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ORIGINAL RESEARCH

Comparative Study of Confirmed versus Suspected Cases of *Vibrio vulnificus* Infection in Chaoshan District, Guangdong, China

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Objective: To compare the epidemiological, clinical, and laboratory data of patients with confirmed and suspected *Vibrio vulnificus* infection in Chaoshan District, Guangdong.

Methods: This retrospective study analyzed 25 confirmed cases and 23 suspected cases of *V. vulnificus* infection at the First Affiliated Hospital of Shantou University Medical College from January 2014 to December 2025. A confirmed case was defined by the presence of a positive result from culture and/or mNGS and a suspected case by the experience of a clear marine trauma followed by rapidly progressive soft tissue manifestations, but without etiological confirmation of *V. vulnificus* infection after exclusion of other infectious etiologies. The epidemiological history, early clinical manifestations, routine blood parameters, and in-hospital outcomes of the two groups were compared.

Results: The confirmed group had a greater severity of soft tissue infection (84.0% vs 26.0%, $P<0.01$) and more involved sites (88.0% vs 47.8%, $P<0.01$). The laboratory data indicated the confirmed group had more abnormalities in markers of tissue injury (creatinine kinase, lactate dehydrogenase), coagulation function (platelets, prothrombin time, international normalized ratio), liver function (aspartate transaminase, total bilirubin), renal function (serum creatinine), and lipid and nutritional markers (all $P<0.05$). The confirmed group also had significantly higher rates of in-hospital mortality (32.0% vs 0%), multi-organ dysfunction syndrome (36.0% vs 0%), and surgical intervention (60.0% vs 30.4%), and a greater economic burden (all $P<0.001$).

Conclusion: There are significant differences in the early clinical manifestations, routine blood parameters, and in-hospital outcomes for patients with confirmed and suspected *V. vulnificus* infection.

Keywords: *Vibrio vulnificus*, soft tissue infection, suspected case, metagenomic next-generation sequencing

Introduction

Vibrio vulnificus infection is an acute and severe disease caused by infection with *V. vulnificus*, a Gram-negative bacterium that occurs in marine environments. Patients with a *V. vulnificus* infection that has progressed to *V. vulnificus*-necrotizing soft tissue infection (Vv-NSTI), have a mortality rate of about 50% and their care is associated with significant public health costs.[1] *V. vulnificus* infection is more common in individuals with underlying health conditions, such as chronic liver disease, diabetes, or an immunocompromised status. Globally, over 95% of fatal *V. vulnificus* infections occur in subtropical regions, including the Chaoshan region of Guangdong, China. *V. vulnificus* infections show a clear seasonal peak from March to November, particularly in the warm summer months when seawater temperatures rise and seafood consumption increases. Recent regional evidence from Asia quantified this burden. In particular, a 2024 systematic review and meta-analysis reported a 10% prevalence of seafood-borne *V. vulnificus*, with oysters as a major source,[2] and another 2024 meta-analysis reported concerning patterns of antimicrobial resistance

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among Asian seafood isolates.[3] Furthermore, a 2025 South Korean study highlighted the substantial health and economic impact of infections associated with raw oyster consumption.[4]

Early identification and timely intervention by a multidisciplinary treatment (MDT) team are critical to the survival of these patients. *V. vulnificus* infection is often diagnosed in individuals with a history of seafood-related puncture or seawater exposure through a wound. These patients develop rapidly progressing skin redness, swelling, pain, and necrotizing soft tissue infection (NSTI) of the extremities.[5] Microbial culture is the gold standard for the etiological diagnosis of *V. vulnificus* infection. However, traditional culture methods are time-consuming, and the overall rate of positive culture in patients with confirmed infection is approximately 30% to 40%.[6] Metagenomic next-generation sequencing (mNGS) has become a valuable adjunctive tool for the identification of infectious pathogens.[7] The increasing use of mNGS may partially overcome the limitation of the low rate of culture positivity, but its role in distinguishing confirmed from suspected *V. vulnificus* infections in routine practice remains unclear.

