1 Antibiotic Resistance of *Vibrio parahaemolyticus* and *Vibrio vulnificus* in Various
2 Countries: A Review
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Abstract

Vibrio parahaemolyticus and *Vibrio vulnificus* are the leading causes of seafood associated infections and mortality in the United States. The main syndromes caused by these pathogens are gastroenteritis, wound infections, and septicemia. This article reviewed the antibiotic resistance profile of *V. parahaemolyticus* and *V. vulnificus* in the United States and other countries including Italy, Brazil, Philippines, Malaysia, Thailand, China, India, Iran, South Africa and Australia. The awareness of antimicrobial resistance of these two pathogens is not as well documented as other foodborne bacterial pathogens. *Vibrio* spp. are usually susceptible to most antimicrobials of veterinary and human significance. However, many studies reported that *V. vulnificus* and *V. parahaemolyticus* showed multiple-antibiotic resistance due to misuse of antibiotics to control infections in aquaculture production. In addition, both environmental and clinical isolates showed similar antibiotic resistance profiles. Most frequently observed antibiotic resistance profiles involved ampicillin, penicillin and tetracycline regardless of the countries. The presence of multiple-antibiotic resistant bacteria in seafood and aquatic environments is a major concern in fish and shellfish farming and human health.

Keywords: *Vibrio parahaemolyticus*, *Vibrio vulnificus*, Antibiotic resistance, Aquaculture environment

1. INTRODUCTION

Vibrio vulnificus and *Vibrio parahaemolyticus* are naturally occurring estuarine bacteria, the leading causes of seafood-borne mortality and illness in the United States (Haendiges *et al.*, 2014; Oliver, 2006). *V. parahaemolyticus* causes the highest number of seafood-associated bacterial gastroenteritis in many countries including United States and Asian countries (Scallan *et al.*, 2011; Newton *et al.*, 2012; Liu *et al.*, 2009), while *V. vulnificus* is responsible for more than 95% of seafood-related deaths in the United States (CDC, 2010), especially among individuals who are immunocompromised or have liver disease (Klontz *et al.*, 1998 and Liu *et al.*, 2006).

Fortunately, the majority of environmental *V. parahaemolyticus* strains are not pathogenic and *V. vulnificus* also exhibits variation in strain virulence (DePaola *et al.*, 2003 and Biosca, 1997). However, it was reported by the United States Centers for Disease Control and Prevention (CDC) that the incidence of *Vibrio* infections increased dramatically since (CDC, 2010).

Each year, an average of 215 culture-confirmed cases of *V. parahaemolyticus*, 30 hospitalizations, and 1-2 deaths are reported in the United States (CDC, 2013 a). Maryland is among the seven coastal states with increased incidences of *Vibrio* infection (vibriosis). In August 2012, a *V. parahaemolyticus* outbreak involving 6 persons occurred in Maryland and the outbreak isolates were linked to the O3:K6 pandemic clone of *V. parahaemolyticus* that had been observed throughout the world (Haendiges *et al.*, 2014).

Increase of *V. vulnificus* infections is particularly concerning due to the high mortality rate associated with this pathogen (Newton *et al.*, 2012; Gulig *et al.*, 2005). Nationwide, there are as many as 95 cases of *V. vulnificus*, 85 hospitalizations, and 35

deaths reported each year, and in Gulf Coast region, an average of 50 cases, 45 hospitalizations and 16 deaths are reported each year (CDC, 2013 b). In July 30, 2014, ABC News reported several cases of *V. vulnificus* occurrence in Florida, where 32 people had contacted the bacteria and 10 had died according to The Florida Department of Health.

Vibrio spp. are usually susceptible to most antibiotics of veterinary and human significance. (Oliver, 2006). Nevertheless, several investigations reported that both *V. parahaemolyticus* and *V. vulnificus* were resistant to ampicillin (Joseph *et al.*, 1978; Zanetti *et al.*, 2001). As a result of excessive use of antibiotics in human, agriculture, and aquaculture systems, antibiotic resistance has emerged and evolved in many bacterial genera including *Vibrio* during the past few decades (Cabello, 2006; Mazel and Davies, 1999).

The recommended antibiotics for the treatment of *V. vulnificus* infections are doxycycline, cephalosporin (e.g. ceftazidime), fluoroquinolone (such as levofloxacin, ciprofloxacin or gatifloxacin) (CDC, 2013 b), and trimethoprim-sulfamethoxazole plus aminoglycosides. Tetracycline or ciprofloxacin can be also used in severe or prolonged illnesses of *V. parahaemolyticus* (CDC, 2013 a).

Some studies that were carried out to characterize the antibiotic susceptibility profile of these two *Vibrio* spp. indicated that *V. parahaemolyticus* and *V. vulnificus* developed multiple antibiotic resistances which may raise a serious public health and economic concerns. Antibiotic resistance within wide range of infectious agents is a growing public health threat of broad concern to multiple countries and sectors (WHO, 2014).

Hundreds of antibiotic agents have been synthesized and applied for either clinical use, animal therapy, or growth promotion since the discovery of penicillin in the 1920s

(Arestrup and Wegener, 1999). However, excessive use of antibiotic agents is reported to be associated with the occurrence of antibiotic resistance of bacteria.

Bacterial resistance to common antibiotics has reached frightening levels in many countries which can lead to failure of the available treatment options for common infections (WHO, 2014; Arestrup, 1999). Thus the development of alternative bio control agents is urgently needed.

