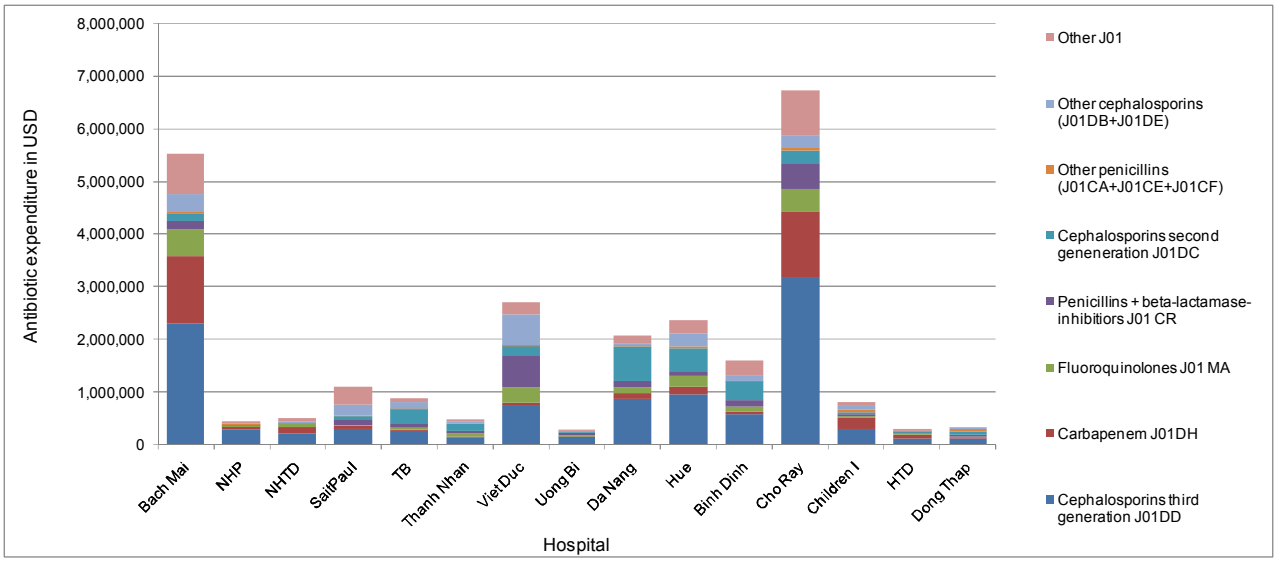

Figure 5. Total antibiotic expenditure for systemic use (J01) in 15 hospitals in Vietnam in 2008 (USD)

Antibiotic Resistance

The number of isolates tested for antibiotic resistance varied by hospital and region with more than 20 kinds of bacterial pathogens isolated from 15 participating hospitals in 2009 (Table 7, see Appendix A). Among pathogens, Gram-negative bacteria accounted for 78.5%, Gram positive 21.5%. In all hospitals, enteric bacteria predominated such as *E. coli* and *Klebsiella* species (Table 8, Appendix A). Other two common tested Gram negative pathogens were *Pseudomonas aeruginosa* and *Acinetobacter* species, which both are common causes of hospital acquired infections. Table 3 also shows the number of tested *S. aureus* strains, the most common detected Gram-positive organism. A total of 489 *Vibrio cholera* isolates were tested in northern hospitals (all in hospitals located in Hanoi except one case in Uong Bi hospital), which correlated with the location of the cholera outbeak in Northern provinces. In addition, 66 *Streptococcus suis* isolates, a common zoonotic disease in Vietnam, were tested in all 3 regions.

Resistance of Gram negative bacteria

In 2009, 30-70% of the gram negative bacteria were resistant to 3rd and 4th generation cephalosporins, approximately 40-60% to aminoglycosides and fluoroquinolones. Almost 40% of *Acinetobacter* species showed decreased susceptibility to imipenem. Resistance rates of four common Gram negative pathogens are presented in Figure 6.

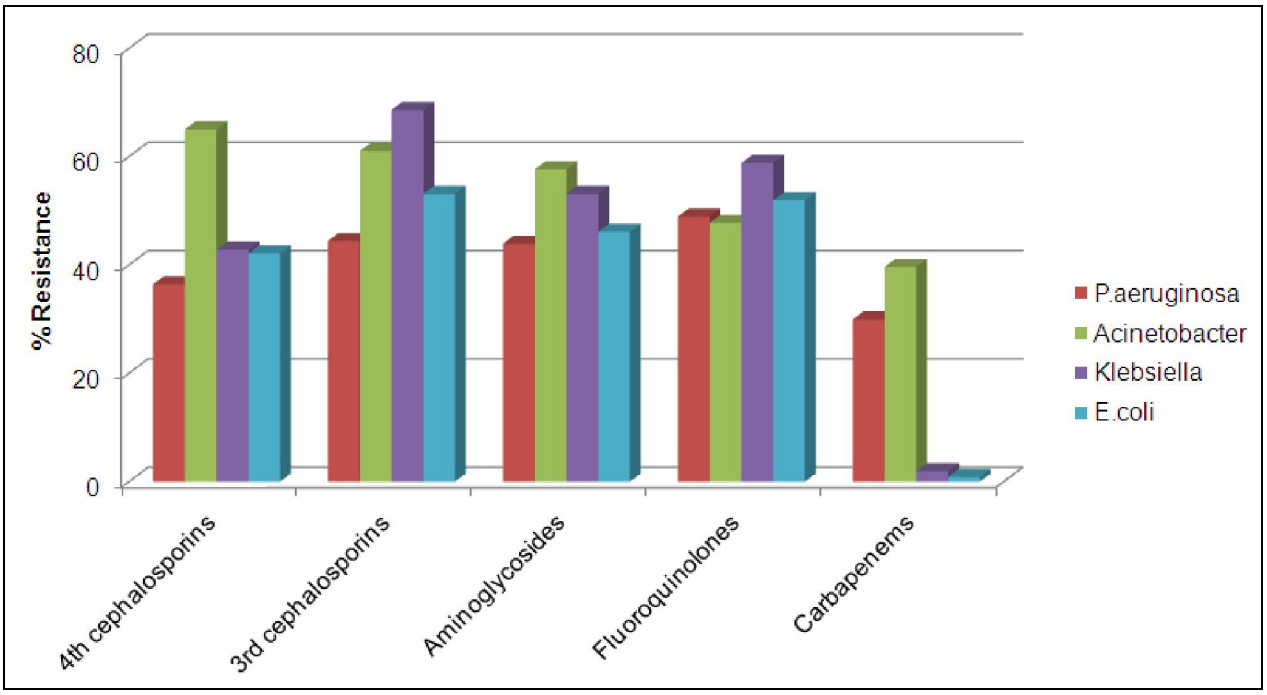

Figure 6. Resistance rate of four common Gram negative bacteria to some new generation antibiotics.

Staphylococcus aureus resistance

Resistance rate of *S. aureus* varied among hospitals and tested antibiotcs. Up to 68.8% strains isolated from Cho Ray hospital were resistant to Gentamicin. Resistance rate to Oxacillin was highest in Hue hospital with 63.8% (See Figure 7). According to report of Cho Ray hospital in 2008, 8% *S. aureus* isolated from Cho Ray hospital were resistant to vancomycin. However, in 2009, most of hospitals including Cho Ray did not have *S. aureus* resistant to vancomycin except some provincial hospitals reporting improbable high resistance rate of *S. aureus* to vancomycin such as 60.9% in Uong Bi hospital, 24.1% in Binh Dinh and 15.6% in Saint Paul (Data not shown). These results indicate that the testing quality needs to be improved, including confirmation of these important resistance strains through other methods.

