PATHOGENS ASSOCIATED WITH BACTERIAL BLOODSTREAM INFECTIONS AT THE FACILITY 2 OF NATIONAL HOSPITAL FOR TROPICAL DISEASES IN DONG ANH DISTRICT (2018 - 2020)

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Summary

Objectives: 1. Identifying the pathogens associated with bacterial BSIs at the ability 2 of NHTD in Dong Anh district from 2018 to 2020. 2. Identifying antimicrobial susceptibility of bacteria isolated from blood samples.

Subjects and methods: A descriptive study was conducted at the National Hospital for Tropical Diseases between January 2018 and December 2020. Cases of BSI were determined from records in the microbiology department with positive two blood cultures in the first episode.

Results: A total of 330 patients with BSI were included for microbiological analysis. The predominant pathogens were: *K. pneumoniae* (15.1%), *E. coli* (14.2%), *S. aureus* (14.2%), *Acinetobacter baumannii* (6.8%) and *Stenotrophomonas maltophilia* (5.3%). There were two species with a high proportion of extended - spectrum beta - lactamase (ESBL) production among *Enterobacteriaceae* were *E. coli* (68.8%) and *K. pneumonia* (15.7%). All of *S. aureus* isolated strains were susceptible to vancomycin and linezolid.

Conclusions: *Enterobacteriaceae* (predominantly *K. pneumoniae* and *E. coli*) is the most common cause of bloodstream infections in a tertiary referral clinic in NHTD (a branch at Dong Anh district) in 2018 - 2020.

Key words: *Bloodstream infections, Gram - negative bacteria, drug resistance, Vietnam.*

BACKGROUND

Bloodstream infections (BSIs) are the major cause of sepsis - related morbidity and mortality worldwide[1]. BSIs were one of the reasons that contributed to death in Europe and North America[2]. Vu Quoc Dat reported that there were 738 patients with BSI at National Hospital for Tropical Diseases (NHTD) from 2011 to 2013 in Vietnam, with over 60% of death associated with *Enterobacteriaceae*[3]. NHTD is a tertiary referral hospital and specializes in infectious diseases. There is the ability 2 of NHTD in Dong Anh district, which has been opened since 2017. Then until 2020, no reports about the pathogens of BSI were published in this branch. Therefore, understanding bacteria cause to BSI and their antimicrobial resistance can help clinicians to use empirical antibiotics effectively. Especially, cases of septic shock should be treated with the right antibiotics quickly. This can help to reduce the mortality rate. Our research was performed with two purposes:

Firstly, identifying the pathogens associated with bacterial BSIs at the ability 2 of NHTD in Dong Anh district from 2018 to 2020.

Secondly, identifying antimicrobial susceptibility of bacteria isolated from blood samples

SUBJECTS AND METHODS

Research subjects: The results of positive blood cultures at NHTD in Dong Anh district between January 2018 and December 2020

Research standards: The results of positive blood cultures associated with BSI patients in the first episode. Selected patients needed to have enough information about identification bacteria and antimicrobial susceptibility testing.

Exclusion criteria: Fungi and *Mycobacterium tuberculosis.*

Study method and data collection: This is a cross - sectional descriptive study about bacterial bloodstream infection at the Microbiology department of NHTD in Dong Anh district from January 2018 to December 2020. Variables in research include age, sex, clinical features, bacteria isolated, antimicrobial susceptibility testing. A standard data collection form was created to extract microbiology records by using Excel 2016. Data were analyzed by SPSS Statistics version 20. Variables are described with percentage and Chi - squared test.

Ethical research: The research was approved by the Hanoi Medical University council. The leader of Microbiology Department and the board of directors accepted our data collection. The information of all patients will be completely kept secret and only use in research. All data was collected and analyzed honestly.

RESULTS

There were 330 results of positive two blood cultures in the first episode from 2018 to 2020. The median age of the group was 51.2 ± 14.8 years. The eldest patient was 89 years old and the youngest patient was 9 years old. The group of patients who were over 60 years old was the highest percentage (30.4%). The group of patients who were under 18 years old was the smallest percentage (1.2%). 74.6% of patients were men, higher than three times to female (25.5%). Common comorbidities were chronic hepatitis or cirrhosis (24.2%). The diagnosis of BSI was 21.8%.