No studies have yet compared patients who have confirmed *V. vulnificus* infection with those who have suspected *V. vulnificus* infection. In clinical practice, many patients are managed as having suspected *V. vulnificus* infection without microbiological confirmation, yet it is unclear whether their early clinical features and prognoses differ from those of confirmed cases. In this study, we define confirmed cases as those with microbiological evidence of *V. vulnificus* (culture and/or mNGS), and suspected cases as those with epidemiological exposure and typical soft tissue manifestations but no etiological confirmation. This retrospective study compared the epidemiological history, early clinical symptoms and key laboratory parameters (within 6 h of emergency department presentation or admission), treatment measures, and clinical outcomes of groups with confirmed and suspected *V. vulnificus* infection. We aim to identify clinical and laboratory indicators associated with confirmed *V. vulnificus* infection and poor outcomes to enable the earlier recognition and risk stratification of high-risk patients.

Materials and Methods

Study Subjects

This retrospective comparative study enrolled patients with confirmed trauma-related infection who were hospitalized at the First Affiliated Hospital of Shantou University Medical College (Guangdong, China) between January 2014 and December 2025. The inclusion criteria for the confirmed *V. vulnificus* infection group (n = 25) were: (1) marine trauma within 7 days before symptom onset; (2) rapidly progressive soft tissue manifestations (eg, erythema, swelling, bullae, NSTI); and (3) a positive bacterial culture or mNGS result from wound tissue or blood. The inclusion criteria for the suspected *V. vulnificus* infection group (n = 23) were: (1) marine trauma within 7 days before symptom onset; (2) rapidly progressive soft tissue manifestations as described above; (3) no etiological confirmation of *V. vulnificus*; and (4) exclusion of other infectious etiologies (eg, *Aeromonas, Streptococcus, Staphylococcus, V. alginolyticus*) based on routine culture or mNGS when available. The exclusion criteria for both groups were: (1) age <16 years; (2) chronic soft tissue infection or pressure ulcer prior to trauma; (3) incomplete or missing medical records affecting outcome assessment; or (4) transfer from another hospital with initiation of antibiotic therapy >24 h before admission.

This study was approved by the Ethics Committee of the First Affiliated Hospital of Shantou University Medical College (Approval No. B-2026-052) and adhered to the principles outlined in the Declaration of Helsinki. Written informed consent was waived due to the retrospective nature of the study. Patient data were anonymized and kept confidential in accordance with ethical guidelines.

Medical records were reviewed, and clinical information on demographics, epidemiology, physical examination findings, presenting symptoms, laboratory parameters, antibiotics, surgical treatment, and outcomes were analyzed.

Outcome Definitions

The primary outcome was the incidence of multiple organ dysfunction syndrome (MODS), defined as a total Sequential Organ Failure Assessment (SOFA) score exceeding 5 at any time within the first 7 days after admission. The secondary outcomes were in-hospital mortality, length of hospital stay, and economic burden. Economic burden was defined as the total direct hospitalization

costs (in Chinese Yuan, RMB) that were billed to the patient, including medication, laboratory tests, imaging, surgical procedures, and intensive care unit fees. Indirect costs, such as lost productivity or post-discharge rehabilitation, were excluded.

Statistical Analyses

SPSS software (version 25.0) was used for statistical analysis. Continuous variables were first tested for normality. Normally distributed data are presented as mean ± standard deviation (mean ± SD), and non-normally distributed data as median with interquartile range (M [IQR]). For baseline comparisons of the two groups, an independent sample *t*-test was applied when the data in both groups were normally distributed and the variances were homogeneous; otherwise, the Wilcoxon rank-sum test was applied. Categorical variables are presented as frequencies and percentages, and were analyzed using the Pearson chi-square test or Fisher's exact test (for small sample sizes). A two-tailed α of 0.05 was considered statistically significant.

Results

Basic Demographic Characteristics, Epidemiology, and Early Clinical Manifestations

All confirmed cases and suspected cases were admitted between March 2014 and November 2025 and were diagnosed with trauma-related infection. There were 25 cases with microbiologically confirmed *V. vulnificus* infection, and 23 controls with suspected but not confirmed *V. vulnificus* infection (Table 1). In the confirmed cases, the median age was 67.0 years (IQR:49.5, 75.5), 96.0% (24/25) were male, 72% (18/25) had a history of marine trauma (eg, fish stabs, shrimp stabs, crab pincer injuries), 8.0% (2/25) had a wound exposed to seafood or seawater, and the remaining 20.0% (5/25) had no clear evidence of marine trauma. In the control group, the median age was 60.0 years (IQR:50.0, 70.0), 78.3% (18/23) were male, and all patients had a history of marine trauma (including fish stabs, shrimp stabs, crab pincer injuries, and fish hook wounds). The two groups had no significant differences in age, sex, or epidemiological characteristics ($P > 0.05$). Analysis of early clinical manifestations (within 6 h of emergency department presentation or admission) indicated the confirmed cases had greater percentages of patients with of severe soft tissue infection (84.0% vs 26.0%, $P < 0.01$) and patients with 2 or more involved sites (88.0% vs 47.8%, $P < 0.01$).

