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# BEYOND THE GUT: NON-O1/NON-O139 VIBRIO CHOLERAE CAUSING BACTERAEMIA — A TWO-CASE REPORT

Clinical Microbiology

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## ABSTRACT

Non-O1/non-O139 Vibrio cholerae bacteremia is an uncommon, life-threatening infection reported chiefly in patients with liver disease, hemolytic disorders, or severe immunosuppression. We report two cases identified via automated blood culture and MALDI-TOF mass spectrometry at a tertiary-care center in coastal India. Case 1, a 23-year-old male mine worker with congenital heart disease and cirrhosis, presented with fever, hypotension, and septic shock; blood culture yielded V. cholerae non-O1/non-O139 resistant to ampicillin but susceptible to third-generation cephalosporins, fluoroquinolones, tetracyclines, and carbapenems, and he recovered fully after antimicrobial therapy. Case 2, a 38-year-old male from a coastal region with decompensated liver disease and chronic kidney disease, presented with fever, septic shock, and lower limb cellulitis following occupational exposure to fish-contaminated water; his isolate was susceptible to all tested agents. Both cases underscore the association of non-O1/non-O139 V. cholerae bacteremia with hepatic disease, the rarity of ampicillin resistance in this serogroup, and the critical role of blood culture and rapid molecular identification in guiding empiric therapy. Early recognition and appropriate antimicrobials achieved favorable outcomes despite severe sepsis.

## KEYWORDS

Vibrio cholerae; non-O1/non-O139; bacteremia; MALDI-TOF; antimicrobial susceptibility

## 1. INTRODUCTION

*Vibrio cholerae* is a curved gram-negative bacillus historically associated with severe diarrheal disease, particularly the pandemic O1 and O139 serogroups [3,12]. Non-O1/non-O139 serogroups, however, are increasingly recognized as causes of extraintestinal infections—bacteremia, otitis media, and wound infections—especially in immunocompromised hosts [6,17]. Non-O1/non-O139 *V. cholerae* bacteremia remains distinctly uncommon, limited to sporadic case reports and small series [1,4,7,9], unlike the epidemic and endemic cholera caused by O1/O139 strains [16,18].

Risk factors include cirrhosis and chronic liver disease, hemolytic anemias (particularly hereditary spherocytosis), hematological malignancies, iron overload states, and profound immunosuppression from malignancy or HIV [4,9,20]. Coastal and tropical geographic distribution reflects the marine reservoir of Vibrio species [8,11]. Presentation typically involves fever, chills, and hypotension evolving to septic shock, distinguishing it from classic cholera's massive watery diarrhea without inflammatory symptoms [17,19].

Microbiological identification has traditionally relied on biochemical assays and serogrouping with O1 and O139 antisera [10]. Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF) now offers rapid, accurate, and cost-effective species-level identification, enabling faster antimicrobial selection [5]. Susceptibility patterns in non-O1/non-O139 *V. cholerae* are variable but often include fluoroquinolones, tetracyclines, third-generation cephalosporins, and carbapenems as reliable options [14,20].

This case series documents two cases of non-O1/non-O139 *V. cholerae* bacteremia at a tertiary-care center in coastal India, highlighting the diagnostic workup, resistance patterns (including rare ampicillin resistance), clinical outcomes, and a literature review.

## 2. Case Presentations

### 2.1 Case 1:

Non-O1/Non-O139 *V. cholerae* Bacteremia with Ampicillin Resistance in a Patient with Congenital Heart Disease and Cirrhosis

#### Patient Demographics and Risk Factors

A 23-year-old male lignite mine worker presented with acute-onset fever and hypotension. His past history included childhood-diagnosed sinus venosus atrial septal defect (ASD) with moderate pulmonary hypertension, congenital extrahepatic portal vein obstruction, and cirrhosis presumed secondary to it. He used alcohol and tobacco, and consumed fish regularly but denied recent seafood or seawater exposure. Travel history was unremarkable.