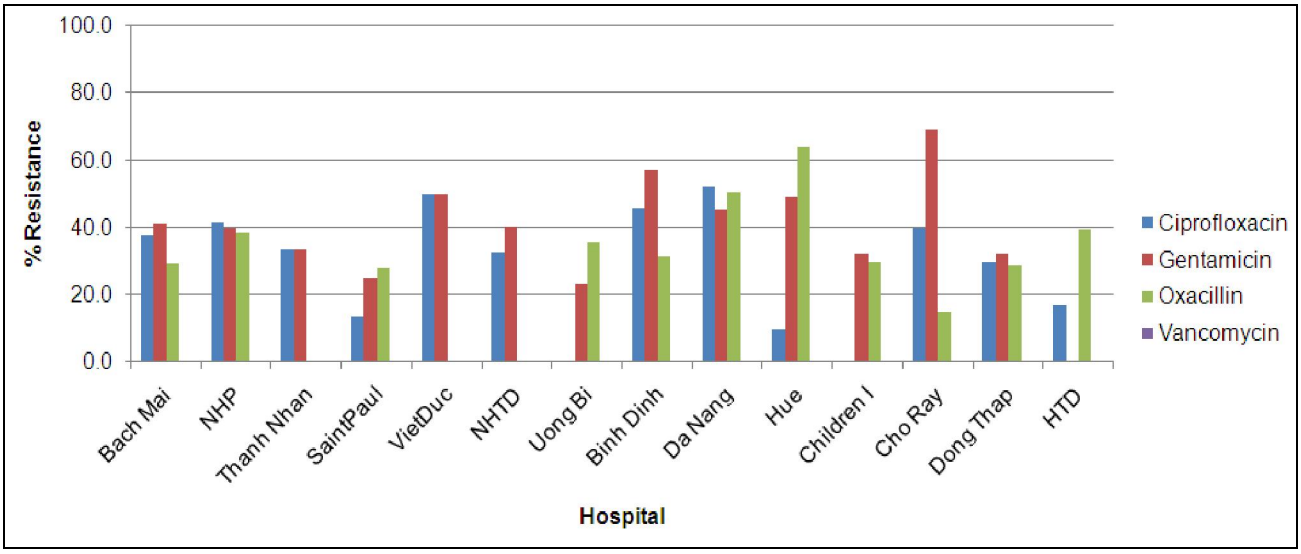

Figure 7. Resistance rate of *S. aureus* in 15 hospitals in 2009

Klebsiella sp. resistance

Antibiotics resistance of *Klebsiella* sp. strongly fluctuated by hospitals but in general, *Klebsiella* sp. showed decreased susceptibility to certains antibiotics such as 3rd generation cephalosporin, particularly ceftazidime, cotrimoxazole, ciprofloxacin and gentamicin. Remaining effective antibiotics included carbapenem and beta-lactamase inhibitors combined beta-lactam. Resistance rate of *Klebsiella* sp. to Imipenem was lower than 10%, except in National TB Hospital with 53.6% (suspected data was not shown in the figure). There are several discontinued points in Figure 8 due to lack of data in respective hospitals.

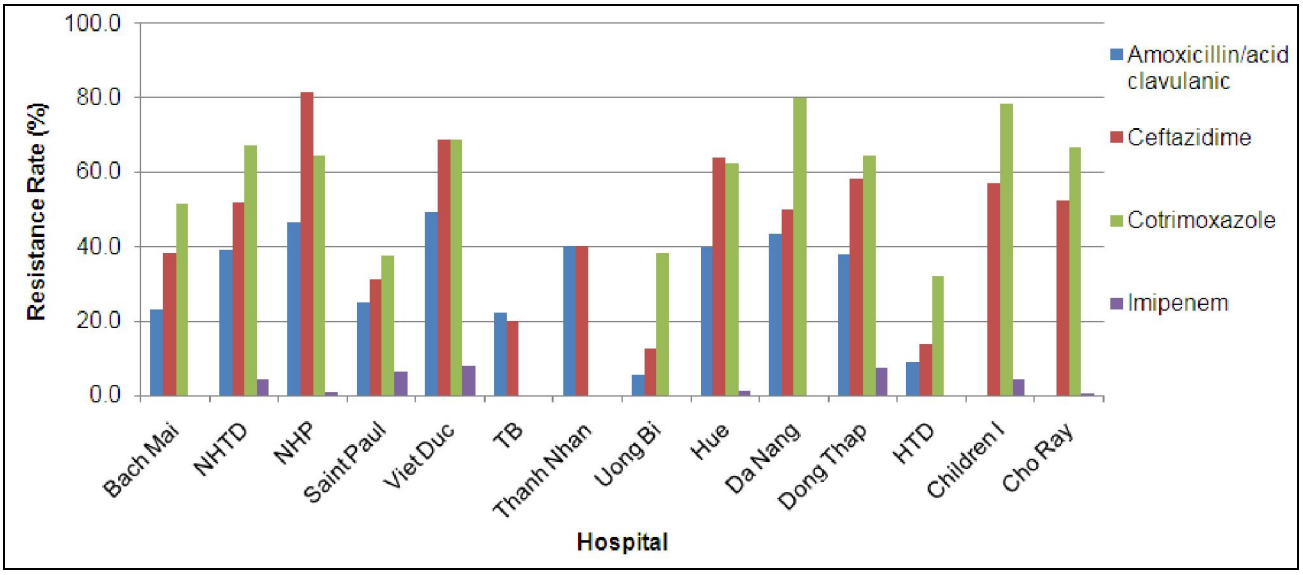

Figure 8. Resistance rate of *Klebsiella spp* to antibiotics commonly used in treatment.

***Escherichia coli* resistance**

In Figure 9, *E. coli* showed reduce susceptibility to 3rd generation cephlosporin and high resistant rates to cotrimoxazole with range from 60-80% in most hospitals. The resistance rate to carbapenems was lower than 2%, except in National TB Hospital which reported a suspected resistance rate of 47.7%.

