

# Comparison of Drug Resistance of Bile Isolated Bacteria in Nanjing from 2017 to 2020

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Received November 11, 2021; Revised December 14, 2021; Accepted December 22, 2021

**Abstract Background:** Analyzed pathogenic bacteria isolated from bile samples of patients with biliary tract infection and their drug resistance in the first Affiliated Hospital of Nanjing Medical University from 2017 to 2020, so as to provide evidence for the treatment of biliary tract infection. **Methods:** Clinical strains isolated from bile specimens of patients suspected of biliary infection in the First Affiliated Hospital of Nanjing Medical University from 2017 to 2020 were collected, The drug susceptibility criteria are based on the standards published by the National Standardization Committee of the US Clinical Laboratories. WHONET 5.6 software was used to analyze the distribution of pathogens and drug resistance. **Results:** From January 2017 to December 2020, a total of 2006 strains of bile pathogenic bacteria were cultured and identified. There were 1253 cases of gram-negative bacilli, 638 cases of gram-positive cocci, 98 cases of fungi, and 17 cases of Gram-positive bacilli. The top five pathogens of Gram negative bacilli were *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter cloacae*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*. The top five pathogens of gram positive cocci were *Enterococcus faecium*, *Enterococcus faecalis*, *Enterococcus gallinarum*, *Enterococcus faecalis* and *Staphylococcus epidermidis*. the resistance rate of *Escherichia coli* to ampicillin, ampicillin / sulbactam, cefotetan, ceftazidime, ceftriaxone, cefepime, itronam, compound trimethoprim decreased, the resistance rate of *Klebsiella pneumoniae* to gentamicin, levofloxacin decreased, the resistance rate of *Enterobacter cloacae* to ciprofloxacin, levofloxacin decreased. the resistance rate of *Pseudomonas aeruginosa* to ceftazidime, cefepime, gentamicin decreased. the resistance rate of *Acinetobacter baumannii* to ceftazidime, ciprofloxacin decreased. the resistance rate of *Enterococcus faecium* to penicillin G, high concentration streptomycin, erythromycin decreased. **Conclusions:** Enterogenic pathogens were the main pathogens in China. Such as *Escherichia coli*, *Klebsiella pneumoniae*, *Enterococcus faecalis* and *Enterococcus faecalis*; Nosocomial infection pathogens. For example, *Pseudomonas aeruginosa* and *Acinetobacter* also need to be paid attention to. Clinicians should improve their awareness of microbiological examination and provide more reliable pathogenic evidence for the selection of clinical antibiotic.

**Keywords:** Biliary tract infection, pathogenic bacteria, drug resistance, Nanjing

**Cite This Article:** Chu Chu, and Hong-Mei Ding, "Comparison of Drug Resistance of Bile Isolated Bacteria in Nanjing from 2017 to 2020." *American Journal of Clinical Medicine Research*, vol. 10, no. 1 (2022): 1-5. doi: 10.12691/ajcmr-10-1-1.

## 1. Introduction

Biliary tract infection is a common clinical infectious disease, which is easy to cause acute or chronic pancreatitis, and even develop into sepsis. At present, biliary tract infection has shown a serious phenomenon of drug resistance. The distribution and drug resistance of bile pathogens can objectively reflect the microbiological status of biliary tract infection. It can guide the clinical rational use of antibiotics and improve the therapeutic effect of antibiotics [1,2,3,4]. Therefore, this study analyzed pathogenic bacteria isolated from bile samples of patients with biliary tract infection and their drug resistance in the first Affiliated Hospital of Nanjing Medical University from 2017 to 2020, so as to provide evidence for the treatment of biliary tract infection.

## 2. Materials and Methods

### 2.1. Source of Bacterial Strain

Non repetitive pathogens isolated from clinical bile samples of the first Affiliated Hospital of Nanjing Medical University from January 1, 2017 to December 31, 2020.

