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Clinical Characteristics and Antimicrobial Resistance among Aeromonas Species in Hepatic Hospital: A 22 Years Retrospective Study

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1. Abstract

1.1. Background: Aeromonas is becoming an increasing pathogen in immunocompromised persons, especially in persons with chronic hepatic disease. However, rare studies have clarified their clinical characteristics and antimicrobial resistance (AMR) patterns. This study aimed to elucidate the distribution of Aeromonas and compare AMR patterns of Aeromonas species from various specimen sources.

1.2. Methods: We conducted a retrospective study in a hepatic hospital in Beijing from 2000-2020. Data were retrieved by the LIS system. Whonet 5.6 and SPSS 22.0 were used to analyze and compare Aeromonas species distribution and AMR patterns.

1.3. Results: Among 374 Aeromonas strains, the predominant Aeromonas were A. hydrophila (146/374, 39.04%), A. sobria (118/374, 30.88%) and A. caviae (87/374, 23.26%). Blood was the most frequent source of strains (46.6%), followed by ascites (28.1%), bile (8.8%), stool (7.1%), hydrothorax (6.0%) and sputum (3.4%). In blood, the most predominant strain was A. hydrophila (47.6%), which was significantly higher than that in ascites, bile, stool and hydrothorax. In ascites, A. sobria (46.5%) was the highest distributed, which was significantly higher than that in other sources. In bile, stool, hydrothorax, A. caviae were most distributed, with 66.7%, 51.6% and 44.0% respectively, significantly higher than that in blood (16.5%). Bloodstream strains exhibited lower resistance rates than ascites to most antibiotics tested. In terms of species, A. caviae demonstrated higher resistance rates to ceftazidime (CAZ), cefepime (FEP), piperacillin/tazobactam (TZP), aztreonam (ATM), Levofloxacin (LVX) than A. hydrophila and A. sobria, while A. sobria harbored resistance rates of most antibiotics significantly lower than the other two Aeromonas species.

1.4. Conclusion: Aeromonas species exhibited different clinical characteristics. Different sources have their dominant Aeromonas, with A. hydrophila in blood, A. sobria in ascites, A. caviae in bile, stool and hydrothorax. Compared with ascites strains, blood strains demonstrated lower resistance rates. AMR patterns varied between species variation, with higher resistance rate in A. caviae and lower resistance rates in A. sobria.

2. Introduction

Aeromonas species inhabit aquatic environments and are responsible for a variety of animal and human diseases, including gastroenteritis, septicemia, skin or soft tissue infections, intra-abdominal infections, respiratory tract infections and urogenital tract infections [1]. A. hydrophila, A. caviae, and A. veronii bv sobria (previously called Aeromonas sobria) are the most frequently isolated species linked to human disease [2, 3]. Through consuming contaminated foods, Aeromonas were carried to gastrointestinal tract with different faecal carriage rate and have been recognized as enteric pathogens [4, 5]. The greatest risk factors for Aeromonas infection are immunocompromised persons with hepatic cirrhosis and malignancy [1, 6, 7]. For the highly prevalent of liver disease in China, infections with Aeromonas are more likely to be severe. However, current studies about clinical distribution patterns of Aeromonas species among different

infectious sources in hepatic hospital were limited. Fluoroquinolones, 3rd and 4th generation cephalosporins and trimethoprim-sulfamethoxazole are recommended as the primary therapeutic regime for Aeromonas infection. However, AMR rates of Aeromonas changes with the use of antimicrobial agents and expression of mobile resistant genes [8]. Compared with other antibiotics, AMR rates of Aeromonas are high to ceftriaxone (CRO) and ciprofloxacin (CIP) [9-12]. 5%-15% resistance rate of Aeromonas bloodstream strains to CRO and CIP are reported in Korea and southern Taiwan [13, 14]. Resistance rates of extra-intestinal Aeromonas to CRO and CIP were 70.6% and 35.3% respectively in Northern China [15]. Moreover, Colistin resistance in Aeromonas has been reported [16]. However, till nowadays, data about AMR patterns with different infectious sources and heterogeneity of AMR patterns of clinically important Aeromonas species in hepatic hospital were rare.

