

## *Vibrio parahaemolyticus*: The Protagonist Causing Foodborne Diseases

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**Abstract :** Food contamination is a worrying condition faced by us today. We often discuss on food safety and how to control food contamination. Food products are easily tainted by bacteria at any level of food production to human consumption, subsequently developing gastroenteritis. The people from developed and developing countries are at high risk from harmful effects of unsafe food. Of all the foodborne pathogens, *Vibrio parahaemolyticus* has been accounted for many outbreaks globally and still at rise even with proper management methods. *V. parahaemolyticus* infection occurs as a result of improper food handling and preparation, ability of the bacterium to withstand human gut to launch virulence, antibiotic resistant bacterium, and failure of regulatory bodies to safe-guard food quality. This scenario poses a global health issue that warrants rapid control measures to ensure food safety from production to consumption by consumers. For that reason, this review aims to provide an overview of the epidemiology of *V. parahaemolyticus* as well as discuss the challenges faced to encounter this bacterium.

**Keywords:** Food safety; contamination; foodborne; *Vibrio parahaemolyticus*; epidemiology

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**Received:** 18<sup>th</sup> May 2019

**Accepted:** 30<sup>th</sup> June 2019

**Published Online:** 02<sup>nd</sup> July 2019

**Citation:** Letchumanan V, Loo KY, Law JWF, *et al.* *Vibrio parahaemolyticus*: The Protagonist Causing Foodborne Diseases. Prog Microbes Mol Biol 2019; 2(1): a0000029.

### INTRODUCTION

FOOD is an essential part of every individuals for survival. It provide us with all the energy and nutrients for our healthy and active life. However, many of us ponder on one matter – How safe is our food? The World Health Organization (WHO) claimed that food is unsafe as it contains harmful bacteria, viruses, parasites or chemical substance, causing various illness ranging from diarrhea to cancers. It is estimated that 1 in 10 people in the world fall ill after consumption of contaminated food and lead to 420,000 die each year<sup>[1,2,3]</sup>. Food products are likely to be contaminated at any stages from production, processing,

distribution, storage and preparation. These unsafe food poses a global health threat, increase hospitalization and healthcare cost, and constrains the national's economic development. Numerous studies revealed that marine and estuarine environments are the ecological niche of many bacteria. Undeniably, these bacteria are often encountered by consumers through seafood products, including *Salmonella* sp.<sup>[4-9]</sup>, *Vibrio* sp.<sup>[10,11,12,13,14]</sup>, *Listeria monocytogenes*<sup>[15,16]</sup>, and *Escherichia coli*, presented with foodborne outbreaks, pathogenicity, and clinical manifestations. Despite the good benefits of seafood, health hazards associated to seafood consumption cannot be ignored<sup>[17]</sup>.

*Vibrio* species are common foodborne pathogen group that's accounted for human gastroenteritis cases worldwide; the most human pathogenic species are *Vibrio cholerae*, *Vibrio parahaemolyticus* and *Vibrio vulnificus*<sup>[14]</sup>. This Gram-negative rod-shaped bacterium is a natural constituents of marine and estuarine environments, and often been associated with seafood<sup>[18]</sup>. The non-cholera *Vibrio* sp., *Vibrio parahaemolyticus*, causes vibriosis and readily isolated from seafood including shellfish, oysters, shrimps, cockles, and fish<sup>[11,12,19]</sup>. The outbreaks of *V. parahaemolyticus* are becoming increasingly common in developed and non-developed countries such as Asia region, United States, Europe, Australia, and other nations<sup>[10]</sup>. According to data published by Centers for Disease Control and Prevention (CDC) in Foodborne Diseases Active Surveillance Network (FoodNet), and Morbidity and Mortality Weekly Report (MMWR), *V. parahaemolyticus* has accounted for approximately 34,664 incidents of domestically developed foodborne infection cases and known as the leading bacterium unlike to other *Vibrio* sp. in the United States (US) in 2016<sup>[20,21]</sup>. The consumption of contaminated food, undercooked or raw seafood leads to *V. parahaemolyticus* gastroenteritis with manifestation of watery diarrhea, stomach pains, nausea, and fever<sup>[22]</sup>. In rare cases, infections of *V. parahaemolyticus* can cause septicemia – leading to an increase in number of fatality cases<sup>[23]</sup>. By taking into consideration of past reports and possibility of severe infections, this review aims to provide an overview of the epidemiology of *V. parahaemolyticus* as well as the rising challenges faced to curb this bacterium.