#### Clinical Presentation

On July 3, 2026, he developed abrupt fever (38.4°C), rigors, and severe hypotension (BP 100/80 mmHg), with a 3-month history of left scrotal swelling.

By July 4, 2026 (Day 2), he developed diarrhea and vomiting. Examination revealed dehydration, clinical icterus, bilateral pitting pedal edema, moderate ascites, and a varicocele.

#### Laboratory and Imaging Findings

Complete blood count: hemoglobin 10.5 g/dL, WBC 7,730 cells/µL, platelets 1.41 × $10^5$ cells/µL. Renal function was preserved (urea 23 mg/dL, creatinine 0.65 mg/dL). Liver biochemistry showed indirect hyperbilirubinemia (total bilirubin 0.6 mg/dL), mildly elevated transaminases (AST 20 U/L, ALT 25 U/L), and low albumin (2.4 g/dL). Arterial blood gas: pH 7.36, $pCO_2$ 20.2 mmHg, $pCO_2$ 60 mmHg, lactate 1.4 mmol/L.

Echocardiography showed ejection fraction 70% with moderate-to-severe tricuspid regurgitation; ECG showed normal sinus rhythm at 100 bpm with right bundle branch block.

#### Microbiological Findings

Blood cultures via the BacT/ALERT Virtuo system showed growth in the aerobic bottle at 7.7 hours; Gram stain revealed curved gram-negative bacilli. Subculture yielded smooth, buff-colored, beta-hemolytic colonies (2–3 mm) on blood agar, non-lactose-fermenting colonies on MacConkey agar, and small yellow colonies on TCBS agar.

MALDI-TOF confirmed *Vibrio cholerae* with high confidence (log score >2.0), supported by biochemical testing (oxidase-positive, arginine dihydrolase-positive, Voges-Proskauer-negative, string test-positive). Serogrouping with O1/O139 antisera was negative, confirming non-O1/non-O139 serogroup.

Susceptibility testing (CLSI M45) showed susceptibility to cotrimoxazole, azithromycin, levofloxacin, tetracycline, ciprofloxacin, and meropenem, but resistance to ampicillin—noteworthy since this is uncommon in non-O1/non-O139 V. cholerae.

Repeat blood culture on July 5, 2026 (Day 2 of therapy) was negative, confirming clearance; stool culture was negative for *V. cholerae*.

#### Treatment and Outcome

He was admitted to the ICU with IV fluid resuscitation and support for septic shock. Empiric piperacillin-tazobactam was escalated to meropenem, then switched to oral doxycycline (100 mg twice daily) after improvement. He recovered completely and was discharged after 8 days.

### 2.2 Case 2: Non-O1/Non-O139 *V. cholerae* Bacteremia with Septic Shock and Cellulitis in Decompensated Liver Disease

**Patient Demographics and Risk Factors**
A 38-year-old male petrol-bunk worker from Cuddalore (coastal Tamil Nadu) presented with acute sepsis. Comorbidities included HBsAg seropositivity, decompensated cirrhosis, ASD, and chronic kidney disease. He denied alcohol and tobacco use, consumed fish regularly, and had daily occupational exposure to fish-contaminated water with bare feet.

**Clinical Presentation**
He developed acute fever with rigors and chills. Within 24 hours, he had severe hypotension (BP 80/60 mmHg) requiring noradrenaline. By Day 2, he developed diarrhea and right lower-limb swelling.

Fever persisted for 4 days. Examination revealed clinical icterus, dependent edema, and pitting edema of the right lower limb to mid-calf with erythema and tenderness consistent with acute cellulitis; he met criteria for septic shock.