To fill this gap, we retrospectively collected data across 21 years in a hepatic hospital of Beijing, capital of China, to elucidate the distributions and AMR characteristics of clinically important Aeromonas species.

3. Methods

3.1. Study Design and Data Enrollment Criteria

This is a retrospective study, in which the patients diagnosed with monomicrobial Aeromonas infection were admitted in Hospital from 2000 to 2020. Only the first isolate of Aeromonas and antibiotic susceptibility data was included.

3.2. Aeromonas Isolates Identification and Antimicrobial Susceptibility Testing

Vitek II (BioMérieux Marcy-l'Etoile, France) combined with biochemical test were used for Aeromonas species identification. Antimicrobial susceptibility tests were conducted according to standard procedures by semi or automated microbial system. The interpretation of breakpoint concentrations was in accordance the Clinical and Laboratory Standards Institute (CLSI). Resistance (R) and Intermediary (I) were all included as resistance rates in this study.

3.3. Statistical Analysis

Raw data were processed with Whonet 5.6 and then statistically analyzed with SPSS 22.0. Chi square test or Fisher's exact test were conducted to examine distribution and antimicrobial susceptibility in blood and ascite. Statistical significance was determined if a two-tailed p value was no more than 0.05. Bonferroni test were used to compare antimicrobial susceptibility patterns in different Aeromonas species. Statistical significance was determined if a two-tailed p value was less than 0.05/3.

4. Results

4.1. Clinical Aeromonas Isolates Distribution

During 2000-2022, 374 Aeromonas were cultured. It was found that a higher percentage of males (81.0%) were infected with Aeromonas compared to females (19.0%). The infection rates varied across different age groups, with the highest rate of 58.2% occurring among those aged between 41-60. This rate was significantly higher compared to other age groups. Additionally, the summer season (Jun to September) saw a higher number of Aeromonas infections, with 60.2% of cases occurring during this period. A. hydrophila (39.04%, 146/374) was the most predominant species, followed by A. sobria (31.55%, 118/374), A. caviae (23.26%, 87/374), A. veronii (4.55%, 17/374) and other Aeromonas species (1.60%, 6/374) (Figure 2.A). 351 Aeromonas were recorded with separating sites. The most common specimen source of Aeromonas was blood (49.86%, 175/351), abdominal fluid (19.66%, 69/351), bile (8.55%, 30/351), stool (9.12%, 32/351), sputum (3.99%, 14/351) and pleural fluid (2.56%, 9/351). Other specimen sources such as aminiotic fluid, shunt fluid, urine, abscess, wound was not included for their few numbers.

In specimens of blood, the most dominant Aeromonas is A. hydrophila (46.86%, 82/175), significantly higher than that in ascites, stool, bile and hydrothorax. Followed by is A. sobria (32.00%, 56/175). In abdominal fluid, the most dominant Aeromonas is A. sobria (49.28%, 34/69), significantly higher than that in blood, bile, hydrothorax, stool and sputum. In stool and bile, the most dominant Aeromonas is A. caviae, with 40.62% and 43.33% respectively, significantly higher than that in blood. (Figure 2.B).