## HISTORY OF *Vibrio* and *Vibrio parahaemolyticus*

*Vibrio* genus was first described by an Italian physician, Filippo Pacini in 1854. He discovered the first *Vibrio* species, *Vibrio cholerae*, the causative agent of cholera while studying outbreaks of cholera disease in Florence<sup>[24]</sup>. Subsequently, this strain was renamed as *Vibrio cholerae*, which is now the type of species of the genus. He further pointed out that cholerae is contagious but his discovery on *Vibrio* was ignored by the scientific community around the world<sup>[24]</sup>. After nearly 30 years, Robert Koch successfully isolated *Vibrio* from pure culture in Calcutta, India. At that time *Vibrio* epidemic was very active in Calcutta, India. Koch's discovery had created an important social consequence and regarded as a public health triumph<sup>[25]</sup>. *Vibrio* genus consist of 142 species that are marine originated and its taxonomy is continuously been revised due to the discovery and inclusion of new species<sup>[26]</sup>. *Vibrio* sp. infects any living being including animals and humans<sup>[27]</sup>. It was reported that a few of the species from this genus have been identified and classified among the top 15 pathogens causing nearly 95% of the foodborne diseases, hospitalizations and even deaths in the United States<sup>[28]</sup>. Recently, the worldwide ocean warming and climate changes have caused emerges of *Vibrio* sp. including the foodborne pathogenic strains with several virulence factors in marine environments.

As a member of the Vibrionaceae family and *Vibrio* genus, *Vibrio parahaemolyticus* has been in limelight for the rising vibriosis and foodborne cases worldwide. *V.*

*parahaemolyticus* was first identified in 1951 by Tsunesaburi Fujino from Research Institute of Microbial Diseases (RIMD), Osaka University from an acute gastroenteritis outbreak. The outbreak occurred in a southern suburb of Osaka, Japan due to consumption of 'shirasu', a type of dried sardine which resulted in 20 deaths and 272 infected patients<sup>[29,30]</sup>. After several bacteriological testing and analysis, Fujino noticed that the strain exhibited hemolytic activity on blood agar and named the strain as *Pasteurella parahaemolytica*, assigning it to genus *Pasteurella*. The progression in taxonomy and various scientific discoveries led to the re-examination of *Pasteurella parahaemolytica* by Fujino. He reported that the genus of the isolate should be *Vibrio* instead of *Pasteurella*. In 1963, Sakazaki investigated Fujino's isolates and confirmed it was the same species belonging to *Vibrio* genus and propose to name the isolate as *Vibrio parahaemolyticus*<sup>[30]</sup>.

