AND TRAINING

National Institute of Hygiene and Epidem

TRAN THI MAI HUNG

ASSESSING THE SITUATION AND SOME
RELATED TO ANTIMICROBIAL RESISTANC
COMMON BACTERIA IN THE COMM
IN VIETNAM 2018-2019

Specialization: Public Health
Code: 62 72 03 01

THESIS SUMMARY

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   Nguyen Tran Hien, Luong Minh Tan, Ngu
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   Anh, Dang Duc Anh (2020): Knowledge,
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   some regions of Vietnam in 2018 - 201
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   Anh, Tran Huy Hoang (2021): Billionaire
   Escherichia coli carrying the gene encoding ES
   with some common diseases visiting primar
   facilities in some provinces and cities of Viet
   Science and Technology Magazine, volume 63

The World Health Organization (WHO) identifies antimicrobial resistance as one of the ten threats to global health, development, and health security. Antimicrobial-resistant bacteria pose an enormous global economic and disease burden. It was estimated that in 2019, there would be 1.27 million deaths from antimicrobial-resistant bacteria worldwide and 4.95 million deaths related to antimicrobial-resistant bacteria. The latest WHO surveillance report in 2021 showed that *E. coli* and *K.pneumonia* were two of the most common antimicrobial-resistant agents and two agents with very high rates of multidrug resistance and sepsis in both community and hospital. This has been the global disease burden and the economy, especially in developing countries. However, most data on antimicrobial-resistant bacteria focus on surveillance and research in the hospital environment.

Vietnam is one of the countries with severe antimicrobial resistance. One of the reasons is the uncontrolled use of antimicrobials in the community and livestock. Over the years, Vietnam has also paid certain attention to the situation of antimicrobial resistance. However, the investment in resources as well as the strategy for the surveillance and management of antimicrobial resistance has not been synchronically implemented. Currently, there is not much data on the extent of antimicrobial resistance in the community; the available data are often from small study sites, which do not estimate the extent and burden of in resistance level, transmission level, and mode of spread, transmission for appropriate interventions. It is necessary to develop communication programs for people and drug sellers about the rational use of antimicrobials following a doctor's prescription.

Information and research data on antimicrobial resistance in the community should be brought to clinicians for reference in the context that in our country, there are no results of microbiological tests in the treatment of hospital infections at the district level, commune health stations to be able to prescribe treatment for patients more effectively.

Continuing to research the transmission and transformation of drug-resistant bacteria; communicate research findings to policymakers and clinicians and develop effective intervention programs

as well as whether or not there is a relatio antimicrobial-resistant bacteria in the communit Because of the necessity and practical significance m we conducted the research topic ***"Assessing the situ factors related to antimicrobial resistance of some c in the community in Vietnam, 2018-2019".*** The stu contribute to determining the priority and level of th appropriate policies, action plans and interventions 2020-2030. The study was carried out with the follow

1. Objective 1: Assess the prevalence and antimic characteristics of some common bacteria of commune health stations in some provinces of 2019.
2. Objective 2: Describe the current situation of kno of antimicrobials of patients visiting commune h some provinces of Vietnam, 2018-2019.
3. Objective 3: Determine the genotypic relatio strains of broad-spectrum antimicrobial-res isolated from patients visiting commune health provinces of Vietnam, 2018-2019.

Novelty in scientific and practical values of the topi

This is the first study of Vietnam on people w acquired infections in many different locations in th and South regions and evaluates different public factors.

The study revealed a picture of the resistance genes and antimicrobial resistance levels of two common and critical bacterial species in the community.

The study resulted in people's knowledge about antimicrobial use, an essential factor contributing to the rational use of antimicrobials and reducing antimicrobial use in the community.

Research has identified several Sequence types (ST) of *E. coli*, *Klebsiella pneumonia*-carrying ESBLs, and carbapenem strains circulating in the community and implications for the association between currently circulating strains in the community and the hospital. This can serve as evidence for the development of overall policies and interventions in both the hospital and the community.

STRUCTURE OF THE THESIS

The thesis consists of 164 pages, excluding references and appendices, with 23 tables, 8 figures, and 20 charts, in which: 2 pages of introduction, 46 pages of literature review, 24 pages of research objectives and methods, 60 pages of results, 26 pages of discussion, 2 pages of conclusion, and 1 page of recommendations.