Key Laboratory Parameters

We also compared the baseline laboratory findings of the two groups, which were recorded at admission (Table 2). These groups had no significant differences in the white blood cell count (WBC), percentage of neutrophils (NE%), C reactive protein (CRP), sodium (Na), glucose (Glu), or triglycerides (TG). In contrast, the confirmed group had clinical parameters indicative of more severe infection and multi-organ involvement. Specifically, the markers of tissue injury (creatinine kinase

Table 1 Baseline Demographic and Clinical Characteristics of Patients with Confirmed and Suspected *Vibrio vulnificus* Infection

Variable	Confirmed Infection (n=25)	Suspected Infection (n=23)	P value
Age (Years)	67.00 (49.50, 75.50)	60.00 (50.00, 70.00)	0.200
Sex (Male)	24 (96.0%)	18 (78.3%)	0.156
Seawater or seafood contact	20 (80.0%)	23 (100.0%)	0.073
Malignancy	4 (16.0%)	0 (0.0%)	0.139
Heart disease	5 (20.0%)	2 (8.7%)	0.484
Liver disease	7 (28.0%)	1 (4.3%)	0.070
Diabetes mellitus	3 (12.0%)	4 (17.4%)	0.905
Body temperature > 37.3°C	17 (68.0%)	11 (47.8%)	0.157
Gastrointestinal symptom	4 (16.0%)	2 (8.7%)	0.743
Necrotizing soft tissue infection	21 (84.0%)	6 (26.0%)	<0.001*
≥2 infectious sites	22 (88.0%)	11 (47.8%)	0.003*
Time from exposure to admission (days)†	1 (1,3)	3 (2,5)	0.055

Notes: †Excluding 5 patients with unspecified causes in the group with confirmed infection. *P<0.05.

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Table 2 Baseline Laboratory Characteristics of Patients with Confirmed and Suspected *Vibrio vulnificus* Infection

Variable	Confirmed Infection (n=25)	Suspected Infection (n=23)	P value
WBC (10^9/L)	15.44 (±1.97)	16.05 (±1.90)	0.827
NE%	87.30 (80.10, 92.85)	83.80 (66.62, 90.50)	0.180
HGB (g/L)	120.36 (±4.22)	134.86 (±3.45)	0.012*
PLT (10^9/L)	135.00 (55.00, 188.50)	214.00 (171.00, 272.00)	<0.001*
PCT (ng/mL)	29.11 (6.10, 73.86)	3.56 (0.16, 10.83)	<0.001*
CRP (mg/L)	110.25 (78.20, 227.14)	100.58 (31.80, 208.00)	0.219
CK (U/L)	189.00 (61.45, 448.8)	96.00 (33.92, 211.00)	0.034*
LDH (U/L)	274.43 (234.00, 448.40)	208.00 (177.00, 251.00)	<0.001*
ALT (U/L)	37.80 (18.60, 115.95)	20.41 (16.48, 44.00)	0.122
AST (U/L)	61.30 (29.75, 134.24)	25.00 (20.00, 29.38)	<0.001*
Tbil (μmol/L)	21.82 (15.69, 47.51)	14.51 (9.58, 19.67)	0.002*
TP (g/L)	55.10 (46.74, 63.60)	62.60 (57.45, 67.60)	0.009*
Alb (g/L)	28.02 (±1.45)	35.51 (±1.03)	<0.001*
Na (mmol/L)	135.79 (±1.05)	137.35 (±0.92)	0.275
Glu (mmol/L)	8.00 (5.35, 11.46)	6.54 (5.30, 8.10)	0.270
Cr (μmol/L)	139.70 (95.90, 235.00)	83.01 (67.44, 99.00)	<0.001*
PT (s)	17.50 (11.85, 19.95)	11.60 (10.80, 12.60)	0.001*
INR	1.53 (1.04, 1.74)	1.02 (0.95, 1.10)	0.001*
HDL (mmol/L)	0.78 (±0.09)	1.09 (±0.07)	0.019*
LDL (mmol/L)	1.01 (0.57, 1.82)	2.57 (1.87, 3.46)	<0.001*
TC (mmol/L)	2.49 (1.69, 3.17)	4.35 (3.43, 4.98)	<0.001*
TG (mmol/L)	1.01 (0.78, 1.40)	0.98 (0.66, 1.23)	0.529

