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The Burden of *Vibrio* sp. Infections – A Scoping Review

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Abstract: *Vibrios* are a group of Gram-negative bacteria ubiquitous in our surrounding environments and responsible for various clinically significant human infections. The three species responsible for human illness are *Vibrio cholerae*, *Vibrio parahaemolyticus*, and

Vibrio vulnificus. *V. cholerae* causes cholera which may result in severe dehydration and death without timely treatment, *V. parahaemolyticus* infection causes gastroenteritis while *V. vulnificus* infections typically manifest as wound or soft tissue infections with poor prognosis, including amputation or death. Available data on the epidemiology and clinical burden of *Vibrio* infections were compiled systematically following a literature review, and 149 relevant studies published between 2010 to 2022 were identified. Cholera represents the majority of *Vibrio* infections, affecting individuals of all ages and gender, while *V. parahaemolyticus* infections were found to affect mostly adult males. *V. vulnificus* infections were mostly reported in males over 50 years old with pre-existing co-morbidities. This review's findings may guide planning and implementing preventative measures in affected regions to prevent future *Vibrio* infections, disease transmission, and major outbreaks.

Keywords: *Vibrio* infections; cholera; *Vibrio cholerae*; *Vibrio parahaemolyticus*; *Vibrio vulnificus*; pathogens; SDG 3 Good health and well-being

1. Introduction

Vibrios are a group of Gram-negative bacteria that can potentially cause infections in various species - from aquatic animals to humans. These bacteria are transmitted to humans by environmental exposure or by consuming contaminated water or seafood [1]. The most common species within *Vibrio* sp., which are pathogenic to humans are *Vibrio cholerae*, *Vibrio parahaemolyticus*, and *Vibrio vulnificus*. These three *Vibrio* species represent those with the most significant impact on human health based on statistics from reports of outbreaks and infections caused by these bacteria [2-8]. These *Vibrios* are autochthonous to aquatic environments, and the warming of the oceans due to climate change has significantly increased their populations and distribution worldwide [9]. As shown by Vezzulli et al., when there is an increase in sea surface temperatures, *Vibrio* concentrations in the waters increase, and subsequently, *Vibrio* infections outbreaks also increase globally [9].

Cholera is a deadly disease caused by *V. cholerae* with serogroup O1 and O139; it presents as an acute diarrheal infection that can lead to potentially fatal dehydration [10]. Symptoms of cholera include watery stool, nausea and vomiting, dehydration, abdominal pain, and leg cramps [2]. It is estimated that there are 1.3 to 4 million cases of cholera, with 21,000 to 143,000 deaths worldwide due to cholera annually [11]. The World Health Organization reported a surge in cholera cases globally since 2021 following years of decline; this increase can be attributed to poor health systems and climate change. In addition, when the COVID-19 pandemic hit in 2021, healthcare systems worldwide were strained dealing with the novel coronavirus, resulting in a lack of resources and medical personnel to care for other disease outbreaks such as cholera [12].

V. cholerae possesses several features which optimize its success as a pathogen – it utilizes biofilms for survival in the environment and provides protection against host gastric acid barriers during infection. This organism is also adapted to maximize its chances of colonizing the gut. During the early stages of infection, where *V. cholerae* cell density is low, virulence gene expression is active for virulence factors such as cholera toxin to cause diarrhea and toxin coregulated pilus for colonization in the gut. Still, as *V. cholerae* begins to proliferate, diarrhea and environmental changes in the gut lead to the clearance of competitor microbes, disrupting the host gut microbiome. The profuse watery diarrhoea at this stage can lead to lethal dehydration. As cell density of *V. cholerae* and quorum sensing molecules increase during late infection, the bacteria detach from the intestinal mucosa, entering the luminal contents to be excreted in the stool and disseminated into the environment, causing further spread of cholera [13]. Rehydration therapy and hydration maintenance are the primary treatment for cholera patients. Antibiotics are recommended for severely ill patients or vulnerable groups such as pregnant patients; antibiotic therapy will be given based on the local antimicrobial susceptibility profile of the pathogen [14]. Cholera vaccines have also been made available, and they are administered via the oral route. The vaccination is recommended for individuals traveling or residing in areas where local transmission of cholera occurs and during cholera outbreaks [15].

