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## ORIGINAL RESEARCH PAPER



# Clinical and microbiological characteristics of *Aeromonas* bacteremia in Turkey

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## ABSTRACT

We investigated the cases with *Aeromonas* bacteremia in terms of clinical and microbiological characteristics, underlying disease and mortality rates. Patients with positive blood cultures were included in this research. *Aeromonas* bacteremia was diagnosed as at least one positive blood culture for *Aeromonas* species. The bacteremia was defined as community origin if the onset was in the community or within 72 hours of hospital admission. The others were considered as nosocomial. All bacteria were defined as *Aeromonas* with conventional method. Species identification was verified by VITEK system. Antibiotic susceptibility tests were analyzed with the disc diffusion, E-test method or VITEK system. Thirty-three patients were diagnosed with bacteremia due to *Aeromonas* spp. Hematologic and solid tumors were the leading underlying conditions, followed by cirrhosis. Two patients (6%) had community-acquired infections. *Aeromonas hydrophila* was the most common isolated bacterium. The crude mortality rate was 36%. 12 patients died and 6 deaths and 4 deaths were detected in patients with bacteremia caused by *A. hydrophila* and *Aeromonas sobria* respectively. All strains were resistant to ampicillin and more than 90% of the strains were susceptible to trimethoprim-sulfamethoxazole, fluoroquinolone, third generation cephalosporins, and carbapenems. *Aeromonas* sp. is not a frequent cause of bacteremia however, it may lead to high mortality rates, especially in the immunocompromised hosts and patients with liver cirrhosis. Nosocomial *Aeromonas* bacteremia is not uncommon in these populations. Broad-spectrum cephalosporins, piperacillin-tazobactam, fluoroquinolones, and carbapenems remain as effective antimicrobial agents for therapy of *Aeromonas* bacteremia.

## KEYWORDS

*Aeromonas* spp, bacteremia, antibiotic, infection, nosocomial

## INTRODUCTION

*Aeromonas* species are members of the family *Vibrionaceae* and these are oxidase and catalase positive, mobile, facultative anaerobe and Gram-negative rods. They are commonly found in

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the natural environments, especially in water resources and can be easily cultivated on basic media [1]. There are more than twenty defined species of *Aeromonas*, causing a wide range of infections in humans, both on land and in aquatic animals, reptiles and fish [2]. In developing countries, these pathogens give rise to self-limiting gastroenteritis in all age groups due to consumption of contaminated water and food especially in the summer months. In developing countries *Aeromonas* spp. are usually manifested as a gastrointestinal disease, however, these may also cause a variety of extra-intestinal infections including sepsis, arthritis, skin and soft tissue infection, meningitis, peritonitis, ocular infections, respiratory tract infections, urogenital tract infections, burn associated sepsis in especially immunocompromised host [2, 3]. *Aeromonas hydrophila*, *Aeromonas veronii*. *Aeromonas sobria* and *Aeromonas caviae* are among the most commonly isolated agents in human infections [4]. In this study, we investigated the cases with *Aeromonas* bacteremia in terms of clinical and microbiological characteristics, underlying disease and mortality rates.