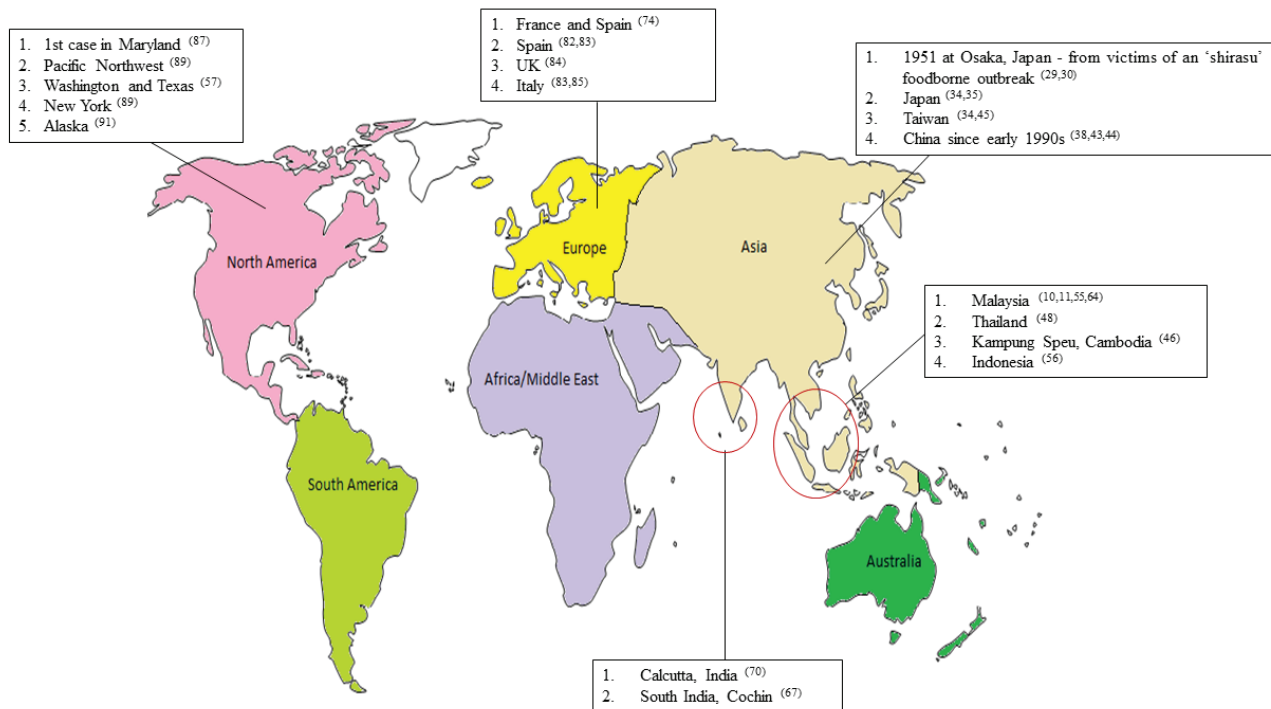
## EPIDEMIOLOGY OF *Vibrio parahaemolyticus*

*Vibrio parahaemolyticus* is largely present in the aquatic environments and often isolated from seafood<sup>[31]</sup>. Since its discovery in 1950, *V. parahaemolyticus* has caused many foodborne outbreaks around the world including in Japan<sup>[32-36]</sup>, in Taiwan<sup>[37]</sup>, in China since early 1990s<sup>[38]</sup>, Bangladesh<sup>[39]</sup>, Laos<sup>[40]</sup>, Hong Kong and Indonesia<sup>[40]</sup> (Figure 1). Despite the advances in hygiene and food processing, this foodborne pathogen still represents a significant threat to human health worldwide.

### Asia

*Vibrio parahaemolyticus* was initially identified as a seafood-associated disease in the Eastern Asia region. This bacterium was first isolated in 1951 from a foodborne outbreak in Osaka, Japan due to consumption of shirasu, which resulted in 272 infected patients and 20 deaths<sup>[29,30]</sup>. Since then, many *V. parahaemolyticus* gastrointestinal cases have been reported in around Japan are due to the habit of eating raw or undercooked seafood such as sushi, sashimi, shellfish, crabmeat, fish, squid and sea urchin<sup>[41,42]</sup>. There was an increasing trend of reported cases from 1993 (837 cases) to 1998 (12, 318 cases), nevertheless the figures drastically dropped to 14 cases in 1999 and 280 cases in 2009<sup>[42]</sup>. The decrease in number of *V. parahaemolyticus* foodborne cases from 1999-2000 is due to the implementation of regulatory actions to improve the hygiene conditions in all seafood production sites in Japan<sup>[35]</sup>. Even with appropriate regulatory measures, there are still many reported *V. parahaemolyticus* cases in Japan.

In the neighboring nation China, *V. parahaemolyticus* was identified as a major cause of foodborne disease since early 1990s. Seafood such as crustaceans was the vehicle for *V. parahaemolyticus* to transmit vibriosis infection in China<sup>[43]</sup>. From 1991-2001, a total of 5770 foodborne cases was reported, which 31% of them was caused by *V. parahaemolyticus*<sup>[44]</sup>. The number of outbreaks decline to 322 cases between 2003 and 2008<sup>[43]</sup>. Li and colleagues found that *V. parahaemolyticus* was the main cause of acute diarrhea during 2007-2012 in southern coastal region of China, with the most prevalent serotype O3:K6 followed by O4:K8 and O3:K29<sup>[37]</sup>. In Taiwan, many foodborne gastroenteritis outbreaks were identified to be caused by *V. parahaemolyticus*<sup>[32,37,45]</sup>.