### 2.2. Pathogen Identification and Drug Sensitivity Test

The pathogen species were identified by manual method or automatic detector, K-B agar diffusion method, agar double dilution method or E-test method were used to determine the minimum inhibitory concentration (MIC).

Drug resistance of different isolates was monitored by different combinations of antibiotics.

### 2.3. Statistical Analysis

WHONET software was used to collect, process and analyze the data. The results of drug sensitivity were analyzed according to CLSI 2007 standard. For the same pathogen isolated from the same part of the same patient, only the first strain data were counted. Anaerobic bacteria and fungi were not monitored in this study.

## 3. Result

### 3.1. Species and Constituent Ratio of Pathogenic Bacteria

From January 2017 to December 2020, the first bacterial strain of patients admitted to hospital was taken as the statistical target. In the First Affiliated Hospital of Nanjing Medical University, a total of 2006 strains of bile pathogenic bacteria were cultured and identified, and drug sensitivity test was carried out. There were 1253 cases of gram-negative bacilli (95 cases in 2017, 227 cases in 2018, 471 cases in 2019 and 460 cases in 2020), 638 cases of gram-positive cocci (62 cases in 2017, 101 cases in 2018, 250 cases in 2019 and 225 cases in 2020), 98 cases of fungi (19 cases in 2017, 19 cases in 2018, 27 cases in 2019 and 33 cases in 2020), and 17 cases of Gram-positive bacilli.

The top five pathogens of Gram negative bacilli were *Escherichia coli* (517 cases, 41.26%), *Klebsiella pneumoniae* (255 cases, 20.35%), *Enterobacter cloacae* (79 cases, 6.30%), *Pseudomonas aeruginosa* (70 cases,

5.59%), *Acinetobacter baumannii* (58 cases, 4.63%).

The top five pathogens of gram positive cocci were *Enterococcus faecium* (226 cases, 35.42%), *Enterococcus faecalis* (164 cases, 25.71%), *Enterococcus gallinarum* (32 cases, 5.02%), *Enterococcus faecalis* (29 cases, 4.55%) and *Staphylococcus epidermidis* (24 cases, 3.76%).

The species and constituent ratio of pathogens in each year are shown in Table 1 and Table 2.

### 3.2. Analysis of Antimicrobial Resistance of Pathogens

#### 3.2.1. Drug Resistance of Gram Negative Bacilli

From 2017 to 2020, the resistance rate of *Escherichia coli* to ampicillin decreased from 93.80% to 78.00%, The drug resistance rate of ampicillin / sulbactam decreased from 84.40% to 59.70%, The resistance rate to cefotetan decreased from 15.60% to 5.90%, The resistance rate to ceftazidime decreased from 66.60% to 35.50%, The resistance rate to ceftriaxone decreased from 81.20% to 61.80%, The resistance rate to ceftazidime decreased from 57.20% to 26.90%, The drug resistance rate to itronam decreased from 69.80% to 46.20%, The resistance rate to compound trimethoprim decreased from 66.64% to 37.60%. The drug resistance rate to piperacillin, cefazolin, cefuroxime and ciprofloxacin remained at a high level (more than 50%).

From 2017 to 2020, the resistance rate of *Klebsiella pneumoniae* to gentamicin decreased from 35.70% to 18.14%, The resistance rate to levofloxacin decreased from 42.90% to 27.56%, The drug resistance rates of ampicillin / sulbactam, piperacillin, cefazolin, cefuroxime and ceftriaxone were still high (more than 45%).