Vibriosis is commonly caused by *V. parahaemolyticus*, and *V. vulnificus*, and can manifest as gastroenteritis or wound and soft tissue infections where necrotizing fasciitis and sepsis are widely reported [1, 16-19]. In the United States, statistics from the Centers for Disease Control and Prevention report 80,000 illnesses and 10 deaths caused by vibriosis annually, with the highest incidence of infection reported during the warmer months from May to October [20]. *V. parahaemolyticus* is often identified as the etiological agent in gastroenteritis outbreaks [17, 21, 22]. Typical symptoms are watery diarrhea, abdominal cramps, nausea and vomiting, fever, and headache. During infection, V. parahaemolyticus utilizes Multivalent Adhesion Molecule 7 to adhere to host cells, leading to up-regulation of other virulence factors. This is followed by upregulation of thermostable direct hemolysin (*tdh*) and TDH-related hemolysin (*trh*) gene expression resulting in hemolysis of red blood cells, formation of pores in the cell membrane as well as alterations in ion flux thus causing gastroenteritis [23]. Gastroenteritis caused by *V. parahaemolyticus* is often self-limiting and resolves within 72 days from onset of symptoms. Medical intervention in the form of antimicrobial treatment commences only when the infection does not resolve or has progressed to systemic infection [14].

V. vulnificus infections include wound or soft tissue infections caused by wound exposure to contaminated water. Wound infections typically present with symptoms such as fever, tenderness, swelling, warmth, pain, and discharge in the affected areas [20]. In addition, ingesting seafood contaminated with *V. vulnificus* can also result in severe systemic infection. The commonly reported clinical characteristics of infection are fever, chills, nausea, hypotensive septic shock, and formation of secondary lesions on the patient's extremities [24]. This opportunistic pathogen can evade destruction by the host’s gastric acid through the upregulation of lysine decarboxylase and manganese superoxide dismutase. These processes ultimately result in acid neutralization and reduction of oxidative stress, thus enabling *V. vulnificus* to evade host defenses in the upper gastrointestinal tract. The bacteria can then penetrate the host intestinal wall and enter the bloodstream. *V. vulnificus* also expresses capsular polysaccharide (CPS) on its cell surface to evade the host immune response. In addition, the exotoxin, *Vibrio vulnificus* hemolysin A (*VvhA*) expressed by *V. vulnificus* causes iron release from hemoglobin, causing a hemolytic effect. *VvhA* also elicits cytotoxic effects on the host cells by causing cell death via pore formation in the cellular membrane. *Vibrio vulnificus* metalloprotease (*VvpeE*) also plays a role in causing tissue necrosis, particularly during systemic infections where edema and bullous lesions form [25]. Furthermore, lipopolysaccharide (LPS) of *V. vulnificus* that are released during cell lysis mediates endotoxic shock in severe disease which can result in anaphylactic shock and death [25, 26]. The rapid development of *V. vulnificus* infections requires prompt diagnosis and delivery of antibiotic therapy to prevent worsening of the infection that can lead to necrosis, resulting in amputation or fatality [14].

An additional challenge is the increased antibiotic resistance of these Vibrio species, which has decreased the efficacy of the current antimicrobial treatments [27-30]. Thus, exploring alternative treatments and preventative methods to manage *Vibrio* infections and disease outbreaks is crucial. In addition, as reports of *Vibrio* populations and spread continue to increase worldwide, an increase in infections or disease outbreaks due to these *Vibrio* species is expected in the foreseeable future. Thus, this review aims to study the clinical burden of infections caused by *V. cholerae, V. parahaemolyticus*, and *V. vulnificus* including the incidence of cases, mortality rates, symptoms, and risk factors. The insight provided by this study can serve as a guideline to implement more effective preventative measures and methods for disease or outbreak management based on the current trends of *Vibrio* infections.