## MATERIAL AND METHODS

From January 2000 to September 2019, patients with positive blood culture for *Aeromonas* spp. were included in this research. As it is a retrospective study, ethical approval and patient consent were not obtained. Thirty-three patients were diagnosed with bacteremia caused by *Aeromonas* spp. This retrospective study was included in two teaching hospitals and two university hospitals in Istanbul, Turkey. To ensure uniformity of definition, a standard form containing limited data was created for this study and they were asked to fill this form. Patients with complete data were analyzed. The diagnoses in the patient file were accepted as the final diagnosis. Their medical records, including demographic characteristics, clinical presentations, underlying diseases, laboratory data, antimicrobial susceptibility test results and patient outcome were recorded for analysis. *Aeromonas* bacteremia was defined as at least one positive blood culture for *Aeromonas* species. Routinely, two sets of blood cultures were taken from each patient with clinical signs or symptoms of infection and culture was taken from the focus if a source was documented as a result of clinical, microbiological and radiological examination. Primary bacteremia was defined as the bacteremia for which no source of infection was detected. When a patient had a focus of infection but no sample could be taken or when the same bacteria were isolated from both focus and blood culture, such infections were considered as secondary bacteremia. The bacteremia was defined as community origin if the onset was in the community or within 72 hours of hospital admission, the others were considered as nosocomial [5]. All bacteria were defined as *Aeromonas* with conventional method. Species identification was verified by VITEK system. Antibiotic susceptibility tests were analyzed with conventional methods (disc diffusion and E-test method) or automated method (VITEK system). Susceptibility of penicillins (ampicillin, ampicillin-sulbactam, piperacillin-tazobactam), cephalosporins (cefotaxime,

ceftriaxone, ceftazidime, cefepime), carbapenems (imipenem, meropenem), trimethoprim-sulfamethoxazole (TMP-SMX) and ciprofloxacin were tested and the results were interpreted according to CLSI. In many cases, the causes of death could not be determined from the patient records. Therefore, we chose to use the crude mortality rate.

## RESULTS

Thirty-three patients with bacteremia were included in this study. Fourteen patients were female and the mean age was  $41 \pm 20$  years (range, 8–74 years). The demographic data and underlying diseases of the patients are shown in Table 1. Three cases were under 16 years, 21 patients (63.6%) were older than 30 years. Hematologic and solid tumors were the leading underlying conditions, followed by cirrhosis (only three patients). Among 25 patients with neoplasm, 19 cases had hematologic cancer (14 leukemia, 4 lymphoma, 1 multiple myeloma). Among 6 solid cancers (2 tongue, 1 pancreas, 1 bladder, 1 breast, 1 lung origin), only three were at metastatic stage. Two patients (6%) had community-acquired infections and the underlying conditions were chronic obstructive pulmonary disease and cholelithiasis, respectively. Of the 33 strains isolated, 4 *Aeromonas* isolates were not identified on species level, therefore these were reported as *Aeromonas* spp. The remaining 29 isolates were identified by VITEK. Altogether 14 were *A. hydrophila*, and 10 were *A. veronii* biovar *sobria*, 3 were *Aeromonas salmonicida* and 2 were *A. caviae*. *A. hydrophila* was the most common isolated organism, followed by *A. sobria* and *A. salmonicida*. Primary and secondary bacteremias developed in 54% and 46% of the cases, respectively. All episodes of primary bacteremia occurred in neutropenic patients and 38% of them were due to *A. sobria*. In patients with secondary bacteremia, the most common sources were intra-abdominal infection and spontaneous bacterial peritonitis, followed by aspiration pneumonia. *A. hydrophila* was responsible for the majority of secondary bacteremia. Of the whole cohort 12 patients died, 8 of them were female. 6 deaths and 4 deaths were detected in patients with bacteremia caused by *A. hydrophila* and *A. sobria*, respectively and the overall 30-day mortality rate was 36% in all patients. All strains were resistant to ampicillin, ampicillin-sulbactam. More than 90% of strains were susceptible to TMP-SMX, fluoroquinolone, third generation cephalosporins, aminoglycosides and carbapenems.

## DISCUSSION

*Aeromonas* bacteremia is a rare disease, accounting for 1.8% of cases of Gram-negative bacteremia [6]. In a study from our country, only one was caused by *Aeromonas* sp. among 122 Gram-negative bacteremias [7]. This is the first study related to *Aeromonas* spp. bacteremia in Turkey comprising thirty-three cases identified in 4 training