Chapter 1. LITERATURE REVIEW

1.1 Some concepts

Antimicrobials are substances secreted by microorganisms or semi-synthetic and synthetic chemicals, with very low

of *E.coli* bacteria are resistant to ciprofloxacin an
intermediate, the resistance rate is quite hig
sulfamethoxazole + trimethoprim with; 88.2%
carrying antimicrobial resistance genes, including
ESBLs- SHV, TEM, and CTX-M and carbapene
Klebsiella spp. isolates with very high resistance to
antimicrobials: entirely resistant to ampicillin and
amoxicillin + clavulanic; 37.3% - 49% resistant to
cephalosporins, 13.7% resistant to meropenem.

2. Knowledge of antimicrobial use of patients

Knowledge about antimicrobial use among study
limited. 64% of respondents have inadequate knowle
the assessment. 37.5% of respondents use antimicrobi
antimicrobials without a doctor's prescription.

3. Genotypic relationship between *E. coli* str ESBLs *and K.pneumoniae* isolated from pati

There are certain associations in genotype and ST
strains *E.coli* was isolated in the study, including b
locality and in different locations. These STs are also S
world and in Vietnam. These strains are also strains th
in community studies in both human and animal samp
of *K.pneumoniae* carrying the NDM-4 gene belonging
in recent outbreaks in hospitals in different regions. Th
all multi-resistant and all-resistant and have a high mor

RECOMMENDATION

communities. More importantly, ST10 is widely distributed in the community and is found in many pigs, chickens, and farm breeds. Hence, the world considers the ST10 strain of *E.coli* as a highly contagious strain from animals such as pigs and chickens to humans.

K.pneumoniae appeared in various ST15, ST16, ST273, and ST1886. We did not find studies on the molecular biology of species in community infections in Vietnam. Compared with *K.pneumoniae strains* analyzed from studies in hospitals in Vietnam, 3 STs have been described in studies at hospitals, namely ST15, ST16, and ST273. ST15 and ST16 were found more frequently in hospital studies. ST273 was found in only 1 study. ST15 and ST16 are high-risk multidrug-resistant species with genes encoding carbapenems such as blaKPCs, blaNDMs, or blaOXAs. Outbreaks caused by ST15 OXA-48 were reported in France and Spain later, and the strain spread worldwide. In Vietnam, in 2017, ST 15 appeared in *K.pneumoniae* strains isolated at a hospital. These ST15 strains carry many resistance genes, especially carpabenem-producing genes such as KPC, NDM-1, NDM-4, and OXA. In our study, the presence of ST15 carrying the NDM-4 gene and many genes resistant to many different antimicrobial groups, such as beta-lactamase, quinolone, etc., in the community proves that there is a certain spread between strains in the community. hospitals and communities in Vietnam.

CONCLUSION

1. Antimicrobial resistance characteristics of some bacteria

60.8% of strains of *E.coli* carry antimicrobial resistance genes

isolated to be resistant to at least one antimicrobial
classes of antimicrobials.

Pan-resistant bacteria: Totally resistant is an age
isolated to be resistant to all antimicrobials currently
classes of antimicrobials.

Community-acquired infection is an infection ou
long-term care facility, or nursing home.

1.2 Disease burden and antimicrobial resistance bacteria of concern in the world

1.2.1 The burden of disease due to antimicrobial

The UK government reckons antimicrobial resista
million people annually by 2050. The United States
6.5% death rate from antimicrobial-resistant bacte
23,000 deaths yearly. It is estimated that the num
deaths in the European Union due to selected antimic
is around 25,000 per year. A new study has estimate
that in 2019, globally, 1.27 million deaths from resist
4.95 million deaths are related to resistant bac
antimicrobial-resistant bacteria. *E.coli and K.pneu*
leading causes of death. According to a new WHO
with data from 68 countries, *E.coli* and *K.pneumonia*
most common antimicrobial-resistant agents; espec
agents have high rates of multi-resistance and infectio
high in both the hospital and the community. *E.*
K.pneumoniae (94%) are present in bacteremia, and