Table 1. Species and constituent ratio of gram negative bacilli in 2017-2020

Name of bacteria	2017		2018		2019		2020		
	Number of bacterial strain(n)	Constituent ratio (%)	Number of bacterial strain(n)	Constituent ratio (%)	Number of bacterial strain(n)	Constituent ratio (%)	Number of bacterial strain(n)	Constituent ratio (%)	
Enterobacteriaceae	<i>Escherichia coli</i>	33	34.74	88	38.77	210	44.59	186	40.43
	<i>klebsiella pneumoniae</i>	14	14.74	49	21.59	76	16.14	116	25.22
	Other <i>Klebsiella</i> species	2	2.11	6	2.64	19	4.03	17	3.7
	<i>Enterobacter cloacae</i>	7	7.37	10	4.41	32	6.79	30	6.52
	<i>Citrobacter</i>	0	0	3	1.32	22	4.67	12	2.61
	<i>Proteus</i>	1	1.05	3	1.32	6	1.27	4	0.87
	<i>Morganella morganii</i>	1	1.05	0	0	3	0.64	3	0.65
	<i>Pandora</i>	0	0	0	0	3	0.64	2	0.43
	Other genera of Enterobacteriaceae	5	5.26	5	2.2	15	3.18	8	1.74
	Nonfermenters	<i>Acinetobacter baumannii</i>	9	9.47	11	4.85	19	4.03	19
Other <i>Acinetobacter</i> species		2	2.11	2	0.88	5	1.06	1	0.22
<i>Pseudomonas aeruginosa</i>		7	7.37	22	9.69	20	4.25	21	4.57
Other <i>Pseudomonas</i>		1	1.05	3	1.32	4	0.85	5	1.09
<i>Stenotrophomonas maltophilia</i>		4	4.21	5	2.2	8	1.70	7	1.52
<i>Shigella</i>		1	1.05	1	0.44	4	0.85	3	0.65
Other non fermenting bacteria		4	4.21	4	1.76	2	0.42	4	1.30
Vibrio, Aeromonas		<i>Hydrophobia / aeromonas caviae</i>	4	4.21	13	5.72	21	4.46	19
	<i>Aeromonas sobria</i>	0	0	2	0.88	1	0.21	3	0.65
	<i>Vibrio fluvialis</i>	0	0	0	0	1	0.21	0	0
Total	95		227		471		460		

**Table 2. Species and constituent ratio of Gram positive cocci in 2017-2020**

Name of bacteria		2017		2018		2019		2020	
		Number of bacterial strain(n)	Constituent ratio (%)	Number of bacterial strain(n)	Constituent ratio (%)	Number of bacterial strain(n)	Constituent ratio (%)	Number of bacterial strain(n)	Constituent ratio (%)
Enterococcus	Enterococcus faecium	22	35.48	41	40.59	87	34.8	76	33.78
	Enterococcus faecalis	11	17.74	31	30.69	71	28.4	51	22.67
	Enterococcus gallinarum	0	0	5	4.95	11	4.4	16	7.11
	Enterococcus casseliflavus	2	3.23	5	4.95	11	4.4	11	4.89
	Other enterococci	3	4.84	2	1.98	18	7.2	15	6.67
Staphylococcus	Staphylococcus haemolyticus	1	1.61	2	1.98	9	3.6	3	1.33
	Staphylococcus aureus	4	6.45	5	4.95	5	2	8	3.56
	Staphylococcus epidermidis	6	9.68	2	1.98	3	1.2	13	5.78
	Other Staphylococcus	3	4.84	2	1.98	3	1.2	4	1.78
Streptococcus	Streptococcus salivarius	1	1.61	1	0.99	6	2.4	4	1.78
	Bradycardia /streptococcus oralis	1	1.61	0	0	4	1.6	2	0.89
	$\alpha$ -Streptococcus haemolyticus	1	1.61	2	1.98	4	1.6	0	0
	Streptococcus sanguis	0	0	0	0	4	1.6	5	2.22
	Streptococcus pharyngitis	1	1.61	0	0	3	1.2	4	1.78
	Streptococcus alactolyticus	0	0	0	0	0	0	5	2.22
	Other Streptococcus	3	4.84	1	0.99	6	2.4	6	2.67
Other cocci		3	4.84	2	1.98	5	2	2	0.89
Total		62		101		250		225	