Table 1. Detailed characteristics of the patients

	Age	Gender	Underlying conditions	Focus of infection	Type of bacteremia	Microorganism	Outcome	Treatment
1	49	Female	Decompensated cirrhosis	Spontaneous bacterial peritonitis	Secondary bacteremia	<i>Aeromonas</i> sp.	Survival	CRO
2	59	Male	Acute myeloid leukemia	None	Primary bacteremia	<i>A. sobria</i>	Death	IMP
3	54	Female	Tongue cancer	Aspiration pneumonia	Secondary bacteremia	<i>A. hydrophila</i>	Death	IMP
4	50	Male	Tongue cancer	Aspiration pneumonia	Secondary bacteremia	<i>A. hydrophila</i>	Survival	TZP, IMP
5	56	Male	Pancreatic cancer	Cholangitis	Secondary bacteremia	<i>A. hydrophila</i>	Survival	CRO, IMP
6	63	Male	Multiple myeloma	None	Primary bacteremia	<i>A. hydrophila</i>	Survival	FEP
7	40	Female	Acute lymphoblastic leukemia	None	Primary bacteremia	<i>A. sobria</i>	Death	MER, AMK
8	40	Female	Acute lymphoblastic leukemia	None	Primary bacteremia	<i>A. sobria</i>	Death	MER, AMK
9	18	Male	Acute myeloid leukemia	None	Primary bacteremia	<i>A. caviae</i>	Survival	MER
10	43	Male	Acute myeloid leukemia	None	Primary bacteremia	<i>A. hydrophila</i>	Death	MER
11	22	Male	Acute lymphoblastic leukemia	None	Primary bacteremia	<i>A. sobria</i>	Survival	TZP, MER
12	22	Male	Acute lymphoblastic leukemia	None	Primary bacteremia	<i>A. sobria</i>	Survival	MER
13	22	Male	Acute lymphoblastic leukemia	None	Primary bacteremia	<i>A. sobria</i>	Survival	MER, CİP
14	58	Male	Alcoholic cirrhosis	Spontaneous bacterial peritonitis	Secondary bacteremia	<i>A. sobria</i>	Survival	TZP, MER
15	16	Male	Lymphoma	None	Primary bacteremia	<i>A. hydrophila</i>	Survival	CAZ
16	8	Male	Acute lymphoblastic leukemia	None	Primary bacteremia	<i>A. hydrophila</i>	Survival	CAZ, TZP, IMP
17	12	Male	Aplastic anemia	None	Primary bacteremia	<i>A. hydrophila</i>	Death	TZP
18	12	Female	Acute lymphoblastic leukemia	None	Primary bacteremia	<i>A. hydrophila</i>	Death	MER
19	68	Male	Lymphoma	Cutaneous Abscess	Secondary bacteremia	<i>A. sobria</i>	Survival	MER
20	57	Female	Acute myeloid leukemia	Necrotizing fasciitis	Secondary bacteremia	<i>A. hydrophila</i>	Death	IMP
21	68	Female	Metastatic bladder cancer	Intra-abdominal infection	Secondary bacteremia	<i>A. hydrophila</i>	Survival	CAZ
22	61	Female	Metastatic lung cancer	Intra-abdominal infection	Secondary bacteremia	<i>A. hydrophila</i>	Death	MER
23	26	Female	COPD	Aspiration pneumonia	Secondary bacteremia	<i>A. salmonicida</i>	Survival	TZP
24	69	Male	Cholelithiasis	Cholangitis	Secondary bacteremia	<i>A. hydrophila</i>	Survival	TZP
25	48	Male	Acute myeloid leukemia	Gastroenteritis	Secondary bacteremia	<i>A. veronii</i>	Survival	TZP
26	37	Male	Lymphoma	None	Primary bacteremia	<i>Aeromonas</i> sp.	Survival	FEP
27	26	Male	Liver cirrhosis	Spontaneous bacterial peritonitis	Secondary bacteremia	<i>Aeromonas</i> sp.	Survival	TZP
28	11	Female	Aplastic anemia	None	Primary bacteremia	<i>A. salmonicida</i>	Survival	TZP
29	74	Female	Metastatic breast cancer	Surgical wound infections	Secondary bacteremia	<i>A. salmonicida</i>	Death	TZP