Notes: *P<0.05. Baseline laboratory parameters were from blood samples obtained within 6 h of emergency department presentation or admission.
Abbreviations: WBC, white blood cell count; NE%, percent neutrophils; HGB, hemoglobin; PLT, platelets; PCT, procalcitonin; CRP, C-reactive protein; CK, creatine kinase; LDH, lactate dehydrogenase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBil, total bilirubin; TP, total protein; Alb, albumin; Na, sodium; Glu, glucose; Cr, creatinine; PT, prothrombin time; INR, international normalized ratio; HDL, high density lipoprotein; LDL, low density lipoprotein; TC, total cholesterol; TG, triglycerides.

[CK], lactate dehydrogenase [LDH]), coagulation (platelets [PLT], prothrombin time [PT], international normalized ratio [INR]), liver function (aspartate aminotransferase [AST], total bilirubin [Tbil]), and renal function (serum creatinine [Cr]) were worse in the confirmed cases (all $P < 0.05$). The lipid profile (high-density lipoprotein [HDL], low-density lipoprotein [LDL], total cholesterol [TC]) and nutritional markers (total protein [TP], albumin [Alb]) were also lower in the confirmed cases (all $P < 0.05$). These results indicate the confirmed cases had a more severe disease state.

Patient Outcomes

We performed pathogen cultures for all 48 patients and mNGS for 10 patients (Table 3). In the 25 confirmed cases, 15 patients were positive by culture only, 8 were positive by mNGS only, and 2 were positive by both methods. In the

Table 3 Outcomes of Patients with Confirmed and Suspected *Vibrio vulnificus* Infection

Variable	Confirmed Infection (n=25)	Suspected Infection (n=23)	P value
Positive culture results	17/25 (68%)	0/23 (0%)	<0.001*
Positive mNGS results	10/10 (100%)	0/0 (0%)	Not applicable
MODS	9 (36.0%)	0 (0.0%)	0.005*
Surgical therapy	15 (60.0%)	7 (30.4%)	0.040*
In-hospital mortality	8 (32.0%)	0 (0.0%)	0.010*
Cost of hospital stay (Yuan)	63,158.00 (21606.00, 120780.00)	10,465.00 (5974.00, 29266.00)	<0.001*
Length of hospital stay (days)	15.00 (5.00, 26.50)	9.00 (6.00, 21.00)	0.542

Notes *P<0.05.

suspected cases, all 23 patients had negative culture results and none of the patients received testing by mNGS. All 48 patients received standard antibiotic therapy, which consisted of piperacillin-tazobactam, imipenem, or a third-generation cephalosporin alone or combined with a fluoroquinolone.

The confirmed cases had significantly higher rates of in-hospital mortality (32.0% vs 0%, P = 0.01), multiple organ dysfunction syndrome (MODS, 36.0% vs 0%, P = 0.005), and surgical intervention (60.0% vs 30.4%, P = 0.04), and a greater economic burden (63,158 vs 10,465 yuan, $P < 0.001$).

Discussion

Patients with *V. vulnificus* infection present with fever and with localized limb erythema, swelling, and pain. Many clinicians are unfamiliar with this disease because of its relative rarity, and this can lead to delayed diagnosis. Early identification of skin and soft tissue involvement is essential for timely intervention and surgical debridement.[8] In our study, each patient with suspected *V. vulnificus* infection had an epidemiological history and signs of limb inflammation that suggested infection by this pathogen. The suspected and confirmed groups had comparable age, gender, and underlying diseases, but the confirmed group had more severe soft tissue infection and a greater involvement of multiple sites.