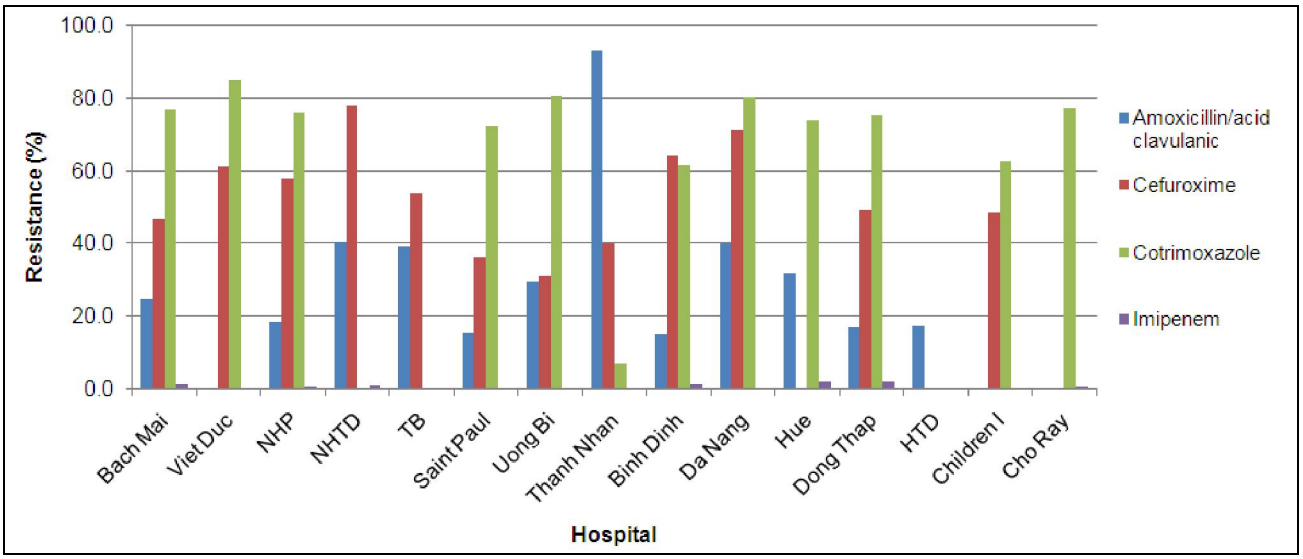

Figure 9. Resistance rate of *E.coli* in 15 hospitals in Vietnam in 2009.

Table 2: Rate of *E. coli* and *K. pneumoniae* producing ESBL in 14 hospitals in 2009 (Uong Bi hospital did not have data)

Hospital	*E. coli*	*Klesiella* sp.
Bach Mai	18.0 (175/970)	3.0 (3/99) (isolated from blood)
NHTD	54.7 (64/117)	72.7 (176/242)
NHP	37.6 (146/388)	51.3 (294/573)
TB	23.4 (11/47)	7.0 (21/298)
Viet Duc	57.3 (63/110)	48.5 (16/33)
Saint Paul	31.7 (52/164)	41.2 (42.102)
Thanh Nhan	41.2 (7/17)	12.5 (1/8)
Hue	33.9 (103/304)	37.5 (69/184)
Da Nang	23.9 (112/468)	13.2 (58/438)
Binh Dinh	35.8 (210/586)	54.3 (227/418)
Children I	38.1 (275/722)	54.1 (392/724)
Dong Thap	14.7 (78/531)	25.0 (56/224)
Cho Ray	49.0 (25/51)	58.2 (139/239)
HTD	34.8 (24/69)	20.5 (9/44)

The prevalence of ESBL in *E. coli* and *K. pneumoniae* was highest in NHTD (the leading hospital in infectious diseases) with 54.7% and 72.7% for *E.coli* and *Klebsiella*, respectively, followed by Cho Ray hospital (the biggest general hospital in the south) with 49% and 58.2%, Viet Duc hospital (Surgical hospital), Bình Định hospital và 2 Bệnh viện Nhi (Nhi TW và Nhi đồng I) with approximately 40% in *E.coli* and above 50% in *Klebsiella*. These hospitals also had the higher rate of cephalosporins third generation of *E. coli* and *Klebsiella* in comparison to other hospitals.

***Pseudomonas aeruginosa* resistance**

Antibiotics resistance of *Pseudomonas aeruginosa* varied with different antipseudomonas agents and different hospitals. Saint Paul Hospital, a provincial general hospital in the north, showed highest rate of ceftazidime resistance with more than 80%, whereas only 20% ceftazidime resistant *P. aeruginosa* was recorded in the National TB Hospital. This hospital also accounted for lowest ciprofloxacin resistance rate of approximately 20% along with two other pediatrics hospitals in the north (NHP) and the south (Children I) region. Other remaining hospitals showed light fluctuation around 40% resistance to ceftazidime and ciprofloxacin. Overall, imipenem resistance rates of *Pseudomonas aeruginosa* were higher than those of *Klebsiella* sp. (Figure 10).

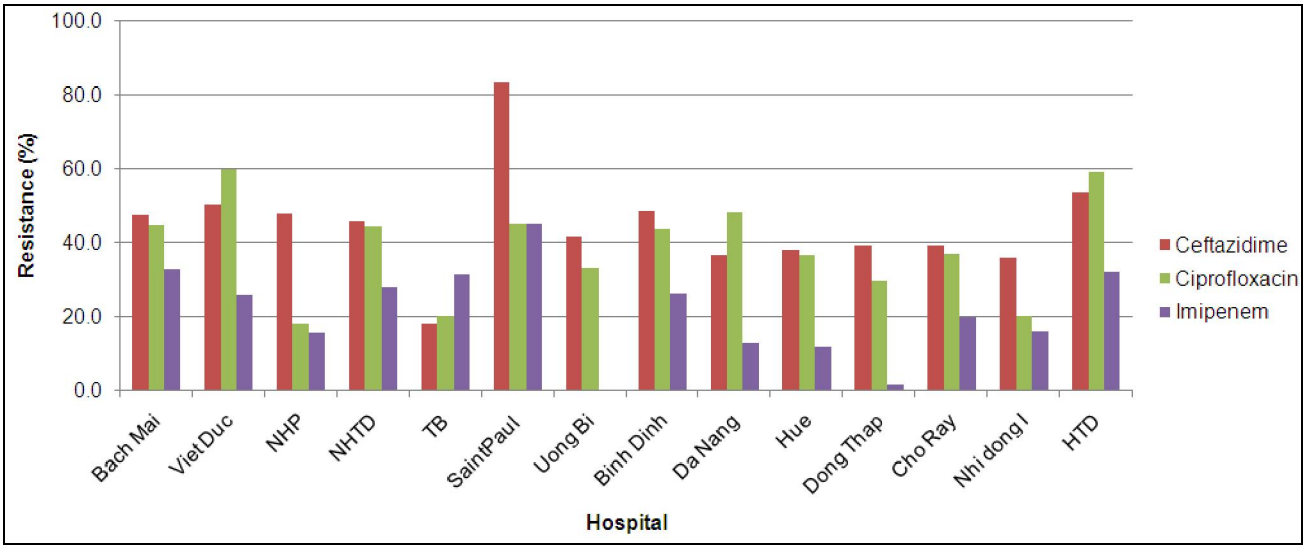

Figure 10. Resistance of *Pseudomonas aeruginosa* to three antipseudomonas agents including ceftazidime, ciprofloxacin and imipenem.

Acinetobacter resistance

Multidrug resistant *Acinetobacter* species is defined as resistance to more than three classes of antibiotics [11]. More than 60% of *Acinetobacter* isolated from some big hospitals such as Bach Mai, Cho Ray and NHTD were multidrug resistant. Saint Paul hospital showed the highest resistance rate to 4 tested antibiotics, completely resistant to ceftazidime and gentamicin and up to 80% were not susceptible to ciprofloxacin and imipenem anymore. In other hospitals, imipenem resistance rate was fluctuated from 18% in TB hospital, Viet Duc or Binh Dinh hospital to 70% to big hospitals like Bach Mai, Cho Ray and NHTD. These results are alarming as these antibiotics have been very effective in *Acinetobacter* treatment (See Figure 11).