Table1. Spectrum of organisms identified during the study period 2018 - 2020

Bacteria	2018		2019		2020		Total in 3 years	
	n	%	n	%	n	%	n	%
Enterobacteriaceae							124	36.8%
K. pneumoniae	10	9.0%	34	20.4%	7	11.9%	51	15.1%
E. coli	14	12.6%	21	12.6%	13	22.0%	48	14.2%
Salmonella species	1	0.9%	2	1.2%			3	0.9%
S. marcescens	2	1.8%	2	1.2%	4	6.8%	8	2.4%
Enterobacterspecies	4	3.6%	5	3.0%			9	2.7%
Other			4	2.4%	1	1.7%	5	1.5%
Non - Enterobacteriaceae							118	35%
Stenotrophomonasmaltophilia	7	6.3%	9	5.4%	2	3.4%	18	5.3%
Aeromonas species	5	4.5%	4	2.4%	3	5.1%	12	3.6%
Burkholderiapseudomallei	3	2.7%	5	3.0%	4	6.8%	12	3.6%
Burkholderia species	7	6.3%	5	3.0%	2	3.4%	14	4.2%
Pseudomonas aeruginosa	3	2.7%	5	3.0%	2	3.4%	10	3.0%
Acinetobacterbaumannii	13	11.7%	9	5.4%	1	1.7%	23	6.8%
Acinetobacter species	2	1.8%	13	7.8%			15	4.5%
Other	6	5.4%	8	4.8%			14	4.2%
Gram positive bacteria							95	28.2%
Staphylococcus aureus	18	16.2%	21	12.6%	9	15.3%	48	14.2%

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Staphylococcus species	4	3.6%	5	3.0%	4	6.8%	13	3.9%
Streptococcus suis	6	5.4%	2	1.2%	1	1.7%	9	2.7%
Streptococcus pneumoniae	2	1.8%	1	0.6%	2	3.4%	5	1.5%
Streptococcus species	4	3.6%	6	3.6%	4	6.8%	14	4.2%
Enterococcus species			3	1.8%			3	0.9%
Corynebacterium afermentans			1	0.6%			1	0.3%
Rhodococcus equi			2	1.2%			2	0.6%
Total amount of bacteria	111	100%	167	100%	59	100%	337	100%

Note: n = amount of bacteria, Strains

During 3 - year period, a total of 337 bacteria isolated from blood samples were identified with 71.8% Gram - negative bacteria and 28.2% Gram - positive bacteria. *Enterobacteriaceae* were the most frequently isolated group of organisms among patients with BSI (36.8%) with the predominant *Enterobacteriaceae* being *K. pneumonia* (15.1%) and *E. coli* (14.2%). *Non - Enterobacteriaceae* was 35% with *Acinetobacter baumannii* (6.8%), which was the fourth - ranking in the pathogens of BSI. In Gram - positive bacteria isolated group, *S. aureus* was the highest percentage (14.2%). There were 7/330 the results of positive blood cultures had 2 pathogens isolated in the same culture bottle. There were 2 cases with *K. pneumoniae and E. coli,* 5 cases with *Acinetobacter baumannii* and *Enterobacter cloacae, E. coli* and *Enterobacter cloacae, K. pneumoniae* and *Acinetobacter baumannii, K. pneumonia* and *Acinetobacter nosocomialis, K. pneumonia* and *E. coli, Acinetobacter baumannii* and *Pseudomonas aeruginosa*.
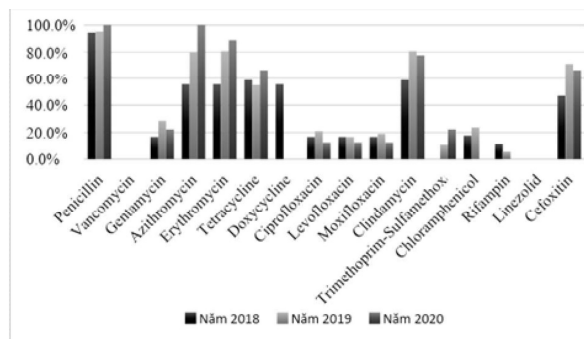
**Picture 1.** Resistance among *S. aureus* from BSI

During 3 - year period, the rate of *S. aureus* isolated resistance to penicillin was highest and increasing gradually (94.4%; 95.2%; 100%). This difference was not statistically significant (p = 0.78). The percentage of resistance to macrolides