2. Methods

This scoping review was done in accordance with the Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines [31]. The search was conducted across three databases: Ovid Medline, EMBASE, and PubMed by using the MeSH terms "*vibrio* OR vibriosis" AND "clinical outbreak OR population surveillance OR incidence OR burden OR epidemiology". The inclusion criteria for the search were original articles in English on *Vibrio* infections, including cholera and vibriosis, with no time or country restrictions. Since the *Vibrio* species with the most significant impact on human health are *V. cholerae, V. parahaemolyticus*, and *V. vulnificus*, publications reporting on infections or disease outbreaks pertaining to these species were included in this scoping review. Publications that report on the incidence of the relevant *Vibrio* infections or outbreaks, attack rates, mortality rates, and risk factors for the disease were included. For example, national surveillance reports, epidemiology studies, and case-control studies were included in reporting on the significance of certain risk factors on disease occurrences. Prevalence studies of *Vibrios* in animals, seafood, environment, and humans without clinical data were excluded. In addition, publications related to *Vibrio* infections that did not contain any inclusion criteria, such as studies on temporospatial effects on *Vibrio* infections, estimation or projection of *Vibrio* diseases, estimation of disease transmission, and *Vibrio* vaccine studies were excluded.

From the search, the publications identified for further assessment were downloaded and imported into Covidence, a primary screening and data extraction tool [32]. In Covidence, duplicates were removed, and the remaining were screened for relevance based on the titles and abstracts. The full-text of the studies that passed the screening process were then assessed for inclusion, and data from included studies were extracted. The search and data extraction were done by one author and cross-checked by another author.

3. Results

3.1. Study selection

A total of 3908 studies were identified from the search and imported into Covidence for duplicate removal and primary screening, with 1416 duplicates removed, leaving 2492 studies for screening based on the article titles and abstracts. A total of 1240 studies were found to be irrelevant, the full-text for the remaining 1252 studies was retrieved and assessed for eligibility for inclusion. A total of 1103 studies were excluded: prevalence studies in humans without clinical data (248), prevalence studies in animals or seafood (165), prevalence studies in the environment (114), studies with irrelevant content for the review (184), publications with wrong study designs (347), articles not in English (32), studies which did not specify Vibrio species (9), and articles with no full text (4) (Figure 1).