The estimated global antimicrobial resistance rate of K.*pneumonia in* 2015 was 23.4% and is forecast to reach 50% by 2030. In Israel and Spain, 40% of K.*pneumonia* isolated in hospitals has been reported. According to WHO, the occurrence of ESBLs-producing *K. pneumoniae* has now reached prevalence rates of up to 50% in many parts of the world, and resistance rates in the community of up to 30% demonstrate the widespread nature of the disease. Overall incidence among *Klebsiella* strains spp. resistance to this drug resistance to carbapenems isolated from nosocomial infections was about 12% between 2009 and 2010. In European countries, the proportion of KPC-producing strains of *K. pneumoniae* isolated in a Greek hospital increased from 0% in 2003 to 38.3% in 2010. In China, strains carrying the KPC gene increased to 63% from 2008 to 2011, mainly KPC-2. In Vietnam, in 2012 and 2013, the ratio *K . pneumonia* carbapenem resistance was 14.9%, of which carbapenem resistance was up to 55%.

In the community, in recent years, several studies have reported the prevalence of ESBLs-positive bacteria in community-onset sepsis in China, 16.5% (46/279) in isolated *K. pneumoniae*. In Turkey, 47% *Klebsiella* spp. born ESBLs in patients with community-acquired urinary tract infections. Similar results were found in other studies in Turkey and India. In addition to ESBLs antimicrobial genes, the studies also found the presence of carbapenemase genes *bla*NDM-1, *bla*NDM-4, *bla*NDM-5, as in South India, 19.4% –22,1% has the NMD-1 gene. These indicated that *Klebsiella* spp. was not only

and muscle/bone/joint pain (15%). Other studies have the flu is a common cause of antimicrobial use. study, the rate was much higher than the study in 27%, sore throat was 16.8%, and fever was 19.2 compared with other studies conducted in Yogy Kuwait (29.8%), and Korea (30.6%). The risk of anti 3 months was 37.5% and in the patient's family w result was similar to the WHO survey in regiona Vietnam in 2015, higher than the survey in the gene Malaysia (16.5% within four weeks) and Serbia and This risk is lower than reported in Egypt; the risk of a in the past 1 month was 54%. The use of antimicrob the community contributes significantly to th antimicrobials used in the country.

4.3. Genotypic relationship of isolated bacterial st detected strains

In our study, the analysis of the phylogeneti the close genotypic relationship between the studied isolated from different patient samples and the study s Some strains belonging to the same ST and having g but coming from other localities such as Khanh Ho Hanoi and Ha Nam show the widespread occurrence carrying drug resistance genes in many provinces of accounted for the majority (23%) and was present i communities, and strains in other locations were si *that the average risk was 32.8%.*

4.1.3. Some factors related to the status of carrying antimicrobial resistance genes in the community

Living conditions, infrastructure, and sanitation are important factors associated with antimicrobial resistance. Our study showed that using dug well water and bore well water has a lower risk of infection with antimicrobial resistant bacteria than tap water and rainwater. Recent concerns suggest that drinking water is the main route of transmission of pathogenic bacteria to humans. Whether treated or not, consumption or treatment of water can lead to colonization of the gastrointestinal tract in humans and animals with bacteria harboring resistance genes. In addition, water is used to irrigate plants and animals, contaminating the products and leading to human/animal colonization with resistant organisms. Our study found that people using antimicrobials with advice from drug sellers had a higher risk of carrying antimicrobial resistance genes. A survey in Ba Vi on 823 children in 2007 showed that seeking medical services at any health facility: pharmacy, public or private clinic increases the likelihood of using antimicrobials to treat urinary tract infections, mild acute respiratory failure, and 82% of unnecessary antimicrobial use was on the advice of a healthcare provider.

4.2. Current status of knowledge and use of antimicrobials of patients and their families visiting the commune health station

Only 57% of respondents answered antimicrobials to treat

promote routine antimicrobial resistance surveillar
changes in resistance patterns.

4.2.2 *The status of Escherichia coli antimicrobial*

E. coli is the leading cause of infection, and E
is highest in Asia and the Middle East (30% to 50
E.coli 3rd generation cephalosporin resistance
countries is 12.8%. The highest was in one of the
Bulgaria, Cyprus, Italy, and Slovakia (with propor
30.2%, 29.8%, and 29.7%, respectively). The majorit
were ESBLs positive (88.4%); this figure in 201
addition, this bacterium is also resistant to many othe
such as aminoglycosides and fluoroquinolones. M
strains of bacteria resistant to 3rd generation cepha
resist to at least three groups of antimicrobials, cau
resistance. Asia is increasingly a hotbed of antimicr
due to large populations, infections in both ho
community, and the extent and control of antimicro
humans and livestock. In 2007, in the Asia-Pacif
resistance surveillance study, the percentage of prod
E. coli, was 42.2%, high in India (79%), China (55%
(50.8%). Countries with the average rate of *E.coli*-pr
were Vietnam (34.4%) and Singapore (33.3%). Coun
risks were Korea, Hong Kong, Philippines, Taiwan
New Zealand, where the rate of *E. coli* producing
22.7%.