(continued)



Table 1. Continued

	Age	Gender	Underlying conditions	Focus of infection	Type of bacteremia	Microorganism	Outcome	Treatment
30	62	Male	Acute myeloid leukemia	None	Primary bacteremia	<i>Aeromonas</i> sp.	Death	TZP, COL
31	30	Female	Acute promyelocytic leukemia	None	Primary bacteremia	<i>A. caviae</i>	Survival	TZP
32	20	Female	Ruptured hepatic hydatid cyst	Intra-abdominal infection	Secondary bacteremia	<i>A. hydrophila</i>	Survival	TZP
33	55	Female	Lymphoma	None	Primary bacteremia	<i>A. sobria</i>	Death	MER, COL

CAZ: Cefazidime, TZP: Piperacillin tazobactam, IMP: Imipenem, MER: Meropenem, CIP: Ciprofloxacin, COL: Colistin CRO: Ceftriaxone, FEP: Cefepime, COPD: Chronic obstructive pulmonary disease

hospitals over a period of 20 years. *Aeromonas* spp. leads to gastroenteritis, meningitis, wounds and respiratory infections, ranging from mild to life-threatening diseases [3, 8]. These infections can be acquired from both community and hospital settings [9, 10]. Several studies stated that the majority of patients acquired *Aeromonas* infection from community, ranging from 71% to 79% but in Taiwan, this rate was 31 percent [10–13]. However, in this study, community-acquired infections were found in only two patients. Since many patients had severe underlying conditions, they were closely associated to taking health care in hospital. Similar to our patients, many studies have shown that *Aeromonas* species are responsible for infections in immunocompetent and immunocompromised host [9–11, 13, 14]. The most common underlying diseases were defined as liver cirrhosis and neoplasm [9–11, 15]. In our cases, the majority of underlying diseases were malignancy followed by cirrhosis. In a literature review of 44 patients, most of the cases were male, the mortality was 48% and 80 percent of the patients had leukemia [16]. In two separate cancer studies, the majority of patients were reported to have acute leukemia, as in the current study [17, 18]. In another study, the mortality rate was 28% in all cases, 82% of patients were male and all except for one were leukemia, as comorbidity. On the other hand, the focus of infection could not be elucidated and the bacteremia was attributed to gastrointestinal translocation [17]. The frequency of primary *Aeromonas* bacteremia varies between 40% and 57% [10, 11]. Neutropenic patients constituted 54% of the cases with the primary bacteremia in our study.

In *Aeromonas* bacteremia, males were more frequently infected than females in the literature and 60%–76% of the infections were monobacterial bacteremia in all reports [10–13]. Similarly, *Aeromonas* was the only agent in our cohort. As reported by Ko et al., the majority of bacteremia were caused by *A. sobria* (51.5%) in secondary bacteremia [10]. In another study, the most common source of secondary bacteremia was biliary tract infection (8/17 patients; 47.1%), followed by spontaneous bacterial peritonitis (4/17 patients; 23.5%) [19]. In our patients with secondary bacteremia, 8 cases were caused by *A. hydrophila* and the most common sources were intra-abdominal infection and spontaneous bacterial peritonitis.

*Aeromonas* species grow easily at increased temperatures and people have more contact with contaminated water and food during the warmer seasons, thereby facilitating colonization and infection [1]. In previous literature, 42–67 percent of patients developed bacteremia during the summer seasons [12, 13]. Similarly, this rate was found to be 54% in our patients.

As a mild, self-limiting infection, *Aeromonas*-associated diarrhea is the most common presentation in daily clinical practice. Yet, only one major outbreak related to *Aeromonas* has been reported to date and stool isolation rates differ among patients with diarrhea [2, 20]. In addition, *Aeromonas* is commonly isolated from asymptomatic individuals, therefore several questions have been raised about the role of *Aeromonas* spp. as etiological agents of bacterial diarrhea [3, 21]. On the other hand, diarrhea accompanying bacteremia is rare. In a study, 53 cases of *Aeromonas* bacteremia were reported over a 10-year period and most patients were immunosuppressive but diarrhea was not found in the majority of patients [22]. Similar to the report of Llopis et al., only one bacteremic patient had gastroenteritis in our cohort [12].