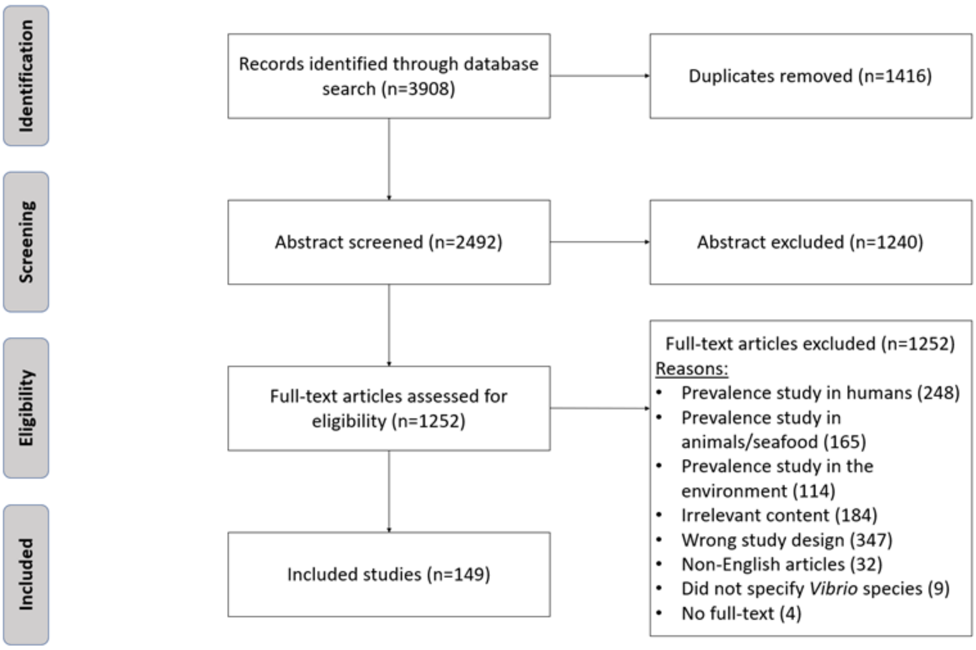

Figure 1. Study selection presented in PRISMA flow diagram.

The results included data from various countries and their respective references where published data were obtained. The countries are: Bangladesh [33-54], Cameroon [55-58], Canada [21], China [3, 5, 16, 19, 59-74], Democratic Republic of Congo [75-78], Ethiopia [79, 80], Ghana [81-85], Guinea [86], Guinea-Bissau [87], Haiti [88-94], India [6, 95-105], Iran [106-109], Iraq [110], Japan [4, 111-113], Kenya [114-119], Korea [17, 18, 120-122], Malawi [123], Mozambique [124, 125], Nepal [126], Niger

[127], Nigeria [128, 129], Pakistan [130], Papua New Guinea [131, 132], Philippines [133], Sierra Leone [134], Singapore [135], South Sudan [136], Sweden [137], Tanzania [138], Thailand [139], Togo [140], Uganda [141-152], United States of America (USA) [7, 153-161], Vietnam [162, 163], Yemen [164-166]. Additional data were obtained from two studies that published data from countries within Africa [2, 167]. The data collected from the included studies were published from 2010-2022. Among the studies included were epidemiological investigation and surveillance reports (100), case-control studies (28), cross-sectional studies (7), prospective studies (3), a prospective cohort study, a randomized controlled trial, retrospective case-control studies (3), a retrospective cohort study, a retrospective cross-sectional study, and retrospective studies (6) were also included.

3.2. Incidence of Vibrio infections

3.2.1 Cholera

Of all the studies included in this review, 101/149 (67.8%) reported the incidence and deaths of *V. cholerae* infections (Table 1). Cholera was mainly reported in Africa, Asia, North America, and Oceania. The Democratic Republic of Congo reported the highest number of cholera cases, with one major study reporting recurrent outbreaks from 2008 to 2017, recording 270,852 cholera cases within that period [78]. Two studies investigating the incidence of cholera in various African countries reported a total of 251,210 cases; 47% (8/17) of the countries included in this review had two or more studies reporting the incidence of cholera, with the highest reporting rates in Uganda, followed by Kenya. In addition, 82.4% (14/17) of the included studies from Africa reported deaths due to cholera. The number of reported deaths is directly proportionate to the number of total reported cases, i.e., the higher the number of total reported cases, the higher the number of total deaths.

In Asia, the highest number of studies on the incidence of cholera cases came from Bangladesh, with 19 studies, followed by India, with 12 studies. In Yemen, a significant research analyzing surveillance data from 2016-2018 related to the cholera epidemic in Yemen reported over 1.1 million cholera cases [166]. Out of the 12 countries which reported cholera cases in Asia, only 50% (6/12) of the studies reported cholera deaths, indicating that fatality rates due to cholera is lower in Asia when compared to Africa. Data from North America came from three countries: the Dominican Republic, Haiti, and the United States. Haiti reported the highest number of cholera cases and deaths, with six studies reporting 1 089 923 cases and 14 112 deaths from 2013 to 2019. In Oceania, two studies from Papua New Guinea reported 61 cholera cases with no deaths recorded.

Table 1. Reports of cholera and deaths caused by cholera by country.