**Figure 1:** Illustration of *V. parahaemolyticus* epidemiology around the world. The first identified case was in Osaka, Japan in 1951 and ever since then the occurrence has spread to whole of Asia region, Australia, Europe, and the United States (US).

In Southeast Asia regions – Laos, Thailand, Indonesia and Cambodia, *V. parahaemolyticus* was accounted for several foodborne outbreaks<sup>[46]</sup>. *V. parahaemolyticus* first outbreak occurred in Kampung Speu, Cambodia resulted in 49 cases of acute diarrhea<sup>[47]</sup>. In Thailand, the pandemic O3:K6 serotype strains was accountable for most of the foodborne cases between 2006 and 2010<sup>[48]</sup>. Thailand is known as the main producer and exporter of cultured shrimp to around the global. This industry is on alert due the occurrence of antimicrobial resistant *V. parahaemolyticus* isolated from white leg shrimp and black leg shrimp from inland ponds<sup>[49]</sup>.

In Malaysia, *V. parahaemolyticus* occurs naturally in the marine and coastal regions. It spreads in the tropical marine surroundings during all seasons and causes foodborne gastroenteritis<sup>[50]</sup>. In the early 1980s, a study revealed the detection of *V. parahaemolyticus* in Malaysian shrimp. It is of interest to note that 21 different serotypes were isolated from Malaysian shrimp, with type 01:K38 and 01:K32 were predominated<sup>[51]</sup>. In 2005, a study reported the isolation of *V. parahaemolyticus* from cockles (*Anadara granosa*) at a harvesting area at Tanjong Karang, Kuala Selangor. The analysis revealed virulent *V. parahaemolyticus* isolates having the thermostable direct hemolysin (*tdh*) and TDH-related hemolysin (*trh*) genes<sup>[52]</sup>. Virulent *V. parahaemolyticus* carrying *tdh* genes and *trh* genes was also identified from frozen shrimp in Malaysia, prompting a possible health risk for people consuming raw shrimp<sup>[53]</sup>. In 2011, a study reported high occurrence of *Vibrio* sp. (98.6%) and *V. parahaemolyticus* (24%) in freshwater fish collected from hypermarket. This outcome indicates a potential source of unsafe food to consumers in Malaysia<sup>[54]</sup>. In addition, recently there was report about European Union (EU) countries rejected frozen black tiger shrimp from Malaysia due to the presences of *V. parahaemolyticus* and this further affected the Malaysian economic<sup>[55]</sup>.

Paydar and colleagues reported prevalence of *V. para-*

*haemolyticus* in the seafood samples from retail and hypermarkets in Malaysia. Out of the 43/150 *V. parahaemolyticus* isolates detected, six isolates carried the *trh* genes and another two carried the *tdh* genes<sup>[55]</sup>. Recently, a comparative study was done to detect the contamination level of *V. parahaemolyticus* in seafood marketed in Thailand, Vietnam, Malaysia, and Indonesia. Interestingly, the study's results revealed that all the four countries had a similar levels of *V. parahaemolyticus* contamination in fish, shrimp, squid, crab, and shellfish. The study did not detect any virulent strains among the seafood samples from Malaysia<sup>[56]</sup>. The findings in agreement with other reports globally that mentioned virulent genes, the *tdh* and *trh* are very low number (1-7%) among environmental and seafood samples<sup>[57-61]</sup>.

The food safety levels in Malaysia further declined due to the prevalence of antibiotic resistant *V. parahaemolyticus* isolated from seafood<sup>[11,12,62]</sup>. In Terengganu, Malaysia, a study reported the detection of cefuroxime and ceftazidime-resistant *V. parahaemolyticus* isolates in shellfish samples<sup>[62]</sup>. In addition, ampicillin resistant profiles are often detected among seafood samples in Malaysia<sup>[11,50,63,64,65]</sup>. Elexson and colleagues reported in their study that all of the *V. parahaemolyticus* isolates from cultured seafood products were resistant to both penicillin and ampicillin<sup>[63]</sup>. In a recent study, high level of penicillin and ampicillin resistant isolates were obtained from short mackerels in Malaysia<sup>[66]</sup>. The ampicillin resistance seen may be due to misappropriation of the first-generation antibiotic for pathogen management in aquaculture, thus reducing the efficacy of ampicillin in the treatment of *Vibrio* infection<sup>[67]</sup>. Hence, it is indeed vital to address and manage the antimicrobial resistance issue.