**Table 3. Drug resistance rate of Common Gram negative bacilli in 2017-2020 (%)**

Name of antibiotics	Escherichia coli				klebsiella pneumoniae				Enterobacter cloacae			
	2017 n=33	2018 n=88	2019 n=210	2020 n=186	2017 n=14	2018 n=49	2019 n=76	2020 n=116	2017 n=7	2018 n=10	2019 n=32	2020 n=30
Ampicillin	93.8	89.5	80.1	78	/	/	/	/	/	/	/	/
Ampicillin / sulbactam	84.4	76.15	62.8	59.7	57.1	57.3	65.8	49.14	/	/	/	/
Piperacillin	71.9	76.7	63.6	59.7	57.1	58.3	53.9	47	57.1	22.2	31.2	36.7
Piperacillin / tazobactam	12.5	10.26	7.2	3.2	21.4	29.2	27.6	21.51	14.3	0	12.5	13.3
Cefazolin	82.2	82.8	67.3	62.9	50	65.2	61.1	49.97	/	/	/	/
Cefuroxime	79.1	82.6	69.4	65.6	50	64.6	64.5	51.75	/	100	35.7	76.7
Cefotetan	15.6	9.3	6.8	5.9	21.4	25	22.4	20	/	/	/	/
Ceftazidime	66.6	51.2	37.8	35.5	35.7	43.8	41.3	32.72	57.1	49.96	53.1	66.7
Ceftriaxone	81.2	79.1	64.1	61.8	50	58.3	53.9	47.8	57.1	66.7	56.2	70
Cefepime	57.2	46.5	32.3	26.9	28.6	33.3	31.6	26.77	28.6	9.99	9.4	13.3
Aztreonam	69.8	66.3	54.33	46.2	50	50	46.1	36.48	57.1	49.96	53.1	53.3
Imipenem	0	4.7	4.3	2.73	21.45	16.31	20	18.13	0	0	6.3	6.67
Meropenem	0	3.5	3.3	2.66	21.4	16.33	20	18.09	0	0	0	0
Amikacin	0	8.4	2	2.8	7.1	15.26	12.3	8.42	0	0	0	0
Gentamicin	60.63	38.4	21.8	27.4	35.7	34.68	32.9	18.14	28.6	29.97	6.2	13.3
Tobramycin	31.2	26.7	10.2	12.9	28.6	29.2	25	12.2	0	11.1	0	13.3
Ciprofloxacin	78.1	75.6	54.4	57	42.9	45.8	38.2	31.3	28.6	22.2	18.8	13.3
Levofloxacin	75.76	66.3	49.5	54.3	42.9	41.7	32.9	27.56	28.6	19.98	15.6	6.7
Compound sulfamethoxazole	66.64	46.5	44.3	37.6	15.4	45.8	43.4	32.72	42.9	29.97	9.4	16.7
Cefoperazone / sulbactam	66.7	23.5	13.2	17.6	25	41.7	42.9	26.1	0	0	18.2	33.3

From 2017 to 2020, the resistance rate of Enterobacter cloacae to ciprofloxacin decreased from 28.60% to 13.30%, The resistance rate to levofloxacin decreased from 28.60% to 6.70%, The resistance rate to ceftazidime, ceftriaxone and aztreonam remained at a high level (more than 45%), as shown in Table 3.

### 3.2.2. Drug Resistance of Non Fermentative Bacteria

From 2017 to 2020, the resistance rate of Pseudomonas aeruginosa to ceftazidime decreased from 42.84% to 14.30%. The resistance rate to cefepime decreased from

28.57% to 9.56%, The drug resistance rate of gentamicin decreased from 14.29% to 4.80%, The resistance rate to imipenem and meropenem showed a downward trend.