Region/Country	Number of studies	Total reported Cases	Total reported Deaths
Africa			
Cameroon	3 [55, 57, 167]	27946	657
Democratic Republic of the Congo	3 [75, 76, 78]	290729	5666
Ethiopia	2 [79, 80]	4329	48
Ghana	5 [81-85]	3002	4
Guinea	1 [86]	2712	N/A
Guinea-Bissau	1 [87]	14222	225
Kenya	6 [114-119]	80144	2917
Malawi	1 [123]	1171	21
Mozambique	2 [124, 125]	27294	220
Niger	1 [127]	16328	578
Nigeria	2 [128, 129]	1649	54
Sierra-Leone	1 [134]	49	N/A
South Sudan	1 [136]	1451	44
Tanzania	1 [138]	11921	N/A
Togo	1 [140]	12676	554
Uganda	11 [141-151]	30297	674
Asia			
Bangladesh	19 [33, 34, 36-48, 51-54]	24475	13
China	1 [74]	46	N/A
India	12 [6, 95-105]	41374	34
Iran	3 [106, 107, 109]	2022	N/A
Iraq	1 [110]	136	3
Korea	1 [121]	3	N/A
Nepal	1 [126]	111	2
Pakistan	1 [130]	83	N/A
Philippines	1 [133]	55	2
Singapore	1 [135]	210	N/A
Vietnam	2 [162, 163]	67	N/A
Yemen	3 [164-166]	1118929	2461
North America			
Dominican Republic	1 [77]	42	N/A
Haiti	6 [88, 90-94]	1082923	14112
United Sates	2 [153, 156]	161	N/A
Oceania			
Papua New Guinea	2 [131, 132]	61	N/A

Data from the included studies indicate no significant difference in the occurrence of cholera between males and females. The incidence of cholera was relatively equally distributed among both genders. The median age for cholera infections ranged between 15 to 44 years. Cholera was most often reported in young adults, followed by adults and young children. Results from this review show that cholera is an important disease in Africa, as many cases and deaths have been reported in this region. Countries in Africa which only have one study reporting on cholera have also reported significantly higher number of cholera cases [87, 123, 127, 140] and deaths than countries in other regions with only one study reporting on cholera [74, 110, 135].

3.2.2 Vibriosis

Data on vibriosis represents a smaller fraction of the included studies, with 25/149 (16.8%) reporting on the incidence of *V. parahaemolyticus* infections (Table 2), and 18/149 (12%) reporting on the incidence and deaths of *V. vulnificus* infections (Table 3). *V. parahaemolyticus* infections were most commonly reported in Asia, with the majority (63.2%, 12/19) of studies from China. Countries in East Asia had the highest number of *V. parahaemolyticus* infections, followed by South Asia and Southeast Asia. However, the United States had five studies presenting 6169 cases of *V. parahaemolyticus* infections in North America. *V. parahaemolyticus* infections are typically non-fatal, thus, zero deaths have been reported. The included studies show that *V. parahaemolyticus* infections occurred more frequently in males than females, and most of these infections were reported in adults. Interestingly, one study showed that the prevalence of *V. parahaemolyticus* infections was higher in males when the age group was less than 15. Still, the prevalence of *V. parahaemolyticus* infections was higher in middle-aged and older women [111].

V. vulnificus infections are most commonly reported in Asia, specifically in East Asia, with the majority (75%, 9/12) of reports coming from China. Despite high numbers of *V. vulnificus* infections in China, only 11 deaths were reported. In North America, six studies on *V. vulnificus* were from the United States, reporting 3400 cases and 76 deaths. Data from the included studies show that males make up most of *V. vulnificus* infections, and the infections typically occur in older adults over 50 years. The severity of *V. vulnificus* infections is apparent as there are fewer reported cases than *V. parahaemolyticus* infections. Still, the reported deaths for *V. vulnificus* infections are significantly higher throughout affected regions.

Table 2. Incidences of *V. parahaemolyticus* infections by country.