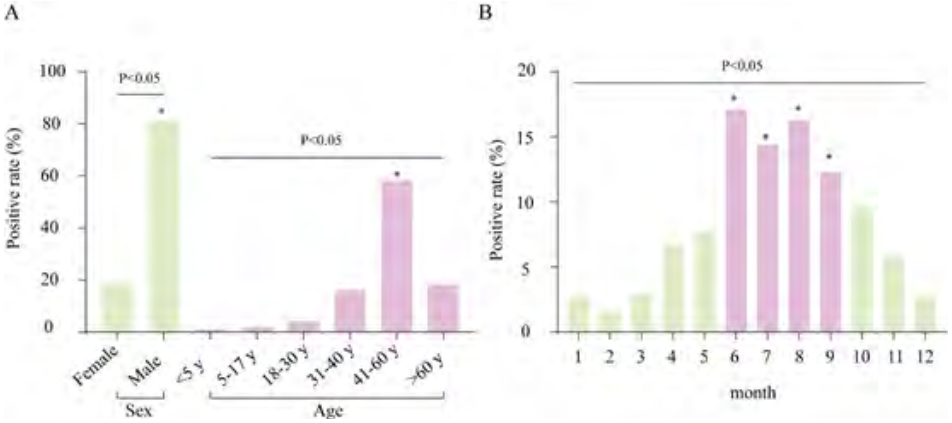
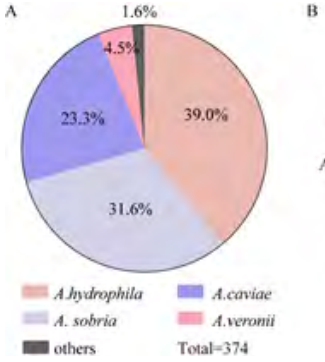


Figure 1: Age ranges of patients studied (A) and distribution of infections by season (B)



B

Sources (n)	*A.caviae*	*A.hydrophila*	*A. sobria*	*A.veronii*	Others	P value
Blood (175)	17.1%	46.9%*	32.0%	2.9%	1.1%	0.000
Abdominal fluid (69)	20.3%	27.5%	49.3%*	2.9%	0.0%	0.000
Stool (32)	40.6%	18.8%	12.5%	25.0%	3.1%	0.003
Bile (30)	43.3%	23.3%	30.0%	0.0%	3.3%	0.000
Sputum (14)	35.7%	50.0%	14.3%	0.0%	0.0%	0.012

>40% 30%-40% 10%-30% <10%

Figure 2: Distribution of *Aeromonas* species in clinical specimen sources

4.2. Antibiotic Resistance Analysis of Aeromonas by Species

To investigate antimicrobial resistance patterns between different Aeromonas species, we compared antibiotic susceptibility patterns among three main species. A. caviae exhibited significantly higher resistance rate to CAZ (27.6%), FEP (24.3%), TZP (29.8%), ATM (19.9%), LVX (13.1%) than A. hydrophila and A. sobria. However, A. sobria demonstrated a resistance rate of less than 20% to most antibiotics tested, with significantly lower resistance rates to PIP (19.5%), CRO (8.0%), CAZ (2.9%) than A. hydrophila and A. caviae. (Figure 3.)