From 2017 to 2020, the resistance rate of Acinetobacter baumannii to ceftazidime decreased from 88.89% to 63.20%, The resistance rate to ciprofloxacin decreased from 75.00% to 63.20%, The drug resistance rates to piperacillin/tazobactam, ceftriaxone, cefepime, imipenem, meropenem, levofloxacin, ampicillin/sulbactam, Cefoperazone/sulbactam and cotrimoxazole remained at a high level (more than 50%), See in Table 4.

**Table 4. Drug resistance rate of common non fermenting bacteria in 2017-2020**

Name of antibiotics	Pseudomonas aeruginosa				Acinetobacter baumannii			
	2017 n=7	2018 n=22	2019 n=20	2020 n=21	2017 n=9	2018 n=11	2019 n=19	2020 n=19
Piperacillin	28.57	36.35	15.03	9.5	/	/	/	/
Piperacillin / tazobactam	28.57	31.8	10.52	0	62.5	81.8	57.9	63.2
Ceftazidime	42.84	36.35	35.01	14.3	88.89	81.8	68.4	63.2
Ceftriaxone	/	/	/	/	75	90.9	68.4	63.2
Cefepime	28.57	22.75	15.03	9.56	75	81.8	68.4	63.2
Imipenem	33.33	42.84	9.96	28.51	77.78	81.8	68.4	66.7
Meropenem	42.84	31.8	14.95	19	77.78	81.8	68.4	66.7
Amikacin	0	9.12	0	0	/	/	/	/
Gentamicin	14.29	9.1	5	4.8	62.5	72.7	63.2	47.4
Tobramycin	0	6.7	5.6	5.3	50	54.5	47.4	47.4
Ciprofloxacin	14.29	22.7	9.99	4.8	75	72.7	63.2	63.2
Levofloxacin	0	9.08	5.04	4.8	74.98	75	60	53.3
Ampicillin / sulbactam	/	/	/	/	77.78	81.8	68.4	63.2
Cefoperazone / sulbactam	20	11.1	0	23.8	87.5	50	75	64.7
Compound sulfamethoxazole	/	/	/	/	71.4	77.8	56.2	60

**Table 5. Drug resistance rate of Common Gram positive cocci in 2017-2020**

Name of antibiotics	Enterococcus faecium				Enterococcus faecalis			
	2017 n=22	2018 n=41	2019 n=87	2020 n=76	2017 n=22	2018 n=41	2019 n=87	2020 n=76
Penicillin G	86.4	80.5	72.1	71.6	0	3.3	2.8	4.2
Ampicillin	81.8	80.5	64.4	67.6	9.09	0	1.4	0
High concentration gentamicin	36.4	43.9	34.5	31.1	18.16	27.61	17.1	13.72
High concentration streptomycin	45.5	43.9	31.4	29.7	11.1	25.9	24.3	22.9
Ciprofloxacin	81.8	82.9	64	70.3	11.1	16.7	15.5	12.5
Levofloxacin	81.8	82.9	62	65.78	9.08	16.16	14.1	11.98
Moxifloxacin	86.4	85.4	100	/	11.1	16.7	16.7	/
Clindamycin	81.8	80.5	90	/	100	100	91.7	/
Erythromycin	86.4	80.5	76	75.02	18.16	45.13	42.3	43.17
Quinuprin / Dapuptin	0	2.4	3.5	0	55.6	66.7	78.9	70.8
Linezolid	0	2.47	0	1.37	0	3.7	1.6	0
Vancomycin	0	0	0	0	0	0	0	1.94
Tetracycline	9.1	26.8	24.4	36.5	55.6	60	52.1	41.7

### 3.2.3. Drug Resistance of Gram-positive Cocci

From 2017 to 2020, the resistance rate of Enterococcus faecium to penicillin G decreased from 86.40% to 71.60%, The resistance rate to high concentration streptomycin decreased from 45.50% to 29.70%, The resistance rate to erythromycin decreased from 86.40% to 75.02%, The resistance rates to ampicillin, ciprofloxacin, levofloxacin, moxifloxacin and clindamycin remained at a high level (more than 50%).