produced ESBLs; in France, it was 6% in 2011, and in Germany, it was 6.3%. In 2009, in China, 50.5% of stool samples of healthy people contained ESBLs-producing *E.coli* bacteria; in Thailand in 2008, the proportion of healthy people carrying ESBL-producing bacteria in stool samples was 61.7%, in which *E. coli* predominates with the rate of 85.1%. In Vietnam, *E.coli*-producing ESBLs appeared in healthy people in the community at relatively high risk, of which 53.7% had ESBLs-producing bacteria in the gastrointestinal tract. Thus, the above studies showed that *E. coli*-producing ESBLs were not only present in hospital patients or outpatients but also in healthy people in communities around the world.

Chapter 2. RESEARCH METHODS

2.1. Research subjects

All patients were examined at the commune health stations and were diagnosed as having one of the following four diseases: skin infection, urinary tract infection, pneumonia, and diarrhea. Patients were in accordance with the selection and exclusion criteria and agreed to participate in the study. Case definition of the urinary tract infections, skin infections, diarrhea, and pneumonia (as defined by CDC, USA and WHO).

2.2. Research period: Data collection in 2018- 2019. Testing and data analysis 2020-2021.

2.3 Research location : 8 communes in 8 provinces: Ha Nam, Hanoi, Bac Ninh and Hai Duong, Thua Thien Hue, Khanh Hoa, Ben Tre and

such as Taiwan, which was 11.9% in 2012, and the
2009-2011. *Klebsiella* spp. carrying genes cod
production, including SHV (76.5%), TEM (23.5%
(21.6%) genes, make up the majority. This result is r
tendency of *Klebsiella* spp to cause communi
neighboring countries China and Taiwan and s
countries of the authors Jing, Lin, and Cartia. Of in
large proportion of *Klebsiella* spp. carrying the
carbapenem; this is a resistance gene that usually
hospitals because carbapenem antimicrobials are ant
in hospitals. Studies and molecular surveillance data
of *Klebsiella* spp. in most community-onset infection
gene is absent. The rate of resistance to 3rd generatio
antimicrobials was 37.3 %, higher than that in a s
(35.8%), Bosnia and Herzegovina (20.3%) and Ethio
particular concern is the group of carbapenem ant
results from this study showed that 13.7% *Klebsiella*
meropenem, however, the intermediate rate with this
very high, up to 31.4%, much higher than studies in
and Portugal (0%). This shows that *Klebsiella* sp
community-acquired infections in Vietnam have mo
of resistance to antimicrobials than those studied in
around the world. The rate of multi-resistant *Kleb*
57.1% (multi-resistant is defined as resistance to mo
of antimicrobial drugs), this is a high rate of multi-

4.1. Antimicrobial resistance characteristics of *E.coli* and *Klebsiella* spp. and some related factors

4.1.1. Antimicrobial resistance characteristics of *E.coli bacteria*

The percentage of *E.coli* carrying genes encoding ESBLs in our study was higher than that of Sudan in 2013, with 30.2%, Hong Kong (48%), and Singapore (33%). Research has shown that the TEM gene is the predominant ESBL gene in *E.coli bacteria*, corroborating with the reports of several other previous studies. The TEM gene was dominant in European countries such as Italy (45.4%) and Turkey (72.7%). Our study is similar to those with TEM predominating (88.2%), followed by CTX-M (51%). *E. coli* resistance to commonly used antimicrobials from our study was lower than that of similar studies in China on community-onset infections. However, compared with similar studies in countries other than China, the results of antimicrobial resistance in our study are much higher, even in low-income countries in Asia and Africa. The results from our study were also much higher than that of studies in developed countries. In studies from OECD countries, overall resistance rates were 53.4% for ampicillin, 23.6% for trimethoprim, 8.2% for co-amoxiclav, and 2.1% for ciprofloxacin. In our study, the risk of multi-resistant strains of *E.coli* isolates was 58.7%. This was a rather high rate compared to studies on community-acquired infection strains. In the Canadian study, this rate is 24.6%, the US is 31-36%, and Taiwan is 37%.