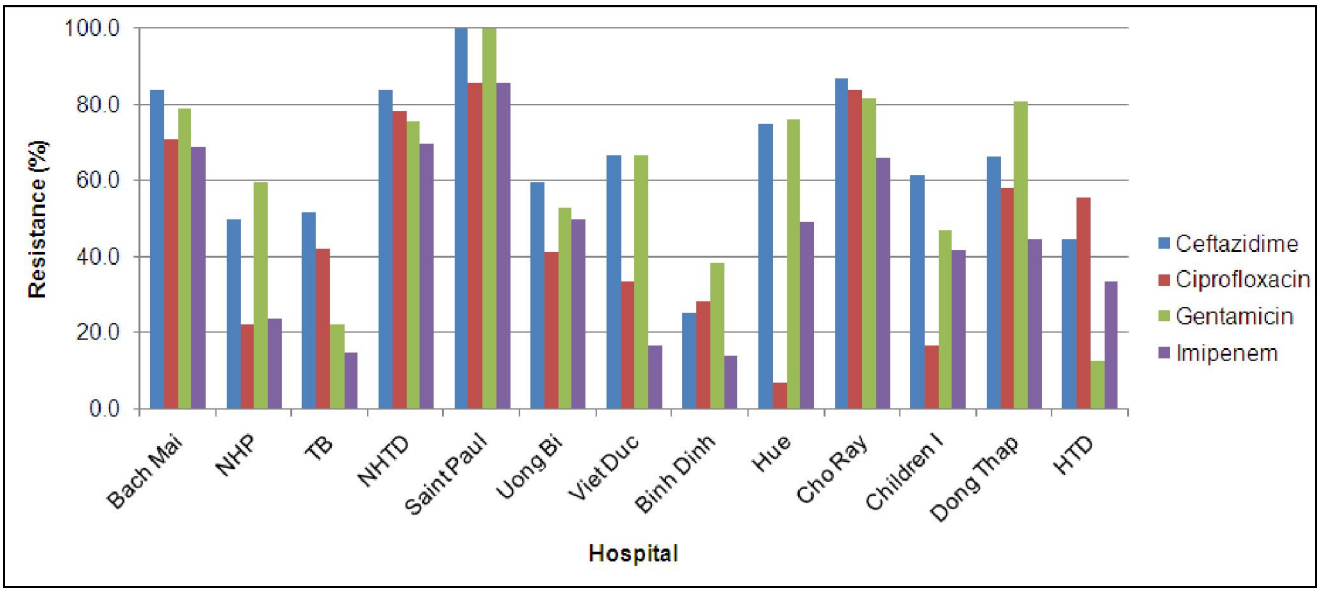

Figure 10. Resistance rate of *Acinetobacter* spp.

Relationship between antibiotic consumption and resistance

Table 3 shows the Spearman correlation between antibiotics use and resistance by organism. Correlations between antibiotics use and resistance were calculated by using two-tailed Spearman's coefficient (r_s) for non-parametric correlations. r_s rank from +1 to -1. A plus r_s means positive correlation and a minus r_s reflect negative correlation. A p value of less than 0.05 was assessed as significant. Two significant correlations were recorded for the combination of cephalosporins consumption and cefuroxime resistant *E. coli* at the 0.01 level (2 tailed Spearman, **r = 0.718, p = 0.003) (See Figure 12) and another combination between carbapenems consumption and ceftazidime resistant *Acinetobacter* at the 0.05 level (*r=0.623, p=0.031). The correlations show that increased cephalosporins 3rd generation resistance rate lead to an increase of carbapenem consumption (See Figure 13). However, analysis results showed, null hypothesis that there was no relationship between ESBL producing *E. coli* and *Klebsiella* spp. and cephalosporin 3rd generation and fluoroquinolones resistance could not be rejected (p value >0.05).

Table 3. Correlation between antibiotics use and resistance by organism

Organisim	AB resistance	AB use, ATC group	Nr. of hospitals	Spearman correlation	P value
E.coli	Cefuroxime	Cephalosporins	15	0,718	0,003**
E.coli	ESBL (+)	Cephalosporins thế hệ 3	14	0,085	0,773

E.coli	ESBL (+)	Fluoroquinolones	14	-0.099	0,737
Klebsiella sp.	ESBL (+)	Cephalosporins thế hệ 3	14	0,002	0,994
Klebsiella spp.	ESBL (+)	Fluoroquinolones	14	-0,086	0,769
Pseudomonas spp.	Imipenem	Fluoroquinolones	14	0,125	0,670
Pseudomonas spp.	Imipenem	Carbapenems	14	0,139	0,636
Acinetobacter spp.	Imipenem	Carbapenems	14	0,517	0,059
Acinetobacter spp.	Ceftazidime	Carbapenems	12	0,623	0,031*

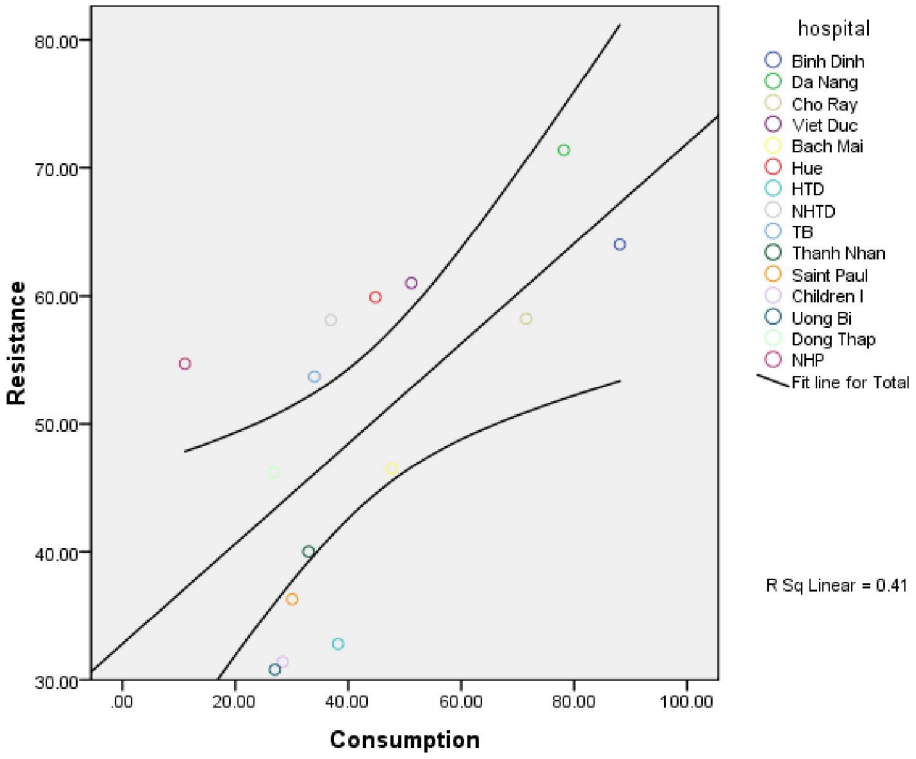

Figure 12: Correlation between cephalosporins use and prevalence of cephalosporin resistant *E. coli*