Previous reports compared patients with NSTI caused by *V. vulnificus* and other pathogens (eg, *Staphylococcus aureus* or *Aeromonas species*).[9,10] Another matched-pair cohort study demonstrated that Vv-NSTI was associated with greater in-hospital mortality,[11] consistent with our findings. Our group with confirmed infection had more pathological laboratory parameters and worse clinical outcomes. Thus, in the absence of etiological confirmation, a diagnostic strategy that considers epidemiological exposure with clinical and laboratory findings may be a reliable adjunctive tool for identifying patients at high risk of *V. vulnificus* infection. Specific laboratory parameters, particularly those indicative of tissue injury, abnormal coagulation, liver dysfunction, renal dysfunction, dyslipidemia, and poor nutritional status, might be most useful for early risk stratification in clinical practice.

In addition to *V. vulnificus*, various other bacterial species (eg, *Aeromonas spp., Shewanella spp., Mycobacterium marinum*, and *Streptococcus suis*) can cause superficial soft tissue and invasive systemic infections following marine-related wounds or seawater exposure.[12–14] A study of soft tissue infections from fish spike wounds found that normal commensal bacteria (eg, methicillin-resistant *Staphylococcus aureus, Enterobacter cloacae, Clostridium spp.)* are more commonly isolated than marine pathogens.[15] These studies demonstrate the microbiological diversity and complexity of post-exposure infections. In the Chaoshan region, *V. vulnificus* infection is an uncommon seawater-related disease, so clinicians must consider this species along with a broad spectrum of other potential pathogens.[16] Failure to recognize and treat *V. vulnificus* infection in a timely manner can lead to severe morbidity or death.[2] Given the considerable heterogeneity and risk of misclassification among "suspected" cases and our lack of adjustment for confounders, such as comorbidities and timing of treatment, caution is needed when attributing infections to *V. vulnificus* without microbiological confirmation. If possible, future studies should incorporate microbiological confirmation, clinical phenotyping, and multivariable adjustments.

All patients with confirmed or suspected *V. vulnificus* infection were admitted from March 2014 to November 2025, but 14 of the confirmed cases occurred in 2024 or 2025, and 8 were identified by mNGS only. mNGS became available at our institution in 2017, so this may account for the greater number of cases during more recent years.[7,17] Due to the limitations of identifying *V. vulnificus* and other pathogens by culture—suboptimal timing of sample collection, prior use of antibiotics, and suboptimal culture conditions—there is a high probability of false negatives. Consequently, some suspected but undiagnosed cases in this study could be attributed to *V. vulnificus*. Future multicenter prospective cohort studies should better define the actual pathogens in a "suspected group" by combining molecular techniques (such as PCR and mNGS) with rigorous clinical assessment. Furthermore, combating neglected zoonotic diseases, such as *V. vulnificus* infection, also necessitates a broader integrated "One Health" approach.[18] As with other zoonoses, this approach promotes coordinated, multisectoral strategies that consider human, animal, and environmental health and includes improved surveillance, data sharing between public health and veterinary sectors, and preventive measures.

Conclusions

In conclusion, this study provides preliminary evidence for the early identification and risk stratification of patients with *V. vulnificus* infection. Our findings demonstrate that early clinical features (severe soft tissue involvement, multiple affected sites) and specific laboratory markers (particularly those indicative of tissue injury, coagulation dysfunction, impaired liver and renal function, dyslipidemia, and poor nutritional status) reliably distinguished confirmed cases from suspected cases. However, this was a single-center study with a relatively small sample size, and statistical matching of the confirmed and suspected groups was not possible. Our results suggest that further large studies are warranted for confirmation. Specifically, future multicenter cohorts using standardized molecular diagnostics are necessary to validate the markers identified in this study and to more fully characterize the heterogeneity of patients with clinically suspected *V. vulnificus* infection. In addition, given the local custom of eating raw marinated seafood in Chaoshan, it is necessary to strengthen public awareness and education regarding *V. vulnificus* infection.

Data Sharing Statement

The datasets generated and analyzed in the present study are available from the corresponding author, Tao Li, upon reasonable request.

Ethics Approval and Informed Consent

This study was approved by the Ethics Committee of the First Affiliated Hospital of Shantou University Medical College (Approval No. B-2026-052) and adhered to the principles outlined in the Declaration of Helsinki. Written informed consent was waived due to the retrospective nature of the study. Patient data were anonymized and kept confidential in accordance with ethical guidelines.

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Author Contributions

Each author made a significant contribution to this study that consisted of study conception, study design, study execution, acquisition of data, analysis and interpretation of data, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests in this work.

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