4.1.2. Antimicrobial resistance characteristics of *Klebsiella* spp.

$$n = Z^2_{(1-\alpha/2)} \frac{1 p}{\varepsilon^2 p}$$

In there: n: Sample size required for 1 diseas commune; Z: parameter related to the risk of corresponding to α = 0.05; ε: relative precision. T proportion of people infected with KKS bacteria of **a in the community**. Choose p=0.5 (some research re that the rate of parasites in the community in from 40-60%) → n = 40; Estimated rejection rate of Thus, the minimum sample size for the whole comm be 44 people x 4 diseases x 8 communes = 1,408 pat

2.6. Sampling method: Select 08 representative p North, Central, and South regions; Select district selected by the Provincial Preventive Medicine Cen capacity to conduct and participate in research.

2.7. Applied laboratory techniques: The technique study were carried out at the Antimicrobial Resistan the National Institute of Hygiene and Epidemiology: identification, and detection of bio-coding gene carbapenems of strains of *E. coli* and *Klebsiella* spp. PCR technique determine the minimum antimicrobi that inhibits bacteria and sequences the whole genom

2. 8. Data analysis and processing: We manage Epidata 3.1 software, and processed and analyzed etc., and basic homology to compare the results of gene sequencing with target gene sequences on the database of NCBI.

2.2.3 Ethics in research

The study was approved by the Ethics Committee in Biomedical Research of the National Institute of Hygiene and Epidemiology in Document No. IRB- VN01057-38/2016, dated October 21, 2016. Ethical principles in biomedical research are maintained in the conduct of research.

Chapter 3. RESULTS

3.1 Antimicrobial resistance rates of some common bacteria

3.1.1. Molecular biology and antimicrobial resistance of *E. coli.* bacteria

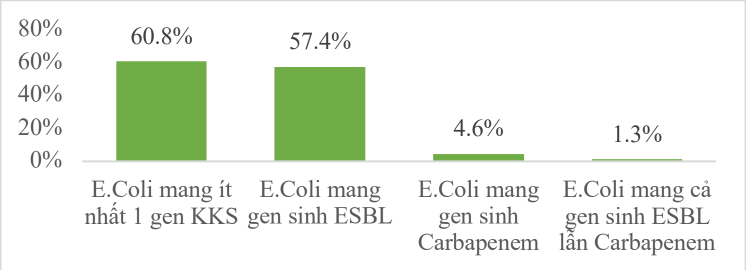

Figure 3.1. Percentage of E. coli carrying antimicrobial resistance genes (N=237)

Of the 237 *E. coli* isolated, 144 (60.8%) carried at least one antimicrobial resistance gene. The number of bacteria carrying genes encoding ESBLs was up to 136 (57.4%), and the number of bacteria carrying the Carpabenem gene was 11 (4.6%).

carried many antimicrobial resistance genes, dive
ST16, ST273 appeared.

is one strain with the same ST as ST10, ST225, ST38 and ST1 appearing at the study sites. There are quite a few strains Similar genotype resistance, including the same site (AHDPH03 a AHDMU12) and different study sites such as two strains in Kha Hoa and Hanoi AKHPH15 and AHNOPH16 or AHNOTH22 a AHNPH48.

Table 3.22. Characterization of AMR genes in *Klebsiella* spp. by genome sequencing techniques

Strain code	Carbapenemase- and ESBL . genes	MLST	Plasmid
ABN-PH33	blaCTX-M-15, blaSHV-100, blaOXA-9, blaNDM-4	-	IncFIB(K)(pCAV1099-114), IncHI1B(pNDM-MAR), IncFII(K)
ABN-PH34	blaCTX-M-15, blaSHV-100, blaOXA-9, blaNDM-4,	-	IncFIB(K)(pCAV1099-114), IncHI1B(pNDM-MAR), IncFII(K)
AHNOPH17	blaSHV-80, blaDHA-1	ST1886	IncR
AKHPH31	blaSHV-78, blaDHA-1	-	IncFIB(K), IncFII(K), IncR, IncFIB(pNDM-Ma
ATTH-MU39	blaSHV-67, blaTEM-1B, blaNDM-4,	ST273	IncFIB(K)
ATTH-MU48	blaCTX-M-14, blaCTX-M-15, blaLAP-2, blaOXA-9, blaNDM-4,	ST15	IncFIA(HI1), IncR, ColRNAI
ATTH-NT30	blaCTX-M-14, blaLAP-2,blaSHV-100, blaOXA-9, blaNDM-4,	ST15	IncFIB(K), IncFII(K)
ACTNT44	blaSHV-148, blaOXA-181	ST16	ColKP3, IncX3, IncFIB(K)