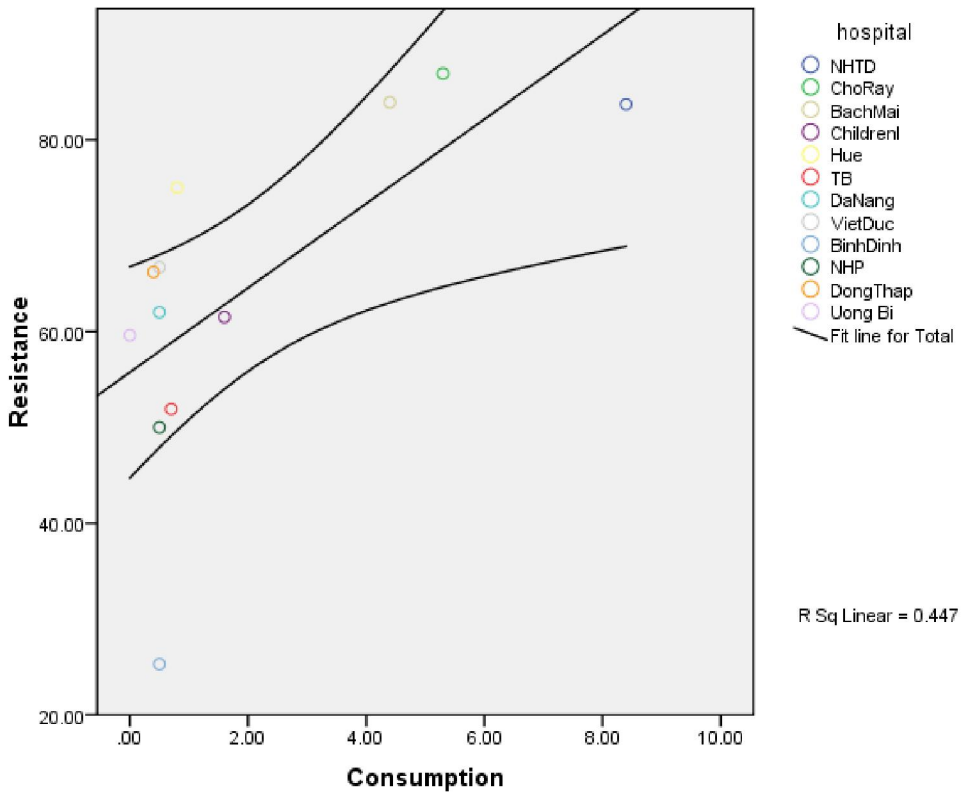

Figure 13. Correlation between carbapenem consumption and ceftazidime resistant *Acinetobacter*

Site assessment

The finding that several hospitals reported unlikely high vancomycin resistance rates for S. aureus, illustrates that the quality of the testing and data reporting is below standard at several hospitals. Therefore, we conducted site visits at the participating hospitals to appraise current antibiotic resistance testing procedures and procurement reports.

Despite that the clinical laboratories test according to CLSI criteria, it was noted that most laboratories test bacteria against more antibiotics than recommended by CLSI. This is due to that the hospitals select the tests themselves without being aware of these recommendations (Table 5a and 5b). Meanwhile, some antibiotics should be tested following by CLSI recommendation but are not done, such as Doxycycline, Minocycline, Tetracycline for *Acinetobacter* spp. Reducing the number of tests will reduce costs and improve the quality of the testing. The recommended tests by CLSI are listed in Tables 5a. In Table 5b we have listed in a similar format what tests are actually performed in Vietnam and are not recommended by CLSI.

The site visits of the clinical microbiology laboratories showed, there was a large variation in the infrastructure, the testing capacity, and the quality systems in place. Two participating laboratories in HCMC are ISO accredits, while all the others are not. Quite a number of laboratories do not have internal quality assurance in place. And those that do have this do it irregularly. Most laboratories in

southern Vietnam and one in northern Vietnam participate in a Vietnamese external quality assurance scheme. However this scheme is quite new and still needs to be improved. All laboratories use recent English CLSI guideline for resistance testing and cut-offs for zone diameters are listed by bacterial group and specimen type. Most laboratoies have drafted local SOPs, however they are often out-dated. Several labs use rabbit blood for making blood agar plates or even human blood. The number of labs that use sheep blood is increasing. The majority of strains are identified with commercial identification kits like API (Biomerieux) and resistance by disk diffusion. Lab personnel usually use a densitometer to measure the McFarland for resistance testing. But common practice shows that most still do it by eye and experience. All microbiology labs draft an annual report about common isolated bacteria and resistance rate. This report is submitted to DTC and Director Board.

Some laboratories need to improve their infrastructure, such as operational safety cabinets for working with infectious materials, computer with internet connection for organizing and storing data and updating knowledge; available McFarland standards for resistance testing; refer to newest CLSI version for antibiograms; weekly internal quality assurance and have different technicians participate in quality assurance schemes to check for differences between technicians. In overall, using external quality assurance is strongly recommended for all microbiology laboratories to improve quality of microbiological testing.

Table 4. Site assesment base on some criteria, findings and suggestions

Criteria	Findings	Suggestions
ISO accreditation	Absent 8/10 visited hospitals	Support development towards ISO accreditation
Internal quality control with Kirby Bauer, E-test or in Vitek	Absent 3/10 Irregular 3/7	Propose control strains to be used, it would be preferred to do this weekly and have different technicians do it each time to check for differences between technicians.
CLSI guide lines	Implemented, using English version 6/10: version 2011 2/10: 2010 1/10:2009 1/10:absent	Implement by translating version and designing one responsible person for quality control of AST
SOP in laboratories	Mostly available: 10/10, however often out-dated	Regular update and survey adherence to SOPs Eg: safety cabinets, data storage units.
Blood culture plate	2 labs. use rabbit blood, 7 labs use sheep blood, 1 lab use human blood	
Use of densitometer for Mc Farland determination	Present in 4/10 labs Absent in 6/10 labs	Implement use of densitometer and Mc Farland standards

Table 5a. Recommended antibiotic tests by micro-organisms according to CLSI

Group	***Enterobacteriaceae***	***S. aureus***	***P. aeruginosa***	***Acinetobacter***
Group A Primary Test and Report	Ampicillin	Azithromycin or clarithromycin or erythromycin	Ceftazidime	Ampicillin-sulbactam
		Clindamycin		Ceftazidime
		Oxacillin (cefoxitin)		Ciprofloxacin Levofloxacin
	Cefazolin	Penicillin	Gentamicin Tobramycin	Imipenem Meropenem
	Gentamicin Tobramycin	Trimethoprim-sulfamethoxazole	Piperacillin	
Group B Primary Test Report Selectively	Amikacin	Daptomycin	Amikacin	Amikacin
		Linezolid	Aztreonam	
	Amoxicillin-clavulanic acid Ampicillin-sulbactam Piperacillin-tazobactam Ticarcillin-clavulanic acid	Telithromycin	Cefepime	
	Cefuroxime	Doxycycline Minocycline Tetracycline		Piperacillin-tazobactam Ticarcillin-acid clavulanic
	Cefepime	Vancomycin	Ciprofloxacin Levofloxacin	
		Rifampin		
	Cefotetan Cefoxitin			Cefepime
	Cefotaxime or Ceftriaxone			Cefotaxime Ceftriaxone
	Ciprofloxacin Levofloxacin			Doxycycline Minocycline Tetracycline
	Doripenem Ertapenem Imipenem			Piperacillin