In India, *V. parahaemolyticus* was detected and identified from both clinical and environmental samples. The first serotype O3:K6 *V. parahaemolyticus* was discov-

ered in an on-going surveillance in Calcutta, India<sup>[68-70]</sup>. Subsequently, the serotype O3:K6 *V. parahaemolyticus* has turned into a widespread around Asia. In a clinical study, 178 *V. parahaemolyticus* strains was isolated from 13,607 diarrheal patients admitted in Infectious Diseases Hospital, Kolkata since 2001 to 2012<sup>[71]</sup>. *V. parahaemolyticus* diarrheal cases were also detected from around the urban slums of Kolkata, India<sup>[72]</sup>. Reyhanath and colleagues have reported detection and isolation of antimicrobial resistant *V. parahaemolyticus* strains from a fishing land in South India<sup>[72]</sup>. In Cochin, a study reported the isolation of *Vibrio* sp. including pathogenic and antimicrobial resistant *V. parahaemolyticus* strains from seafood. Most of the isolates was seen resistant to ampicillin and multidrug resistance was prevalent among the isolates<sup>[73]</sup>. The prevalence of multidrug resistant *V. parahaemolyticus* isolates in environment and clinical setting is of public health concern, thus require continuous monitoring and management.

## Europe

In European countries, *V. parahaemolyticus* infections are seldom reported, unlike Asia and US countries where *V. parahaemolyticus* infections are commonly reported<sup>[74]</sup>. However, there were several sporadic outbreaks reported over the last 20 years in countries such as France and Spain<sup>[32,74]</sup>. *V. parahaemolyticus* was isolated from the Baltic Sea, the North Sea, the Mediterranean Sea<sup>[75]</sup>, and Black Sea<sup>[76]</sup>. In 1978, studies were conducted in coastal waters of Guadeloupe and isolated *V. parahaemolyticus* from 53/100 water samples that was investigated<sup>[77]</sup>. Over the years, many cases of *V. parahaemolyticus* gastroenteritis were detected and isolated in Spain, Greece, Britain, Turkey, Denmark, Yugoslavia, the Scandinavian areas, and Italy<sup>[78,79]</sup>.

In 1989, *V. parahaemolyticus* was accounted for 8 acute gastroenteritis cases linked with intake of fish and shellfish in Spain<sup>[80]</sup>. In 1997, a major outbreak of *V. parahaemolyticus* involving 44 patients had occurred in France and it was associated with the consumption of shrimps imported from Asia<sup>[81]</sup>. In 1999, the first large outbreak of *V. parahaemolyticus* occurred in Galicia, Spain. This outbreak involved 64 illnesses and it was associated with consumption of raw oysters<sup>[82]</sup>. A more recent outbreak of *V. parahaemolyticus* was reported in Spain in 2004, whereby it involved 80 illnesses among the guests who attended weddings in a restaurant. The investigation revealed that the outbreak was caused by consumption of boiled crab prepared under unsanitary conditions<sup>[83]</sup>. In 2004-2005, only 57 cases of *V. parahaemolyticus* infections was reported in United Kingdom and most of the infections were obtained through travel to endemic areas<sup>[84]</sup>. In addition, serotype O3:K6 *V. parahaemolyticus* strains were isolated from patients of outbreak in Spain and patients of gastrointestinal infection in Italy<sup>[83,85,86]</sup>.