Region/Country	Number of studies	Total reported cases
Asia		
China	12 [3, 5, 16, 60-64, 66, 67, 70, 74]	16501
India	1 [104]	137
Japan	2 [111, 112]	1223
Korea	3 [17, 120, 122]	1014
Thailand	1 [139]	32
North America		
Canada	1 [21]	82
United States	5 [7, 153, 159-161]	6169

Table 3. Incidences of *V. vulnificus* infections and deaths due to *V. vulnificus* infections by country.

Region/Country	Number of studies	Total reported cases	Total reported deaths
Asia			
China	9 [19, 59, 65, 68-70, 72-74]	530	11
Japan	2 [4, 113]	49	7
Korea	1 [18]	5	N/A
North America			
United States	6 [7, 153, 157, 159-161]	3400	76

*N/A: Data is unavailable.

3.3 Risk factors

Among the included studies in this review, 55/149 reported *Vibrio* infections' risk factors (Table 4). The risk factors identified for cholera among the studies were the source of drinking water, source of water for domestic activities, sanitation or hygiene practices, age, education level, eating out, exposure to cholera patients, household income, consumption of raw food, residing in slums, consumption of food contaminated with *V. cholerae*, and accessibility to healthcare. Risk factors associated with *V. parahaemolyticus* were consuming raw or undercooked seafood, shellfish, and eating outside the home. As for *V. vulnificus* infections, the identified risk factors are underlying co-morbidities, male gender, consumption of raw or undercooked seafood, age, exposure to contaminated seawaters, extensive skin lesions, and low platelet count. It is also vital for local governments to strengthen food safety measures by targeting food handlers, vendors, and eating places. Also, education on this disease should be given to all food handlers and the community.

Table 1. Risk factors for *Vibrio* infections were identified from all studies.

Vibrio **species/Risk factor**	**Number of times reported**
Vibrio cholerae	
Source of drinking water	22
Source of water for domestic activities	15
Sanitation/Hygiene practices	15
Age	12
Education	9
Eating out	8
Exposure to person with cholera	7
Household income	4
Consuming raw food	3
Residence in slum	1
Consumption of contaminated food	1
Vibrio parahaemolyticus	
Consumption of raw seafood	2
Shellfish consumption	2
Eating out	1
Vibrio vulnificus	
Underlying chronic disease	5
Male	2
Consumption of raw or undercooked seafood	2
Age	2
Exposure to contaminated seawater	1

4. Discussion

Vibrio infections are without doubt a global public health concern, causing significant numbers of diseases and deaths over recent years. Data from this review shows that *V. cholera* remains the most significant *Vibrio* infection based on the incidence of cholera cases, followed by *V. parahaemolyticus*, and *V. vulnificus*.

In terms of risk factor analysis which may assist with targeted preventive methods for cholera, many studies which report high incidences of cholera also reported that there was a lack of access to clean water sources for drinking or domestic activities and poor sanitation and hygiene practices were also identified as the contributing factors for disease outbreaks [51, 103, 116, 129, 133, 142, 149]. The primary water sources of the residents who reported cholera infections were rivers or lakes. The waters were often contaminated by fecal matter due to open defecation or being near the latrines of the residents [51, 83, 147, 151]. The bacterial flora from fecal matter can potentially alter the bacterial flora in the nutrient-rich environments of rivers and lakes, resulting in plankton blooms often associated with cholera outbreaks [168]. Water retrieved from wells or public taps for drinking or domestic use was contaminated with *V. cholerae* in several instances [34, 134, 144]. Thus, it is essential to educate the residents in the local area on the importance of proper sanitation of latrines and to refrain from open defecation in rivers or lakes to prevent the spread of *V. cholerae*. It was found that cholera affects all age groups, with the highest occurrence in young adults, followed by adults and young children. The lack of information and knowledge on the disease and its risk factors among affected populations has also contributed to the prevalence of cholera cases [41, 42, 56]. For instance, exposure or contact with persons infected with cholera increases the chances of disease spreading; hence, it is important to practice hand washing with soap and water when caring for a cholera patient. It is also essential to sanitize the toilets used by cholera patients to prevent the rampant spread of the disease [15]. Therefore, educating individuals of all ages and demographics on cholera and the importance of practicing good hygiene, such as hand washing with soap and water, is crucial in preventing infections. Consumption of contaminated foods and eating out are also risk factors for cholera. Thus, local authorities need to implement better food safety measures to monitor the cleanliness and safety of the food sold by restaurants and street vendors to prevent outbreaks.