	Meropenem			
	Piperacillin			Trimethoprim-sulfamethoxazole
	Trimethoprim - sulfamethoxazole			
Group C Supplemental Report Selectively	Aztreonam Ceftazidime	Chloramphenicol[c]		
		Ciprofloxacin or levofloxacin or ofloxacin Moxifloxacin		
	Chloramphenicol	Gentamicin		
	Tetracycline	Quinupristin-dalfopristin		
Group U Supplemental For Urine Only	Cephalothin	Lomefloxacin Norfloxacin	Lomefloxacin or ofloxacin Norfloxacin	
	Lomefloxacin or ofloxacin Norfloxacin	Nitrofurantoin		
		Sulfisoxazole		
	Nitrofurantoin	Trimethoprim		
	Sulfisoxazole			
	Trimethoprim			

Table 5b. Antibiotics tested in Vietnam, but not recommended by CLSI

S. aureus	***P. aeruginosa***	***Acinetobacter* spp**	***E. coli***	***Klebsiella***
Amikacin	Amoxicillin/ clavulanic acid	Amoxicillin/ clavulanic acid	Cefoperazone	Netilmicin
Amoxicillin/ clavulanic acid	Ampicillin/ sulbactam	Ampicillin	Cefoperazon/ sulbactam	Cefoperazone / sulbactam
Ampicillin	Cefoperazone	Cefoperazone	Fosfomycin	Cefoperazone
Ampicillin/ sulbactam	Cefoperazon/ sulbactam	Cefoperazone/ Sulbactam	Netilmicin	
Cefepime	Cefotaxime	Cefuroxime	Amoxicillin	
Cefoperazone	Ceftriaxone	Cephalothin		
Cefotaxime	Cefuroxime	Chloramphenicol		
Cefoxitin	Chloramphenicol	Ertapenem		
Ceftazidime	Ertapenem	Netilmicin		
Ceftriaxone	Netilmicin	Norfloxacin		
Cefuroxim	Nitrofurantoin	Ofloxacin		
Cephalexin	Trimethoprim/ Sulfamethoxazol			
Cephalothin				
Ertapenem				
Fosfomycin				
Imipenem				
Piperacillin/ tazobactam				

Regarding antibiotic procurement reporting, audit results showed that purchasing data of antibiotics reflects antibiotic use in participating hospitals according to the local pharmacist. It was also found that the purchased antibiotics are mainly used for in-patients and only for a limited number of out-patients. Hospitalized patients rarely get antibiotics from other sources than the hospital pharmacy. All visited pharmacy departments have their own computerized database system for monitoring drug use in their hospital, facilitating the data extraction of actual antibiotic use. All hospitals also require that the dispensing of 2nd line drugs, like carbapenems, need to be approved by the local acting Drug and Therapeutic committee (DTC). During the visits it became clear that in those hospitals that also perform surgery, antibiotic prophylaxis during surgery was commonly 2nd and 3rd generation cephalosporins and administered for 7-10 days. This was also done for 'clean procedures'. Generally a single dose of surgical prohylaxis just before the surgical procedure is sufficient. In several southern hospitals, there is an effective mechanism of controlling antibiotic prescription by providing feedback to prescribers to reduce inappropriate antibiotic use. According to the interviewed pharmacists, areas of improvement are enhancing capacity of clinical pharmacist, provide up-to-date guidelines and antibiotic formularies and these documents should be distributed

among prescribers, microbiologists and pharmacists, enhance infection control; strengthen the DTC in controlling antibiotic resistance.

Since colistin it is not currently registered in Vietnam, it is not available to hospital pharmacies and is only available for purchase from market at relatively high prices. The lack of colistin availability and high price is leading to inadequate dosing of patients, with a serious risk that the bacterial pathogens will also develop colistin resistance. This would be a disastrous, since the infections would then become untreatable. Recent studies also show that a loading dose of colistin should be administered for serious resistant infections requiring colistin treatment [12], which is currently not done in Vietnam.

DISCUSSION

This surveillance project is the first for Vietnam to report on both antibiotic use and resistance. In 15 hospitals, the pharmacy data showed that average total antibiotic use per hospital was 274.7 DDD per 100 bed days. In comparison, antibiotics consumption in Vietnam was approximately five fold higher than a figure reported in Netherlands which found only 58.1 DDD per 100 bed-days in the same year [2] and median total antibiotic use reported from 139 hospitals in 30 European countries with 49.6 DDD per 100 bed-days in 2001[3]. In pediatrics hospitals, with average of 65 DDD per 100 beddays, overall antibiotics consumption in Vietnam was slightly higher than the figure in 5 children's hospitals in China in 2006 which was recorded in 49.9 DDD/100 bed-days [4]. With the increased common use of new generation antibiotics such as cephalosporins or 2nd line drugs like carbapenems for more severe diseases, the use of older antibiotics such as phenicols, beta lactamase sensitive penicillins, lincosamides gradually are replaced in treatment.

Average antibiotic expenditure per hospital in 2008 was 1.93 million USD, while the average annual income per capita was 1,024 USD and gross national income was approximately 77.7 billion USD [13]. These figures reflect that cost for antibiotic in treatment is an economic burden to the national health budget. Increasing resistance rates will lead to higher consumption of the more expensive 2nd line drugs like imipenem. Already we see that with little carbapenem usage, the costs have already increased considerably because of this. Controlling resistance also means that you will prevent increasing use of more expensive drugs.

Although the number of isolates varied by hospital and region with more than 20 kinds of bacterial pathogens, enteric bacteria predominated including *E. coli, Klebsiella* species, *Pseudomonas aeruginosa* and *Acinetobacter* which are common causes of hospital-acquired infections.

The notable increases in the prevalence and the level of cephalosporins 3rd and 4th generation resistance among clinical Gram-negative pathogens are of particular concern. 56.4% *E. coli* isolated in middle region hospitals were resistant to ceftazidime. According to the data from the surveillance,

the prevalence rate of carbapenem resistance was alarmingly high in northern hospitals where more than 50% of *Acinetobacter* species were resistant to imipenem. Data from this study also showed that fluoroquinolones resistance among *Klebsiella* strains isolated in southern hospitals was more than 60%.

The associations between antibiotic use and resistance in participating hospitals were found . There were two positive correlations between high consumption cephalosporins J01DA and higher resistance rate of *E.coli* to cefuroxime-3rd generation cephalosporin ($r = 0.718$, $p = 0.003$) and higher consumption carbapenems J01DH in hospitals where ceftazidime resistant *Acinetobacter* being high ($r=0.623$, $p=0.031$). These findings indicate that if we can improve antibiotic use, we may reduce or delay further spread of resistance.

There may be some limitation in interpreting the data from this study. For instance, the consumption data that was collected from purchasing report may not reflect true consumption and is aggregated. To improve AB use reporting, we should collect the actual use of antibiotics on patient level in the hospital in the future. As most hospitals have computerized systems, this should be feasible, and would allow even to do this by month so seasonal patterns may be observed. Consumption data was collected for 2008 meanwhile resistance rate represented for 2009, therefore data from this study may not reflect exactly the relationship between the amounts of antibiotics used and the emergence of resistance. Beside this, DDDs do not consider different dosage for children (patients in two pediatrics hospitals). Therefore, using DDDs for adults to express consumption in children leads to an underestimation for pediatric hospitals.