The drug resistance rate of Enterococcus faecalis to clindamycin and quinupine / daprotin remained high (over 50%) in 2017-2020, as shown in Table 5.

## 4. Discussion

Biliary tract infection refers to the bacterial infection of the biliary system, including acute and chronic cholecystitis,

acute and chronic cholangitis, acute obstructive suppurative cholangitis, etc. It is a common, multiple and refractory disease in surgery [5,6]. Therefore, understanding the distribution and drug resistance of pathogens in biliary tract infection can provide a basis for guiding the rational use of antibiotics and improving the therapeutic effect of antibiotics [7,8,9,10].

The results of this study show that Escherichia coli, Klebsiella pneumoniae and Enterococcus are still the main pathogens of biliary tract infection from 2017 to 2020, and the detection rate of Escherichia coli is increasing year by year, which may be related to the distribution of intestinal flora [5,6]. In addition, although the detection rate of pathogens of nosocomial infection, such as Pseudomonas aeruginosa and Acinetobacter, showed a downward trend, it should also be paid attention to. From 2017 to 2020, the resistance rate of Escherichia coli to ampicillin, ampicillin / sulbactam, cefotetan, ceftazidime, ceftriaxone,

cefepime, aztreonam and cotrimoxazole showed a downward trend. However, the resistance rates to piperacillin, cefazolin, cefuroxime and ciprofloxacin remained at a high level. Whether it is related to the use of antibiotics in hepatobiliary surgery in our hospital needs further study. The resistance rate of *Escherichia coli* to carbapenems is low (< 10%), which can be used as an empirical drug in clinic. From 2017 to 2020, the resistance rate of *Klebsiella pneumoniae* to gentamicin and levofloxacin showed a downward trend. However, the drug resistance rates of ampicillin / sulbactam, piperacillin, cefazolin, cefuroxime and ceftriaxone still maintain a high level, which should be paid attention to in clinic.

Among non fermenting bacteria, *Acinetobacter baumannii* has a high resistance rate to a variety of antibiotics, It is worth noting that *Acinetobacter baumannii* is particularly resistant to carbapenems and most aminoglycosides. The resistance rate to imipenem and meropenem was more than 65%. In view of the high detection rate of *Acinetobacter baumannii* in the bile of elderly patients in our hospital and the high resistance rate to a variety of antibiotics. In addition to the rational selection of antibiotics according to the drug sensitivity results, we should also pay attention to hand hygiene and strictly follow the principle of sterility.

Among gram-positive cocci, the resistance rate of *Enterococcus faecium* to penicillin G, ampicillin, ciprofloxacin, levofloxacin, moxifloxacin, clindamycin and erythromycin was as high as 80%. It deserves our attention, which is related to the medication habits of clinicians. The resistance rate of *Enterococcus faecium* to quinuprin / dafuptin, linezolid and vancomycin is low, which can guide clinicians to take empirical drugs. The overall resistance rate of *Enterococcus faecalis* is low. Vancomycin is one of the most effective antibiotics for Gram-positive bacteria. Previous studies have suggested that the drug resistance rate to Gram-positive bacteria in biliary tract is as low as zero. However, this study suggests that there is a certain degree of drug resistance rate, which should be paid attention to.

The results showed that enterogenic pathogens were still the main pathogens in China. Such as *Escherichia*

*coli*, *Klebsiella pneumoniae*, *Enterococcus faecalis* and *Enterococcus faecalis*; Nosocomial infection pathogens. For example, *Pseudomonas aeruginosa* and *Acinetobacter* also need to be paid attention to. The drug resistance of pathogens of biliary tract infection is similar to the overall situation of the hospital, but the drug resistance of individual pathogens is more prominent. At the same time, compared with the clinical proportion of biliary tract infection, the rate of microbial culture is low. Clinicians should improve their awareness of microbiological examination and provide more reliable pathogenic evidence for the selection of clinical antibiotics.

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