(Azithromycin và erythromycin) was increasing. The proportion of MRSA (Methicillin - resistant *Staphylococcus aureus*) was 61.7%, which was more than 2 times MSSA (Methicillin - resistant *Staphylococcus aureus*) with 38.3%. All of *S. aureus* isolated strains were susceptible to vancomycin và linezolid.
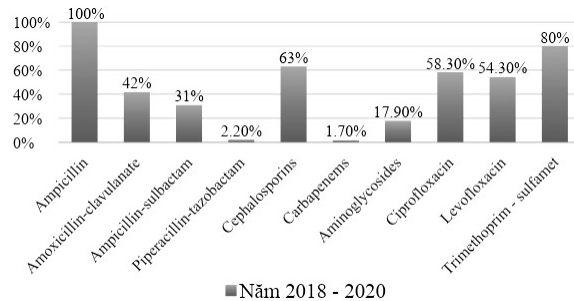
Picture 2. Resistance among *E. coli* from BSI

E. coli isolated were resistant to ampicillin (100%), cephalosporins (63%), ciprofloxacin (58.3%), levofloxacin (54.3%) and trimethoprim - sulfamethoxazole (80%). However, *E. coli* isolated resistance to carbapenems was the smallest rate with 1.7%.
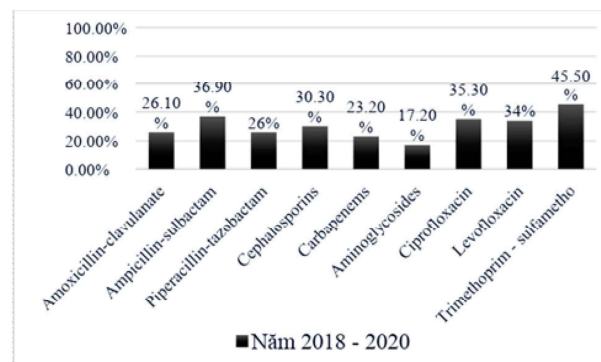
Picture 3. Resistance among *K. pneumonia* from BSI

K. pneumoniae isolated has a medium rate of resistance with all antibiotics (< 50%). The *K. pneumonias* trains had the highest rate of resistance to trimethoprim - sulfamethoxazole (45.5%) and the smallest proportion of resistance to aminoglycosides (17.2%).

Table 2. Rates of *E. coli* và K. pneumonia extended - spectrum beta - lactamase (ESBL) - producing

Bacteria Year		E. coli		K. pneumoniae	
		ESBL (+)	Total of E. coli	ESBL (+)	Total of K. pneumoniae
2018	n	13	14	2	10
	%	92.9%	100%	20%	100%
2019	n	11	21	5	34
	%	52.4%	100%	14.7%	100%
2020	n	9	13	1	7
	%	69.2%	100%	14.3%	100%
Total 3 years	n	33	48	8	51
	%	68.8%	100%	15.7%	100%

Note: n = amount of bacteria

There are 68.8% (33/48) of all *E. coli* isolated were extended - spectrum beta - lactamase (ESBL) - producing. By contrast, only 15.7% (8/51) of *K. pneumoniae* isolated were ESBL producers.

DISCUSSION

Analysis of microbiological dataset

During the 3 years, a total of 330 BSI patients with 137 bacteria were isolated from blood samples. The most popular pathogen was Gram - negative bacteria (71.6%). *Enterobacteriaceae* were the most frequently isolated group of organisms with the predominant species being *K. pneumonia* (15.1%) and *E. coli* (14.2%). Gram - positive bacteria isolated group had a lower proportion than Gram-negative bacteria with 28.4%. Among them, *S. aureus* was the leading pathogen (14.2%). According to Pham Chi Lan's research at Ho Chi Minh Medical Hospital, Gram - negative bacteria was isolated from BSI patients with 76.6%. The most popular pathogen isolated of BSI patients in this study was *K. pneumonia* (12.4%) and *A. baumannii* (8.6%)[4]. An amount of *A. baumannii* isolated in this study was higher

than ones in our research. All BSI patients had invasive procedures, so they had a high risk of nosocomial infection with *A. baumannii.* From Tran Thi Thanh Thu's research (2018) at Children Hospital 1, the most common pathogen was *Streptococcus pneumonia* (17.8%)[5]. In contrast, *S. pneumonia* has a smaller rate in our research (1.5%) because of the different BSI patients age groups between 2 studies. The research subject of Tran Thi Thanh Thu focused on children. However, our BSI patients with medium age were 51.2 years.