For *V. parahaemolyticus* infections, it has been well-documented that consuming raw or undercooked seafood is the primary infection source. This can be seen in data from Asia, where *V. parahaemolyticus* infections are most common. Eating seafood raw in several Asian cuisines contributes to food-poisoning cases caused by *V. parahaemolyticus* [169]. The consumption of shellfish is also commonly reported to be the source of *V. parahaemolyticus* infections; which is perhaps expected given that bioaccumulation of *V. parahaemolyticus* often occurs in shellfish due to filter feeding. One study found that oysters may contain up to 100-fold higher concentration of *V. parahaemolyticus* than their surrounding environment due to filter feeding, which is further exacerbated during the warmer months in summer [170]. In order to prevent *V. parahaemolyticus* infections, it is vital to avoid consuming raw or undercooked seafood and to ensure that the seafood consumed is cooked thoroughly before consumption. Moreover, when storing raw seafood for future use, keeping them separate from other fresh produce or food is vital to prevent cross-contamination [17].

Although *V. vulnificus* infections have the lowest incidence among the three, the severity and prognosis of the infection still raise concerns [14, 24, 25]. Infections of *V. vulnificus* often occur when the individual is exposed to the pathogen via seafood consumption or when a wound is exposed to waters contaminated with the bacteria [18, 19, 69]. *V. vulnificus* infections can manifest as gastroenteritis which is usually self-limiting, and by ensuring the seafood is cooked thoroughly before consumption, the risks of *V. vulnificus* gastroenteritis can be reduced. However, wound infections involving *V. vulnificus* are severe and can potentially cause death. This review described data that shows males over the age of 50 contribute to the majority of *V. vulnificus* infections, and a number of those infected succumb to the disease [4, 59, 113]. Pre-existing medical conditions are a significant risk factor for *V. vulnificus* infections, especially chronic illnesses, including hepatic dysfunctions, renal disorders, diabetes, heart diseases, and hematological disorders [4, 19, 59, 65, 113, 157]. The majority of *V. vulnificus* infections affect wounds and cause soft-tissue infections such as cellulitis and necrotizing fasciitis [25, 69, 72, 157]. These infections typically require hospitalization, debridement of the affected areas, and possibly even amputation of the limbs should the infection continue to spread [4, 69, 72, 73]. The poor prognosis of *V. vulnificus* infections renders it a critical *Vibrio* infection as it can result in severe health consequences such as amputation, which will negatively impact the quality of life and reduce life expectancy. To prevent exposure to *V. vulnificus* in the environment, persons handling raw seafood should wear protective clothing, such as gloves, to prevent injuries to minimize exposure to the opportunistic pathogen. Persons with open wounds should avoid exposing the wounds or broken skin to open waters inhabited by *V. vulnificus*. Furthermore, protective footwear should be worn when participating in water-related recreational activities to prevent *V. vulnificus* from entering any open wounds [25, 171].

It is imperative to prevent these *Vibrio* infections to minimize fatalities and to improve global public health. As these *Vibrio* species are ubiquitous in our surrounding aquatic environments, pathogenic strains of the bacteria can easily be transmitted to humans, making primary prevention very challenging. An alternative strategy to improve outcomes is through early detection of these *Vibrio* species in the early stages of infection using rapid detection methods to identify the specific causative agent, allowing the initiation of appropriate treatment promptly. For example, lateral flow immunoassays in dipsticks or immunochromatographic strips can detect the presence of *V. cholerae* from clinical samples in a few minutes. A positive test result can then prompt early treatment of infections and prevent significant outbreaks in the area. This can be very useful in low-resource settings where access to laboratories and expensive equipment is limited [172, 173]. Cholera vaccines have also been developed and distributed to countries frequently plagued by cholera outbreaks. The vaccines have effectively protected against cholera and prevented the development of severe disease in individuals who have received the immunization [174-176].