**Laboratory and Imaging Findings**
Complete blood count: hemoglobin 11 g/dL, WBC 9,710 cells/µL, platelets low at 43,000 cells/µL. Renal function was impaired (urea 74 mg/dL, creatinine 1.5 mg/dL). Liver function tests: direct bilirubin 2.35 mg/dL (total 5.4 mg/dL), AST 71 U/L, ALT 35 U/L, albumin 2.15 g/dL; INR was elevated at 2.94.

Arterial blood gas: pH 7.45, $pCO_2$ 19.3 mmHg, $pO_2$ 71 mmHg (on 2 L $O_2$), $HCO_3$ - 13 mmol/L, lactate 4.8 mmol/L. Echocardiography showed reduced ejection fraction (25–50%), elevated cardiac index (49%), and IVC diameter 1.7 cm.

**Microbiological Findings**
Blood culture via BacT/ALERT Virtuo showed growth in the aerobic bottle at 8.7 hours; Gram stain revealed curved, comma-shaped gram-negative bacilli. Blood agar yielded smooth, grey, beta-hemolytic colonies; MacConkey agar showed NLF colonies; TCBS agar showed small yellow colonies.

MALDI-TOF confirmed *Vibrio cholerae* (log score >2.0), supported by biochemical assays (oxidase-positive, arginine dihydrolase-positive, Voges-Proskauer-negative, string test-positive). Serogrouping was negative for O1/O139, confirming non-O1/non-O139 serogroup.

Susceptibility testing (CLSI M45) showed susceptibility to all agents tested: ampicillin, cotrimoxazole, azithromycin, levofloxacin, tetracycline, ciprofloxacin, and meropenem.

Repeat blood cultures on Day 4 were negative, confirming clearance; stool culture was negative for *V. cholerae*.

**Treatment and Outcome**
He was admitted to the ICU with aggressive hemodynamic support—vasopressors (noradrenaline), IV fluids, and blood products for coagulopathy. Empiric piperacillin-tazobactam was escalated to meropenem, then switched to oral doxycycline after improvement. Cellulitis resolved gradually with therapy; renal function stabilized and thrombocytopenia resolved. He was discharged in stable condition after approximately 10 days.

Baseline clinical and demographic details are summarized in Table 1.

**Table 1: Baseline Clinical and Demographic Characteristics**

| Variable | Case 1 | Case 2 |
|---|---|---|
| Age (years) | 23 | 38 |
| Sex | Male | Male |
| Primary Risk Factor | Cirrhosis + CHD | Decompensated Cirrhosis + CKD |
| Etiology of Cirrhosis | Congenital portal vein obstruction | Hepatitis B (HBsAg+) |
| Fever Duration (days) | 2 | 4 |
| Septic Shock | Yes | Yes |
| Occupational Exposure | Lignite mining | Fish-contaminated water |

*Note: CHD = Congenital Heart Disease; CKD = Chronic Kidney Disease.*

Microbiological characteristics and antimicrobial susceptibility are summarized in Table 2.

**Table 2: Microbiological Characteristics and Antimicrobial Susceptibility**

| Parameter | Case 1 | Case 2 |
|---|---|---|
| Time to Positivity (hours) | 7.7 | 8.7 |
| Colony Morphology (Blood Agar) | Smooth, buff, 2–3 mm, beta-hemolysis | Smooth, grey, beta-hemolysis |
| TCBS Agar | Small yellow colonies | Small yellow colonies |
| MALDI-TOF Identification | *V. cholerae* (score >2.0) | *V. cholerae* (score >2.0) |
| Serogroup | Non-O1/non-O139 | Non-O1/non-O139 |
| Repeat Blood Culture | Negative (Day 2) | Negative (Day 4) |
| Ampicillin | R (Resistant) | S (Susceptible) |
| Levofloxacin | S | S |
| Tetracycline/Doxycycline | S | S |
| Ciprofloxacin | S | S |
| Meropenem | S | S |
| Stool Culture | Negative | Negative |

*Note: S = Susceptible; R = Resistant.*

## 3. DISCUSSION

### 3.1 Epidemiology and Clinical Significance
Non-O1/non-O139 *V. cholerae* bloodstream infection is rare, with fewer than 100 well-documented cases in the literature [6,7], and our two cases highlight its epidemiologic distinctiveness. While O1 and O139 serogroups cause fulminant diarrheal disease via cholera toxin, non-O1/non-O139 strains are primary bloodstream pathogens that may or may not cause diarrhea [13,16]—an absence that can delay recognition [17].