Of the 33 isolates, 4 strains were not identified in species level and reported as *Aeromonas* spp. *A. hydrophila* was the most commonly isolated organism (42%), followed by *A. veronii* biovar *sobria*. Earlier studies found that more than 85% of the human infections were caused by *A. hydrophila*, *A. sobria* and *A. caviae* [4]. *A. hydrophila* was the most frequently isolated organism in many reports and it can also harbor antibiotic resistance genes [9, 11, 16, 23]. *Aeromonas* spp. may have higher index of gastrointestinal colonization in neutropenic cancer patients and this may be responsible for the source of bacteremia in most cases [24]. Additionally, *A. sobria* is more common than the other genus in neutropenic patients [17]. In our study, bacteremia caused by *A. hydrophila* had the highest mortality rate and it was the most commonly isolated species. Also, *A. sobria* was the most common cause of bacteremia in neutropenic patients. Interestingly, aspiration pneumonia was the source of bacteremia in three patients. *Aeromonas* spp. have been encountered as a rare pathogen of aspiration pneumonia in the recent years [3, 25, 26].

*Aeromonas* infections are more common in far eastern countries other than Japan but are very rarely reported from

Europe. Turkey is located near the European countries and has very close contact with them. Likewise, both in European countries and in Turkey, *Aeromonas* infections were frequently acquired from hospital settings and had male predominance [12, 15, 17, 27]. Community-acquired infection was rare in our study, probably due to the lower frequency of environmental aeromonads in European regions in comparison to far eastern countries.

The mortality rates of *Aeromonas* bacteremia have been reported as 36% in 59 cases, 26% in 116, 28% in 17, 19% in 36, 35% in 17, 32.6% in 41 cases [9, 13, 15, 17, 18, 28]. In this study, just 12 patients died, the mortality rate was 36% and this rate was relatively higher than in several previous reports. The majority of fatal cases had cancer and hospital-acquired infections which may explain the higher rate of mortality.

All strains in our cases were resistant to ampicillin, ampicillin-sulbactam and more than 90% of the strains were susceptible to TMP-SMX, fluoroquinolone, third generation cephalosporins, aminoglycosides, carbapenems. Monitoring local antimicrobial susceptibility patterns of isolates is essential for antibiotic selection. In our study, piperacillin-tazobactam, carbapenems and third generation cephalosporins were more commonly preferred in empirical treatment, in order to cover nosocomial pathogens. Although several reports indicated that there have been emerged resistance in fluoroquinolone following leech therapy, fluoroquinolone resistance was not detected in our strains [29]. Though two weeks of therapy is usually recommended, the optimal duration of the treatment for bacteremia is still unclear and it should be adjusted based on individual conditions and clinical response.

This study has some limitations. It is a retrospective research and includes low number of cases. The methodology for the identification and susceptibility test for *Aeromonas* species were not homogeneous throughout the study. However, as a first study related to *Aeromonas* bacteremia it provides valuable epidemiological data to guide antibiotic selection in further cases.

In conclusion, though *Aeromonans* sp. is not a frequent pathogen of bacteremia, it may give rise to high mortality rates, especially in immunocompromised patients and patients with liver cirrhosis. Physicians should be aware of nosocomial *Aeromonas* bacteremia which is not uncommon in these populations. Broad-spectrum cephalosporins, piperacillin-tazobactam, fluoroquinolones, and carbapenems remain as effective antimicrobial agents for treatment of *Aeromonas* bacteremia.

**Declarations:** Authors declare no conflict of interest.

All authors meet the ICMJE authorship criteria.

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