Rates of antimicrobial resistance for the common bacteria identified

Some studies showed that *E. coli* was the leading cause of BSIs. The hospital costs and mortality associated with *E. coli* BSIs are significantly increased by antibiotic-resistant *E. coli* strains and ESBL production[6]. In our study, *E. coli* isolates were resistant over 50% to cephalosporins III (except ceftazidime), ciprofloxacin and levofloxacin, trimethoprim - sulfamethoxazole. 100% of *E. coli* isolates were resistant to ampicillin. No record was reported resistance to meropenem. *E. coli* isolates had a low resistance rate under 10% to piperacillin - tazobactam, carbapenems, and amikacin. During 3 years, there was 68.8% of *E. coli* isolates produced ESBL. The rate of ESBL - producing *E. coli* isolates in our study was higher than that in Vu Quoc Dat's research (45%), which was performed at NHTD from 2011 to 2013[3]. Following Mita's research from 2011 to 2015 in Japan, the percentage of ESBL - producing *E. coli* was 90.1%[7]. It would seem that ESBL - producing *E. coli* isolates tended increasingly.

The proportion of resistance to *K. pneumonia* isolates was under 50% with all antibiotics. The rate of ESBL - producing *K. pneumonia* isolates was 16.3%. *K. pneumoniae* isolates were resistant to cephalosporins (30.3%), carbapenems (23.2%) and aminoglycosides (17.2%). From the result of Vu Quoc Dat's study (2017), the rates of antimicrobial resistance were lower than our study with cephalosporins (14.3%), carbapenems (0.8%) and aminoglycosides (13%)[3]. According to other research by Anh Tram Que (2020), the percentage of resistant *K. pneumonia* was under

20% with all antibiotics and lower than that in our study. Especially, no case was reported resistance to carbapenems as well as producing ESBL[8].

Production of beta - lactamases was the most prevalent mechanism of resistance against beta - lactam antibiotics except carbapenems and cephamycins. The global emergence and spread of ESBLs producing *Enterobacteriaceae* had been threatening the ability to treat an infection associated with high mortality[9]. From the study of Leistner (2014), there were 18.8% of ESBL - producing strains of *E. coli* and 11.9% ESBL - producing strains of *K. pneumoniae*. Mortality of those who suffered from BSI caused by *E. coli* and *K. pneumonia* was 18.5% and 25%. Increased hospital costs and length of stay were significantly associated to BSI with ESBL - positive *K. pneumoniae*[10]. In conclusion, ESBL - producing *Enterobacteriaceae* became a severe problem in healthcare. Thus, we needed to give strategies to combat antibiotic resistance of these strains.

S. aureus was the leading pathogen of Gram - positive bacteria in our study. The rate of methicillin - resistant *Staphylococcus aureus* (MRSA) was 61.7%. MRSA strains became serious trouble with the worldwide epidemic of antibiotic resistance because of resistance to the newer antimicrobial agents such as linezolid, vancomycin, teicoplanin anddaptomycin[11].

MRSA strains in our study were much more than Vu Quoc Dat's study from 2011 - 2013 (37%)[3]. Our study showed the trend of MRSA isolates was increasing in NHTD. This created a huge challenge with infection control in the hospital. Fortunately, no resistance was observed to vancomycin and linezolid.

Our study has two limitations. Firstly, NHTD was a terminal hospital and specializes in infectious diseases. Therefore, the level of antibiotics resistance pattern and spectrum of bacterial BSI is different from that seen in district and provincial level hospitals. Secondly, the rate of bacterial pathogens was disparate between years because a small number of patients admitted to the hospital in 2020. Thus, the result of positive blood cultures decreases, and only one - third of the previous results in 2019.

CONCLUSIONS

Gram - negative bacteria were the most common cause of BSI with predominant pathogens were *K. pneumonia* and *E. coli*.

The extended - spectrum beta - lactamase (ESBL) producing *Enterobacteriaceae* was associated with the ability of antibiotics resistance. The trend of MRSA was increasing. However, a total of *S. aureus* isolates was susceptible to vancomycin and linezolid.

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