Both cases had significant hepatic dysfunction: Case 1 had cirrhosis from congenital portal vein obstruction, and Case 2 had decompensated cirrhosis from hepatitis B—a well-established association [1,4,9]. Proposed mechanisms include portal hypertension causing portosystemic shunting, splenic dysfunction impairing phagocytic clearance, complement/opsonin deficiency, and iron overload favoring Vibrio growth [2,13].

This vulnerability in decompensated cirrhosis reflects several converging derangements. Increased intestinal permeability and portal hypertensive enteropathy promote bacterial translocation across the gut mucosa into the portal circulation [22], while impaired Kupffer cell function and portosystemic shunting let translocated organisms evade hepatic clearance and reach systemic circulation [22,23]. Cirrhosis-associated immune dysfunction—reduced complement synthesis, poor opsonization, defective phagocytosis—allows even small inocula to survive and proliferate [21], and the iron-overloaded, hepcidin-deficient state further favors growth of these strongly iron-dependent organisms [4]. Unlike toxigenic O1/O139 strains, confined largely to the gut lumen, many non-O1/non-O139 isolates carry invasive determinants such as hemolysin, RTX toxin, and adhesins that facilitate tissue invasion once host defenses are breached [23].

### 3.2 Microbiological Diagnosis and Species Identification
Both cases illustrate blood culture's critical role as the diagnostic method of choice. Non-O1/non-O139 *V. cholerae* is not reliably isolated from stool in bacteremia—indeed, both patients' stool cultures were negative [4,10]—so blood culture must be obtained promptly in any septic patient with risk factors, particularly cirrhosis.

The BacT/ALERT Virtuo system detected both isolates within 7–9 hours; both grew only in aerobic bottles, not anaerobically, characteristic of Vibrio species.

MALDI-TOF identified both isolates as *V. cholerae* with high confidence (log score >2.0)—faster than biochemical profiling, more cost-effective than 16S rRNA sequencing, and more species-specific than biochemical panels [5]—enabling identification within 24 hours of culture positivity and accelerating targeted therapy.

PCR-based virulence gene characterization (ctxA, tcpA, toxR, ompW, hlyA, rtxA) was not performed, a limitation of this study [10].

### 3.3 Antimicrobial Susceptibility and Resistance Patterns

A notable finding in Case 1 was ampicillin resistance, since non-O1/non-O139 serogroups have historically shown high ampicillin susceptibility [14,20]. This resistance is distinctly uncommon and may reflect intrinsic mechanisms or plasmid-acquired resistance genes [14]; it was confined to ampicillin, with the isolate remaining susceptible to carbapenems.

Both isolates were fully susceptible to tetracyclines, fluoroquinolones, macrolides, and carbapenems—the preferred agents for *V. cholerae* bacteremia [14,20]—and both patients responded well to doxycycline as step-down therapy.

### 3.4 Literature Review

A structured literature review identified more than 40 published cases of *V. cholerae* bacteremia over the last 20–30 years [1,4,7,9,20], with key themes as follows:

- Most cases (>90%) occur with cirrhosis, chronic hemolytic anemia, or hematological malignancy; immunocompetent individuals are rarely affected [4,9].
- Geographic distribution is strongly linked to coastal, tropical climates where Vibrio species thrive; inland cases are exceptions [11,15].
- O1 serogroup bacteremia is extremely rare; most strains are non-O1/non-O139 [16].
- Septic shock occurs in 60–80% of cases; mortality historically ranged 20–50% despite treatment, improving to 10–30% in modern series with earlier diagnosis and critical care [4,9].
- Most isolates are susceptible to fluoroquinolones, tetracyclines, and carbapenems; ampicillin resistance is uncommon (<10%), making Case 1's isolate noteworthy [14,20].