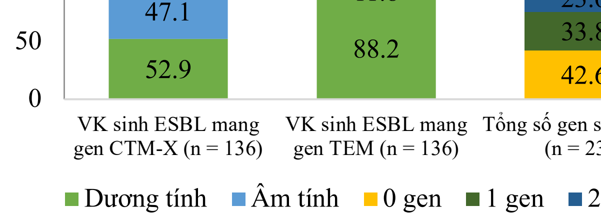

Figure 3.2. Characteristics of carrying the ESBL

(n = 237)

Among ESBLs-producing strains, TEM and were the two primary genes, in which TEM accounte CTX-M was 52.9%. The percentage of *E.coli* bacter genes was 23.6%.

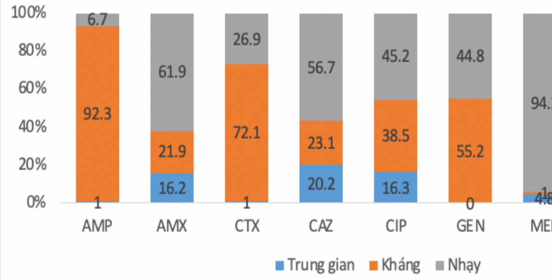

Figure 3.5. Rate of resistance of *E.coli strains* antimicrobials

92.3% *E.coli* resistant to ampicillin, 21.9 amoxicillin/clavulanic acid. With broad-spectrum antimicrobials, 72.1% were resistant to cefotaxime, resistant, and 20.2% were intermediate to ceftazidi resistance to the second-generation Quinolone ciprofloxacin was also 38.5% and 16.3% at the int

Number of antimicrobial-resistant groups	**Number of strains**	**Ratio (%)**	**Clas**
0	4	3.9	Non-ı resist (MDR)
1	11	10.6	
2	28	26.9	
3	24	23.1	Multi-re (MDR)
4	23	22.1	
5	14	13.5	

4/104 strains were not phenotypically resistant to any antimi accounting for 3.9%, and 10.6% of strains were resistant to a group of antimicrobials. The remaining 58.7% were resistant to 3 or more gro

3.1.3. Molecular biology and antimicrobial resistance of *Klebsiella* spp.

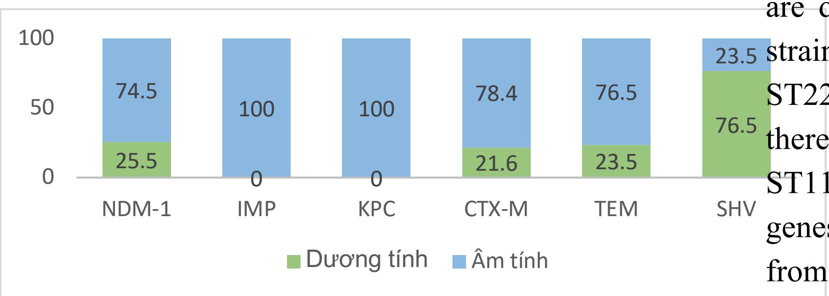

Figure 3.9 . Antimicrobial resistance gene carrier characteristics of *Klebsiella* spp. (N=51)

21.6% of strains carrying genes CTX-M and SHV (76.5%).

There were 13/51 strains carrying the NDM-1 gene (25.5%) and mo

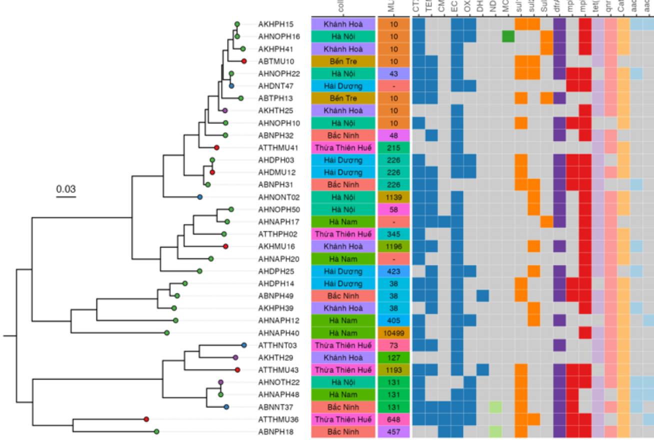

Figure 3.20. The phylogenetic tree shows th relationship of the studied strains and the heat p genotypes of the isolated ESBL s -bearing *E.*