The current resistance report form included many bacterial indicators which makes both reporting and analysis difficult. Resistance rates of some bacteria were reported for genus levels such as *Klebsiella* spp., *Acinetobacter* spp. which is too crude and could not reflect the emergence resistance rate of particular common nosocomial pathogens. In the future, the report should focus on several indicator bacteria with sufficient numbers such as *E. coli, K. pneumonia, P. aeruginosa, Acinetobacter baumannii, S. aureus, S. pneumoniae* and from relevant specimens including blood, CSF, sputum, stool and urine. Data should be collected consistently for all three categories of susceptibility testing: resistant (R), susceptible (S) and intermediate (I). In the current report, some hospitals submit data in number of resistant strains without providing the number of tested strains, which makes a proper assessment impossible due to lack of a denominator. In the Appendix B revised form is proposed which can be used for future reporting (Appendix B). As some hospitals showed improbable resistance rates and thus poor quality resistance data, only hospitals which pass an external assessment should be selected to participate the surveillance program in the future.

CONCLUSION

The report showed high consumption of antibiotics in most hospitals in Vietnam with an increased use of new generation and expensive antibiotics like carbapenems. This shift in treatment has lead to an increased economic burden of the national health budget. Furthermore, common pathogens showed alarming resistance rates to common used antibiotics and decreased susceptibility to last resort antibiotics such as carbapenems. We found significant positive correlations between

cephalosporins consumption and cefuroxime resistant *E. coli* and carbapenems use and ceftazidime resistant *Acinetobacter*. These correlations reflect the fact that antibiotic pressure drives resistance, and resistance drives doctors to use newer and often more expensive last resort antibiotics. Currently, all laboratories base their susceptibility testing on CLSI guidelines. On site assessments revealed that most labs perform too many resistance tests, for instance for antibiotics that would not be used for treatment or for several antibiotics in the same class. A positive development is that quality assurance is being increasingly performed, but does need further improvement. Participating in an internationally recognized external quality assurance scheme is highly recommended. Areas of improvement are enhancing capacity of clinical pharmacists, clinical microbiologists and clinicians. Up-to-date antibiotic guidelines should be drafted with local data and widely circulated among prescribers, microbiologists, pharmacists and infection control staff. Furthermore the capacity of local Drug Therapeutic Committees should be strengthened to be able them to both monitor and control antibiotic use in their hospital based on local consumption and resistance data. On the basis of the information from this study, further national surveillance for both actual antibiotic use and resistance rate of few common bacterial pathogens in same period is strongly warranted to develop the evidence base for action on antibiotic resistance in Vietnam. Antimicrobial stewardship program also should be built and implemented in hospitals.

RECOMMENDATIONS

A. Develop an antibiotic stewardship program that is coordinated by the Drug Therapeutic Committees and includes

1. Develop a database for antibiotic use and resistance in hospitals

   This database requires the following data;

   - Collect monthly bed occupancy rates (for DDD/ 100 bed-days calculation)

   - Collect the actual use data of antibiotics in the hospitals to improve antibiotic use report which reflex the real consumption data for in-patients only.

   Provincial and district hospitals, which previously showed improbable high resistance rate and poor quality resistance data, should have site visits and coaching before participating at the surveillance program in the future.

   - Consumption data and resistance data should be collected for the same year to evaluate the relationship between the amounts of antibiotics used and the emergence of resistance. –

   - **Analyze** data by month so seasonal patterns can be observed. Annually report of antibiotic use and resistance in hospitals should be distributed to all large hospitals as well as made available online.

2. Develop evidence based national antibiotic guidelines as component of standard treatment guidelines (STGs) with regular updates and can be adjusted locally based on local epidemiology and resistance rates for each hospitals.

3. Perform clinical audits of doctors/departments to assess compliance to guidelines and appropriate practice on antibiotic use.

4. Enhance the hospital quality systems for pharmacy, laboratory, infection control and clinical departments.

5. Resistance testing

   Assessment of Resistance including %R, %I and % S, and the number of samples tested, to avoid misinterpretation of resistance rates due to low patient numbers investigated.

   a. Internal quality control of resistance tests needs to be performed on a regular (e.g. weekly) basis and have different technicians do it each time to check for differences between technicians.

   b. Available McFarland standards in lab for resistance testing

   c. Active use and understanding of up-to-date CLSI guidelines, which preferably needs to be translated into Vietnamese and widely disseminated.

   d. Antibiotics selection for resistance test should be based on CLSI guidelines. Reducing the number of unnecessary tests will reduce costs and improve the quality of the testing (eg antibiotics of the same group, antibiotics are not recommended by CLSI, antibiotics will not be used in treatment).

   e. Supplemental recommendations, particularly: (1) replace disk diffusion test by MIC method for vancomycin against *S. aureus* (MIC $\geq$ 2 indicate high risk of failure in treatment); (2) apply new criteria of break points and MIC for third generation cephalosporins against *E. coli* and *K. pneumoniae* as well as other Enterobacteriaceae to detect ESBL producing strains;, (3) apply new criteria of break points and MIC for carbapenem against *E. coli* and *K. pneumoniae* to detect carbapenem-resistant strains, NDM1 and KPCbla; (4) oxacillin should be replaced by cefoxitin to detect methicillin-resistant *staphylococcus*.

   f. External quality assurance is recommended for all testing performed in the laboratory (e.g. NEQAS, or RCPA).

6. Infection control: Effective infection control is difficult in over-crowded and poorly resourced health care settings. However, infection control guidelines should be updated and strictly applied with the right leadership and resources to reduce transmission of multi-drug resistant bacteria.

As most hospitals have computerized systems, this should be feasible, and would allow to do analyzed data by month so seasonal patterns can be observed. Monthly bed occupancy rates would be needed for this as well.

B. Forms improvement:

- Purchasing form should be revised to consumption form for in-patients and may be done digitally with the current systems already in place.

- The current resistance report form included many bacterial indicators and some bacteria to genus level which is too crude makes both reporting and analysis difficult. It should be reduced to several key common nosocomial pathogens including *E. coli, K. pneumonia, P. aeruginosa, Acinetobacter baumanni, S. aureus, S. pneumoniae* isolated from relevant specimens such as CSF, blood, urine, sputum, and stool. Draft revised forms are shown in the appendix.

Appendix A.