Vibrio infections may require antimicrobial treatment, but the rapid emergence of antibiotic resistance in these bacteria dramatically reduces the efficacy of antibiotics currently available [27, 177-181]. Therefore, alternative antibiotics such as probiotics should be explored to manage *Vibrio* infections effectively. The use of antibiotics to prevent vibriosis in aquaculture, which produces seafood for human consumption, is a significant contributor to antibiotic resistance in these *Vibrio* species [27, 182]. Probiotics are known for modulating host gastrointestinal microflora by enhancing beneficial strains' growth and suppressing pathogenic bacteria such as *Vibrio* species. Thus, probiotics are an excellent alternative to control vibriosis and maintain a safe bacterial load in these marine animals to reduce transmission of pathogenic bacteria to humans [183, 184]. *Streptomyces* sp., a filamentous, Gram-positive bacteria, has been the focal point of many researchers in developing a probiotic to treat *Vibrio* infections in the aquaculture industry [180, 185-187]. The bacteria produce a variety of secondary metabolites, which have been useful in drug discovery [188-194]. These compounds possess many properties, such as antibacterial, antifungal, antiviral, antioxidant, and cytotoxic properties [195, 196]. For this context, their anti-*Vibrio* properties can be beneficial in developing probiotics to fight against *Vibrio* infections [197-199]. Studies on the effects of *Streptomyces* sp., on animal models have produced positive results, as it was demonstrated that the administration of *Streptomyces* sp. enhanced immunity and provided protective effects from *Vibrio* infections [200-202]. As positive data from animal models continue to increase, clinical trials on the impact of *Streptomyces* sp. in humans can be done in the near future, providing an optimistic outlook for public health. The potential application of *Streptomyces* sp. as a probiotic in aquatic life and humans can prevent *Vibrio* infections and the further spread of antibiotic resistance in the environment. In addition, using probiotics in humans can help maintain a healthy gut microbiome [203]. The gut microbiome acts as a protective barrier to prevent colonization of pathogenic bacterium such as *Vibrio* sp. in the GIT to maintain balance in the gut microbiome [204-206]. Furthermore, when exposed to pathogens, the highly diverse gut microflora defends the host from infections via immunoregulatory responses [207]. Interestingly, research has shown an association between the human gut microbiome and various diseases other than gastrointestinal diseases, such as infectious diseases, metabolic disorders, and cognitive disorders [208-210]. Therefore, enhancing the gut microbiome via probiotics reduces the disease burden of *Vibrio* infections on the immune system and lowers the risk of developing medical conditions attributed to microbiome disruption.

5. Conclusions

This review of 149 studies demonstrated that *Vibrio* infections remain a persistent and significant public health threat globally. A broad spectrum of the population is at risk, with some variations between the key pathogenic species: for cholera, persons of all ages and gender can be infected, whereas in *V. parahaemolyticus* infections, mainly adult males are affected, and *V. vulnificus* infections primarily affected males over the age of 50 years old. The collected data can prompt continuous surveillance and monitoring within nations that are greatly affected by *Vibrio* infections. The data can also be used to plan, implement and strengthen preventative measures in the relevant regions to protect the local communities. For example, quality assessment of drinking water and water used for daily activities should be done diligently and periodically to ensure the waters are free from contamination. Local government authorities should also implement more stringent food safety measures to ensure the public's food source is safe to consume. In addition, a focus should also be put on providing education regarding the importance of maintaining good personal hygiene, sanitation of living spaces, risks of consuming raw or undercooked food, and the risk of exposing wounds to open waters. Empowering individuals with such knowledge may be the critical link to the primary prevention of *Vibrio* infections in vulnerable communities.

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