## United States (US)

In 1971, *V. parahaemolyticus* was first identified as an etiological food borne pathogen in Maryland, US after three outbreaks of 425 gastroenteritis cases associated with consumption of improperly cooked crabs<sup>[87]</sup>. Ever since then, intermittent *V. parahaemolyticus* outbreaks have been reported throughout the US coastal regions due to the consumption of raw shellfish or uncooked seafood. In 1973

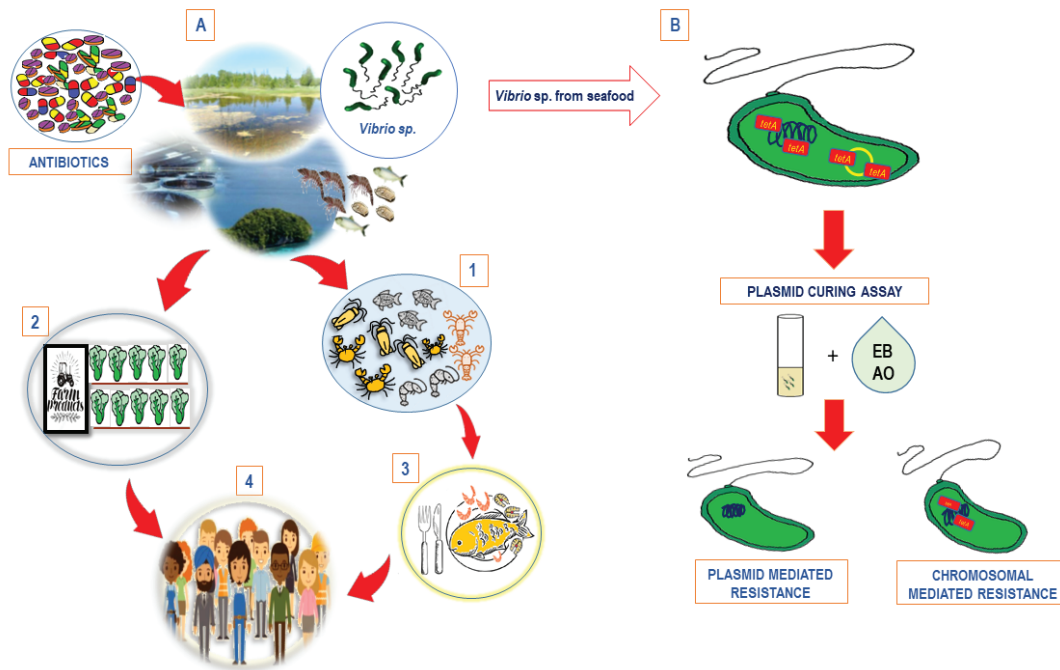
to 1998, a total of 40 outbreaks of *V. parahaemolyticus* infection was reported by the CDC<sup>[88]</sup>. Four out of 40 outbreaks involved over 700 cases of diseases linked with consumption of raw oyster in the Gulf Coast, Pacific Northwest, and Atlantic Northeast regions between the years 1997 to 1998. In 1997 summer, 209 (including one death) of *V. parahaemolyticus* infection cases was reported involving consumption of raw oyster in around the Pacific Northwest (Oregon, Washington, California and British Columbia of Canada)<sup>[89]</sup>. In 1998, there were two separate reports on *V. parahaemolyticus* infection cases in Washington (43 cases) and Texas (416 cases)<sup>[90]</sup>. In between July to September 1998, there was eight *V. parahaemolyticus* infection cases reported in around Connecticut, New Jersey, and New York as a result of eating oysters and clams harvested from Long Island Sound of New York<sup>[89]</sup>.

In summer 2004, 14 passengers on a cruise ship in Alaska experienced gastroenteritis symptoms after ingestion raw oysters produced in Alaska<sup>[91]</sup>. The O6:K18 isolates from the Alaska outbreak were in differentiated by PFGE from those isolated in the sporadic cases from Pacific Coast states over the previous decade. From July to October of 2004, 96 ecological samples were collected from 17 Alaska oyster farms, and 32% of the samples were *V. parahaemolyticus* with the prevalent serotypes of O1:K9, O4:K63, and O6:K18<sup>[92]</sup>. In summer 2006, there was an outbreak involving 177 gastroenteritis cases resulted from ingestion of oysters contaminated with *V. parahaemolyticus* in Washington and British Columbia<sup>[93]</sup>. In summary, the prevalence of *V. parahaemolyticus* in both clinical and environmental samples potentially rises a serious food safety concern in the US.