Table 6. Total antibiotics consumption (J01) by ATC group in 15 Vietnamese hospitals in 2008

Antibiotics group	**ATC code**	**North**	**Middle**	**South**	**Average**
Tetracyclines	J01AA	6.8	3.0	2.2	4.0
Phenicol	J01BA	0.5	0.3	0.4	0.4
Penicillins with extended spectrum	J01CA	51.2	25.6	37.7	38.2
Betalactamase sensitive penicillins	J01CE	0.7	1.7	1.1	1.2
Betalactamase resistance penicillins	J01CF	2.0	1.4	3.8	2.4
Penicillins + beta-lactamase-inhibitiors	J01CR	30.8	18.0	13.8	20.9
Cephalosporins first gen.	J01DB	17.7	8.3	7.5	11.2
Cephalosporins second gen.	J01DC	27.9	135.3	29.9	64.4
Cephalosporins third gen.	J01DD	31.4	70.3	41.2	47.7
Cephalosporins forth gen.	J01DE	4.1	2.7	1.3	2.7
Carbapenem	J01DH	1.9	0.6	2.5	1.6
Sulfanamides + trimethoprim	J01EE	7.3	1.9	3.4	4.2
Macrolides	J01FA	41.2	26.7	15.5	27.8
Lincosamides	J01FF	0.5	1.2	1.0	0.9
Aminoglycosides	J01GB	8.9	14.4	9.1	10.8
Fluoroquinolones	J01MA	27.1	28.9	33.1	29.7
Other quinolones	J01MB	0.0	0.7	0.1	0.2
Vancomycin	J01XA	0.5	1.1	1.0	0.9
Polymyxin	J01XB		5.0	0.0	2.5
Metronidazole	J01XD	5.0	0.0	1.9	2.3
Fosfomycin	J01XX	0.4	0.2	0.8	0.5
Total	J01	**270.0**	**347.3**	**206.7**	**274.7**

Table 7. Bacterial pathogens tested for antibiotic resistance in 15 hospitals in Vietnam in 2009.

Bacteria name	BM	NHTD	NHP	TB	VD	SP	TN	UB	BD	DN	Hue	HTD	ND I	CR	DT
Acinetobacter	583	250	393	82	40	40	25	73	281	123	149	66	806	964	157
Burkholderia cepacia		2	185	219		6			1		26	91	18		1
Escherichia coli	933	156	402	51		155	32	322	560	468	304	70	722	1493	531
Haemophilus influenzae	11		92					392							
Klebsiella sp.	681	242	587	310	134	68	19	56	95	438	184	44	724	1129	496
Moraxella catarrhalis		3	23			1		784	20		20				
Neisseria gonorrhoeae			2					19							
Neisseria meningitidis			1			1									
Pseudomonas aeruginosa	500	98	382	204	192	107	26	98	210	254	190	19	234	818	183
Salmonella typhi		11						2				10			
Shigella flexneri						153		5							
Staphylococcus aureus	288	85	246		11	141	35	305	113		276	51	319	1353	313
Streptococcus pneumoniae	12	18	113			20		524	1		14	18	58		12
Streptococcus suis	35	38									23	23			
Vibrio cholearea	35		217			236		1							
Other Gram negative	25	315	311	4	92	175	10	246	808	284	363	1	228		244
Other Gram positive		23	10		19			128	508		415	52	930		40

Table 8. Bacterial pathogens tested for antibiotic resistance in Vietnam by region in 2009

Bacteria name	North		Middle		South	
	Number	**%**	**Number**	**%**	**Number**	**%**
Klebsiella sp.	2097	16.3	717	11.7	2393	19.6
Escherichia coli	2051	16.0	1332	21.7	2816	23.0
Pseudomonas aeruginosa	1607	12.5	654	10.7	1254	10.3
Acinetobacter	1486	11.6	553	9.0	1993	16.3
Staphylococcus aureus	1111	8.7	389	6.3	2036	16.7
Moraxella catarrhalis	811	6.3	40	0.7	0	0.0
Streptococcus pneumoniae	687	5.4	15	0.2	88	0.7
Haemophilus influenzae	495	3.9	0	0.0	0	0.0
Vibrio cholearea	489	3.8	0	0.0	0	0.0
Burkholderia cepacia	412	3.2	27	0.4	110	0.9
Shigella flexneri	158	1.2	0	0.0	0	0.0
Streptococcus suis	40	0.3	23	0.4	23	0.2
Neisseria gonorrhoeae	21	0.2	0	0.0	0	0.0
Salmonella typhi	13	0.1	0	0.0	10	0.1
Neisseria meningitidis	2	0.0	0	0.0	0	0.0
Other Gram negative	1178	9.2	1455	23.7	473	3.9
Other Gram positive	170	1.3	923	15.1	1022	8.4
Total	**12828**	**100**	**6128**	**100**	**12218**	**100**

All hospitals used CLSI guidelines for antibiotic susceptibility testing.

Appendix B

MoH (Health Bureau)
Hospital's name : …… **Form No. 2**

Report of Antibiotic Purchase

No	Active ingredient name/Concentration (content)	No of drug	Generic name/Brand name	Country/ Manufacturer	Unit	1/6/2008				7/12/2008				1/6/2009			
						Total of drug (in unit)	Total of drug (in content)	Price/unit	Total of money	Total of drug (in unit)	Total of drug (in content)	Price/unit	Total of money	Total of drug (in unit)	Total of drug (in content)	Price/unit	Total of money
(1)	(2)/(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)	(18)	(19)
							3 x 8		8 x 10		3 x 12		12 x 14		3 x 16		16 x 18
1		1															
		2															
		3															
		4															
		…															
	T?ng s?																
2		1															
		2															
		3															
		4															
		…															
	T?ng s?																
3		1															
		2															
		3															
		4															
		…															
	T?ng s?																
…																	
X	**Proportiong of AB expenditure**																
Y	**Drug expenditure (excluding chemistry, reagents, blood, vaccine and other biological products)**																

Ngày …../……./2009

Pharmacy Department *(Sign and stamp)*

Finance-Account Department *(Sign and stamp)*

Director *(Sign and stamp)*

Ministry of Health (Health Bureau): ……

Hospital's name: ……

REPORT OF ANTIBIOTIC RESISTANCE

(attached with Document No. 139/KCB-VN on 26/2/2010)

(Specimen ……....)

Form …./……. To……/…….

			Bacteria																					
		Antimicrobial Susceptibility Test*	*Escherichia coli*	*Salmonella sp.*	*Shigella sp.*	*Enterobacter sp.*	*Klebsiella sp.*	*Proteus sp.*	*Pseudomonas aeruginosa*	*Burkhloideria cepacia*	*Acinetobacter sp.*	Gram (-) Bacilli	*V. cholearae*	*Haemophilus sp.*	*Staphylococcus aureus*	*Coagulase negative staphylococci*	*Streptococcus pneumoniae*	*Enterococcus sp.*	*Viridans streptococci*	*Streptococci khác*	*Moraxella catarrhalis*	*Neisseria meningitidis*	*Neisseria gonorrhoeae*	*Others*
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
Nr. of strain																								
(+)	ESBL																							
	b-lactamase (nitrocefin)																							
1	Amikacin																							
2	Amoxicillin																							
3	Amoxicillin																							
4	Amoxicillin/ clavulanic acid																							
5	Ampicillin/ sulbactams																							
6	Azithromycin																							
7	Aztreonam																							
8	Cefaclor																							
9	Cefepime																							
10	Cefixime																							
11	Cefoperazone																							
12	Cefoperazone/ sulbactams																							
13	Cefotaxime																							
14	Cefoxitin																							
15	Cefdopoxime																							
16	Ceftazidime																							
17	Ceftriaxone																							
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
18	Cefuroxime																							
19	Cephalexin																							
20	Cephalothin																							
21	Chloramphenicol																							
22	Ciprofloxacin																							
23	Clarithromycin																							
24	Clindamycin																							
25	Colistin																							
26	Doxycycline																							
27	Ertapenem																							
28	Erythromycin																							

Proposed new forms for antibiotic resistance (attached)

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