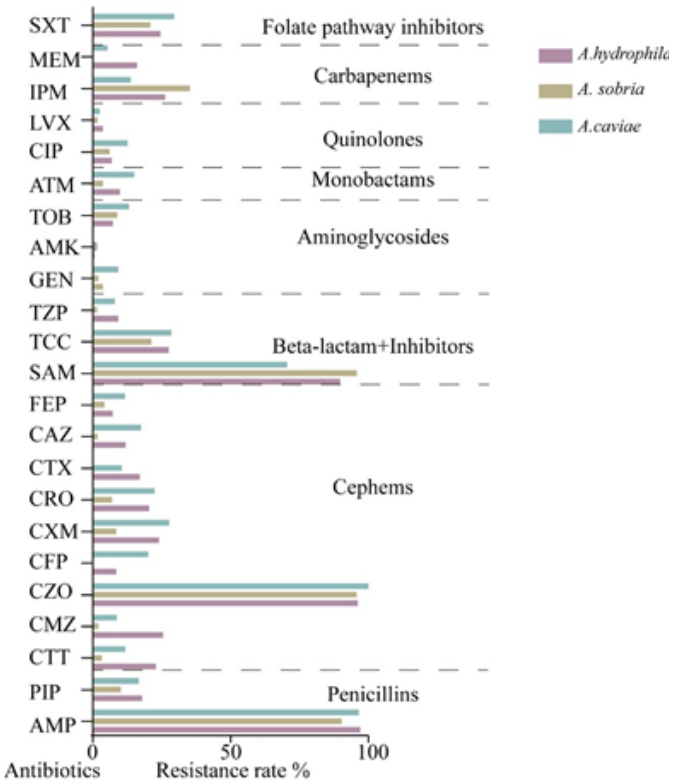


Figure 3: Antimicrobial resistance patterns of *Aeromonas* by species

5. Discussion

The most common specimen sources of Aeromonas in this study were blood (46.6%) and ascites (28.1%). As the largest hepatic hospital of China, our hospital possesses a big population of patients with hepatic disease, including cirrhosis and hematologic malignancy. According to studies, the first underlying illnesses associated with Aeromonas bacteremia is hepatic cirrhosis (54%) [17]. In Taiwan, 14.2% of Gram-negative-bacillus bacteremia in patients with liver cirrhosis is caused by Aeromonas [18]. 97% patients with primary Aeromonas peritonitis were detected with liver disease and 50% patients were detected with bacteremia at the same time. The underlying reason was the impaired function of hepatic reticuloendothelial system and neutrophils, portal-caval shunts and a decreased opsonic effect on the ascites [19, 20]. Moreover, persons with liver disease may more easily cause break of gastrointestinal mucosa and cause transmigration of Aeromonas from bowel into bloodstream and ascites by expressing exoenzymes and enterotoxins [1, 21, 22]. The above findings suggest that Aeromonas are more likely invading to blood and ascites in persons with hepatic disease.

Our results demonstrated that A. hydrophila and A. veronii bv sobria were the leading pathogens causing septicemia, rather than A. caviae, in accordance with the study of Han-Chuan Chuang et al, in which A. hydrophila and A. veronii bv sobria accounted for 55.49% and 29.22% of Aeromonas septicemia [23]. Accumulated evidence has shown that A. hydrophila and A. sobria were able to invade intestinal cells and infect bloodstream. Toxins such as cytotoxin enterotoxin may help bacterial translocation by inducing apoptosis of intestinal epithelial cells. Compared with the widely distribution of cytotoxin enterotoxin genes in A. hydrophila and A. sobria, the genes in A. caviae were less. In vitro study, A. caviae was less toxic to HEp-2 cell and lost the ability of persistent colonization to mouse models [23]. Based on this, poor ability of producing enterotoxin maybe the reason of poor virulence and lower chance of A. caviae translocating to blood [24, 25]. Different Aeromonas species harbored distinct antimicrobial susceptibilities. A. sobria was most susceptible to cephalothin antibiotics, in contrast, the resistance rate of cephalothin to A. caviae was highest [26]. This finding is consistent with a study in Southwest China among 1135 Aeromonas strains, with relatively

high resistance rate of A. caviae and low resistance rate of A. sobria [8]. The susceptibility of antibiotics differs based on the species of Aeromonas tested and the geographical location [27]. It is deduced that the emergence and transmission of CTX-M-3, TEM-1 and a new plasmid-mediated MOX-4 AmpC in Aeromonas caviae may be blamed for this phenotype [28].

6. Conclusion

This study elucidated distinct clinical distribution and AMR patterns of Aeromonas species in a hepatic hospital based on a large sample size of data. A. hydrophila and A. veronii bv sobria dominated in blood and bloodstream isolates showed low antimicrobial resistance rates to most antibiotics including 3rd and 4th generation cephalosporins and ciprofloxacin. Compared with A. hydrophila and A. veronii bv sobria, A. caviae were proved as the predominant isolate in bile, stool and hydrothorax and they performed different AMR patterns, with higher resistance to CAZ, FEP, TZP, ATM and LVX. In summary, different Aeromonas species have different clinical and AMP pattens, and the determination of Aeromonas species in this study will offer important guidance for species-oriented therapy.

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