## MAJOR CHALLENGERS OF *Vibrio parahaemolyticus*

The regulatory bodies and healthcare sector is continuously challenged by increasing numbers of antibiotic resistant *V. parahaemolyticus* strains in the environments. The occurrence of multidrug-resistant (MDR) towards clinically used antibiotics is a major health issue and deprives the global drug discovery programs<sup>[94]</sup>. Each year, more and more pathogenic *Vibrio* sp. have been reported to develop resistance towards most of the clinically used antibiotics (Figure 2). Drug resistance is an alarming issue worldwide and is spreading rapidly due to overuse, self-medication or the non-therapeutic use of antimicrobials<sup>[95]</sup>. The countries around the world have reported the detection of MDR *V. parahaemolyticus* in seafood, prompting the need for continuous surveillance and monitoring in the aquaculture industry<sup>[96-99]</sup>.

It is reported that over 90% of the marine originated bacteria isolates display resistance towards more than one type of antibiotic. In addition, 20% of them exhibited resistance towards five types of antibiotics<sup>[100]</sup>. The marine environments are more prone to antibiotics and antibiotic resistant genes due to the misuse of antibiotic agents in hospital or veterinary treatment, aquaculture and agriculture locations, and their successive release into wastewater treatment plant<sup>[101]</sup>. The elevated levels of antibiotic agents in the aquatic could play a role as a



**Figure 2:** Illustration of *Vibrio parahaemolyticus* transmission to humans and plasmid curing assay. (A) *Vibrio parahaemolyticus* is found in the marine, estuarine, and aquaculture settings. Antibiotics are incorporated in feed and water to control *Vibrio parahaemolyticus* infections on aquatic animals such as shrimp, cockles, fish, and shellfish. This bacterium eventually develops antibiotic resistance and carries the resistance genes in them. 1) *Vibrio parahaemolyticus* uses seafood as a vehicle to transmit the carries the antibiotic resistance and resistant genes. 2) The antibiotics resides in water and transmitted to agriculture area thru irrigation. 3) Undercooked and raw seafood potentially carry pathogenic *Vibrio parahaemolyticus* and resistant strains. 4) Consumers will eat contaminated seafood and vegetable, thus exposing themselves to gastroenteritis. (B) *Vibrio parahaemolyticus* is isolated from seafood. Antibiotic susceptibility test is performed to determine the resistance profile. The antibiotic resistance could be either in the plasmid or chromosomal of the bacterium. The strain would be subject to plasmid curing assay to determine the antibiotic resistance mediation. Intercalating agents such as ethidium bromide or acridine orange can be used to cure the bacteria plasmid. After the assay, antibiotic resistance mediation could be determine either it is plasmidial or chromosomal mediated.

selective pressure contributing to the rise and distribution of resistant and pathogenic bacteria within the same aquatic environment<sup>[102]</sup>. Additionally, bacteria in the environments are able to produce antimicrobial compounds, thus making them capable of acquiring or expressing antimicrobial resistant genes to protect themselves from the toxicity of antibiotics present in the environments<sup>[103]</sup>. Therefore, the presences of aquatic bacterium may function as reservoirs for antibiotic resistance genes and plays a crucial role in the spread of antibiotic resistance in aquatic environments<sup>[101]</sup>.

*Vibrio parahaemolyticus* – both as a pathogenic strain carrying virulence genes (direct hemolysin (*tdh*) and/or *tdh*-related hemolysin (*trh*) and as a MDR strain, is difficult to be controlled. Recently, there is a discovery on the ability of *V. parahaemolyticus* to withstand the bile salts, then utilize bile as signaling cue to launch its virulence<sup>[104]</sup>. The human bile in gastrointestinal system is known as the first defense mechanism against bacteria invasion in human. Bile salts in human not only aid during digestion of food but possess antimicrobial activities as they have the ability to inhibit the survival of bacteria in the human gastrointestinal tract. However, this usual defense is interrupted with the ability of *V. parahaemolyticus* to sense bile salts. The bacteria enters into the human gastrointestinal system, two major complex protein VtrA and VtrC will interact and forms complex protein on host cell, binds with bile salts and triggers the cell to produce toxins. Upon binding of bile salts to the VtrA/VtrC complex, the cytoplasmic DNA binding domain of VtrA is activated which in turn induces VtrB to activate, resulting in the T3SS2 expression. T3SS2 virulence is secreted thus causing illness to human. This mode of mechanism ensures the survival of pathogenic *V.*