Our cases align with published literature on demographics, risk factors, geographic origin, and response to targeted antimicrobials; both patients recovered, consistent with modern series.

This comparison is summarized in Table 3.

**Table 3: Comparative Literature Review of Published Cases**

| Study/Case | Country | Year | Primary Risk Factor | Outcome |
|---|---|---|---|---|
| Case 1 (present report) | India | 2026 | Cirrhosis + Congenital Heart Disease | Recovered |
| Case 2 (present report) | India | 2026 | Decompensated Cirrhosis + CKD | Recovered |
| Srivastava et al. [1] | India | 2009 | Cirrhosis (Portal vein obstruction) | Recovered |
| Chowdhury et al. [4] | Bangla desh | 1998 | Cirrhosis (70%), Hemolytic anemia (30%) | Variable (Mortality 30–40%) |
| Bhattacharya et al. [9] | India | 1999 | Mixed (Cirrhosis predominant) | High mortality (40–50%) |
| Monma et al. [20] | Japan | 2009 | Hemolytic anemia, Cirrhosis | Mixed outcomes |
| Baker-Austin et al. (Review) [11] | Global | 2017 | Coastal populations, Seafood consumption | Variable |

*Note: CKD = Chronic Kidney Disease*

### 3.5 Clinical Implications and Diagnostic Challenges

(1) *V. cholerae* bacteremia should be considered in any septic patient with cirrhosis, hemolytic disease, or occupational exposure to brackish water or raw seafood, even without diarrhea [17].
(2) Blood culture is essential; stool culture is insensitive for non-O1/non-O139 serogroups [4,10].
(3) MALDI-TOF enables rapid species identification (within 24 hours), facilitating early, targeted antimicrobial therapy [5].
(4) Empiric therapy should avoid ampicillin monotherapy; fluoroquinolones or tetracyclines provide excellent coverage pending culture results [14,20].
(5) ICU admission and aggressive hemodynamic support are critical; outcomes improve significantly with vasopressors, fluid resuscitation, and appropriate antimicrobials.

### 3.6 LIMITATIONS

This report is limited by its small sample size (n=2), which constrains statistical analysis, and by the absence of molecular typing and PCR-based virulence gene characterization [10]. Our experience is limited to a single institution; multicenter studies are needed.

## 4. CONCLUSION

Non-O1/non-O139 *Vibrio cholerae* bacteremia is a rare but life-threatening infection with significant mortality if not promptly recognized. This case series underscores its continued relevance in coastal regions and the critical role of blood culture with MALDI-TOF identification—both patients presented with septic shock and cirrhosis as the predominant risk factor, yet achieved favorable outcomes through early recognition, aggressive supportive care, and targeted antimicrobial therapy. Clinicians managing sepsis with hepatic disease should maintain high suspicion for Vibrio bacteremia, and microbiologists should adopt rapid identification methods such as MALDI-TOF.

## 5. Future Scope

Future studies should incorporate PCR-based virulence gene profiling (ctxA, tcpA, toxR, ompW, hlyA, rtxA) to better delineate the pathogenic potential of non-O1/non-O139 *V. cholerae* isolates [10]. Whole-genome sequencing may clarify the mechanisms underlying the atypical ampicillin resistance seen in Case 1 and track emerging resistance genes across strains [14]. Multicenter, prospective surveillance across coastal and tropical regions is needed to define the true incidence, risk-factor profile, and outcomes of this likely underreported infection [6,7,11]. Wider adoption of rapid platforms such as MALDI-TOF, particularly in hepatology and critical-care units, may shorten time to targeted therapy and further improve survival [5].

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