The phylogenetic tree diagram shows that th
are divided into two main groups: the upper grou
strains belonging to 13 STs, including common ST
ST226, and ST38; The remaining group was locate
there were eight strains belonging to 6 different STs
ST1193, ST131, ST646, ST457. Phylogenetic analys
genes has shown a close relationship between *E. coli*
from different types of patient samples and from oth
areas; ST10 was classified as made from latex, faece
from 3 different cities and provinces: Hanoi, Khanh
ST226 isolated from stool and pus samples in Hai D
ST38 isolated from fecal samples in all three province

antimicrobials and antimicrobial resistance

The study used 11 questions to determine people's knowledge about antimicrobials, antimicrobial usage, and antimicrobial resistance. Only 59.6 % of people answered correctly, "Antimicrobials are used to treat bacteria," and 31.4% of people incorrectly answered, "antimicrobials are used to treat viruses" "don't know.", 57% of the respondents answered incorrectly about the disease requiring antimicrobial treatment. The selected wrong answers included "sneezing, runny nose, headache, stomachache, musculoskeletal pain, don't know."

Table 3.18. Status of antimicrobial use of subjects within 3 months before the time of the study by 3 regions (n=1432)

Characteristics	Total (n=1432)	North (n=796)	Central Region (n=337)	The South (n=299)	p-value
Use of antimicrobials					<0.001
No	895 (62.5%)	463 (58.2%)	243 (72.1%)	189 (63.2%)	
Have	537 (37.5%)	333 (41.8%)	94 (27.9%)	110 (36.8%)	

Patitents commonly used antimicrobials within 3 months and there was a statistically significant difference between regions, the North has the highest rate of antimicrobial use (41.8%), followed by the South (36.8%) and the Central region with the lowest rate (27.9%).

Figure 3.10. Resistance percentage of *Klebsiella* with antimicrobials

Klebsiella spp. was resistant to 8 out of 9 tested, 100% of strains were resistant to ampici resistant to amoxicillin + clavulanic acid; 37.3% with 49% with ceftazidime; 13.7% resistant to meropene group, however, the intermediate rate with this antin high, up to 31.4%;

51)

Amount of antimicrobials	**Number of strains**	**Frequency (%)**	**Single-resistance/Multi-resistance**
1	18	35.3	Non-multiple resistance (MDR) 52.9%
2	9	17.6	
3	7	13.7	
4	5	9.8	Multiple Resistance (MDR) 4 7.1%
5	8	15.7	
6	4	7.8	

Prevalence of multi-resistance of *Klebsiella* spp. accounted for 47.1% of whole bacteria *Klebsiella* spp. All were resistant to at least one antimicrobial group, and the risk of resistance to 5 and 6 antimicrobial groups was up to 23.5%.

Table 2.15. Some factors related to the non-resistance gene in 2 strains *E.coli and Klebsiella* spp. (n = 279); n (%)

Element	**Not carrying the KKS gene (n=91)**	**Carries the KKS gene (n=188)**	**Univariate RR (95% CI)**	**Multivariable RR (95**
Main source of water used for drinking				
Machine water	72 (38.3)	116 (61.7)	1	
Rainwater/river/str	12	35	0.7 (0.4-	0.9 (
Well water/dug	7 (15,9)	37 (84.1)	**0.4 (0.2-0.8)** *	
Get advice from the drug dealer for KS				
Have	57 (27.9)	147 (72.1)	1	
No	34 (45.3)	41 (54.7)	**1.6 (1,2-2,3)** *	

(*) : p< 0.05

People living in households that used dug/dr for drinking were 0.4 times less likely to carry the than those that used tap water or rainwater. Those advised on antimicrobials by drug sellers were 1.5 ti to carry no antimicrobial resistance genes (95 % CI: counseled group .

3.2. Current status of patients' knowledge of ar