*parahaemolyticus* in the environments and increase in the bacterial infections<sup>[104,105]</sup>. In addition, the T3SS2 is associated with *tdh*- and/or *trh*-positive *V. parahaemolyticus* strains<sup>[106]</sup>. Hence, this information is significant to all healthcare personnel in order to know the mechanism of *V. parahemolyticus* infections and able to decide the best treatment for the infection.

## CONCLUSION

*V. parahaemolyticus* infection is a predominant global health threat to both developed and developing countries. The pathogenesis of infection and symptoms are minor or self-limiting upon ingestion of unsafe food. However, the rising number of people falling ill with *V. parahaemolyticus* has constrained the socioeconomic and healthcare systems. There are various factors contributing for foodborne diseases to remain as a global public health challenge. Although many foodborne diseases have been controlled with proper management methods, new threats do continuously emerge. The changes among microorganism leads to the emergence of new pathogens, increased antibiotic resistant strains in the environment, and alteration in pathogen's virulence. In addition, people in many countries eat food prepared outside their homes which potentially exposing themselves to high risks of poor hygiene in retail food service surroundings. In many situations, foodborne diseases go unrecognized, underreported, unreported, or not investigated at all<sup>[107]</sup>. All these challenges involve a constant monitoring of foodborne pathogens and management food safety to ensure human wellbeing.

Hence, adequate management of *V. parahaemolyticus* is required to control the widespread of this bacterium. Aquatic products are one of the main reservoirs for pathogenic and multidrug resistant *V. parahaemolyticus*. Therefore, there is an urgent prerequisite for the expansion of non-antibiotic technique to manage multidrug resistance (MDR) among pathogens due to declining efficacy of antibiotics and deficiency of new antibiotic in development pipeline<sup>[108-110]</sup>. Hence, further research can be done using bacteriophages and exploring the usefulness of it the management of *V. parahaemolyticus*. Phages are approved and recognized by the US regulatory bodies as a potential bio-control agent to control and prevent pathogens including *Vibrio* sp<sup>[111-117]</sup>. In addition, it can be utilized in the agriculture and aquaculture industries instead of antibiotics to control bacterial infections that occur in the farms. This will sooner or later reduce the dependency towards antibiotics that leads to resistant genes profile in the environment<sup>[118]</sup>.

In addition, the antibiotic resistance mediation of *V. parahaemolyticus* could be detected by plasmid curing assay (Figure 2). This fast, reliable and inexpensive method uses curing agent to eliminate bacteria plasmids and determine antibiotic resistance mediation. Mostly food safety studies involve a huge number of sample thus hindering the use of costly NGS. Hence, many researchers have utilized and reported the use of plasmid curing assay to determine antibiotic resistance mediation among environmental isolates<sup>[119-124]</sup>. The results from this curing assay may influence an effective antibiotic management policy in the aquaculture sector. With this valuable knowledge, farmers could alternate the antibiotics used in their farms occasionally which will allow the bacteria to lose its resistance to a specific antibiotic<sup>[11,12]</sup>. Furthermore, the study of *V. parahaemolyticus* genome could provide vital information on the particular strain and further strengthen the management strategies<sup>[125,126]</sup>. In summary, the public should be given adequate information on *V. parahaemolyticus* thru awareness campaigns in order to ensure food safety thru out the whole food industry from production to consumption<sup>[127]</sup>.

## AUTHORS CONTRIBUTION

The literature review and manuscript writing were performed by VL and K-YL. JW-FL, N-SAM, SHW, B-HG and L-HL provided vital guidance and support as content expert and proofread of the writing. L-HL and VL founded the research project.

## CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## ACKNOWLEDGEMENTS

This work was supported by PVC Award Grant (Project No. PVC-ECR-2016), External Industry Grant (Biotek Abadi – Vote No. GBA-808138 and GBA-808813) awarded to L-HL.

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