2. GEOGRAPHICAL ANTIBIOTIC RESISTANCE PROFILES OF *V. PARAHAEMOLYTICUS* AND *V. VULNIFICUS*

2.1. United States

In contrast to the extensive antibiotic resistance investigation in other pathogens such as *V. cholera* and *Salmonella* spp., the awareness of antibiotic resistant in *V. vulnificus* and *V. parahaemolyticus* is not well documented (Cabello, 2006). Most of the studies investigated the antibiotic resistance in non-cholera vibrios were conducted outside of the United States.

According to CDC, at least 2 million people became infected with antibiotic-resistant bacteria and at least 23,000 people died as a direct result of these infections in the United States (CDC, 2014 a). An important study on the antibiotic resistance of *V. parahaemolyticus* and *V. vulnificus* in the United States was carried out during 2005 and 2006 on 168 *V. parahaemolyticus* and 151 *V. vulnificus* isolates recovered from Louisiana Gulf and retail oysters. The two *Vibrio* spp. were susceptible to the majority of antibiotic tested, except for 95 (57%) ampicillin-resistant and 41 (24%) ampicillin-intermediate resistant strains of the *V. parahaemolyticus*. *V. vulnificus* isolates showed lower Minimum Inhibitory Concentration (MICs) for cefotaxime, ciprofloxacin, and tetracycline compared to *V. parahaemolyticus* (Han *et al.*, 2007).

Clinical and environmental *V. vulnificus* isolates from South Carolina and Georgia estuaries were screened against 26 antibiotic agents. Unexpectedly, 45% of the environmental isolates were resistant to three or more classes of antibiotics and 17.3% were resistant to eight or more antibiotic agents including doxycycline, tetracycline, aminoglycosides and cephalosporins which are usually prescribed for *V. vulnificus* infections (Baker-Austin *et al.*, 2009). Shaw *et al.* (2014) carried out a study to evaluate antibiotic susceptibility of the *V. vulnificus* and *V. parahaemolyticus* isolated from Chesapeake Bay and Maryland Coastal Bays surface-water. Most of the isolates were susceptible to antibiotics recommended for treating *Vibrio* infections, although the majority of isolates, 78% of *V. vulnificus* and 96% of *V. parahaemolyticus*, expressed intermediate resistance to chloramphenicol. Sixty eight percent (68%) of *V. parahaemolyticus* strains also demonstrated resistance to penicillin. In contrast to *V. vulnificus*, sampling location or month did not significantly impact *V. parahaemolyticus* resistance patterns. This was the first antimicrobial susceptibility data of *V. vulnificus* and *V. parahaemolyticus* recovered from the Chesapeake Bay.

A very high ampicillin resistance rate was observed in *V. parahaemolyticus* in the United States as early as 1978, even before recognition of *V. vulnificus* as a food-borne pathogen (Blake *et al.*, 1979).

2.2. Italy

The previous finding in the United States was confirmed by the study of antibiotic resistance in many *Vibrio* strains including *V. parahaemolyticus* and *V. vulnificus* isolated from the coastal waters of Italy, where 80% of these isolates were resistant to ampicillin (Zanetti *et al.*, 2001). Another study was conducted in fish farms located along the Adriatic

Sea (Italy) to detect the multi-antibiotic resistance occurrence on the autochthonous marine bacterial strains including *Vibrio* spp. due to frequent use of antibiotics to treat and prevent the infectious diseases in fish and shellfish. In this study resistance to tetracycline (17%), trimethoprim–sulfadiazine (7%) and only trimethoprim (2%) were the most frequent patterns obtained (Labella *et al.*, 2013). Likewise, Ottaviani *et al.*, (2013) investigated the antibiotic susceptibility of *V. parahaemolyticus* by analyzing the toxigenic and non-toxigenic strains isolated from shellfish and clinical samples in Italy. This was the first large-scale study on antimicrobial susceptibility and the distribution of resistance genes in environmental and clinical *V. parahaemolyticus* strains in Europe. A total of 107 *V. parahaemolyticus* strains were analyzed including 20 clinical isolates (8 from Italy and 12 from Japan, a non-European origin). No significant difference was observed in the distribution of multiple resistances with respect to pathogenic potential and 62% of all strains were resistant to four different classes of antibiotic. All isolates (100%) were resistant to ampicillin and amoxicillin but susceptible to chloramphenicol and doxycycline. Intermediate resistance to tetracycline (11.2%), oxytetracycline (8.4%) and trimethoprim/sulfamethoxazole (SXT) (3.7%) were observed.

In a previous study, Ottaviani and his collaborators investigated the susceptibility patterns to 27 antibiotic agents in potentially pathogenic halophilic vibrios (including *V. parahaemolyticus* and *V. vulnificus*) isolated from fresh and frozen seafood in Italy. All isolates were resistant to lincomycin, and highly sensitive to oxolinic acid, trimethoprim–sulphamethoxazole, doxycycline, flumequine, cefotaxime, nalidixic acid and ciprofloxacin (Ottaviani *et al.*, 2001).

2.3. Brazil

De Melo *et al.* (2011) investigated the antibiotic resistance of *V. parahaemolyticus* isolated from fresh and refrigerated samples of vannamei shrimp collected from retailers in Natal, Brazil. According to their results, 50% of the isolates presented multiple antibiotic resistance, 90% to ampicillin and 60% to amikacin. All strains were sensitive to chloramphenicol. The study conducted in Ceara, Brazil, revealed similar results. A total of thirty-one *Vibrio* strains isolated from shrimp farms (13 from water and 18 from shrimp hepatopancreas) were tested using a standard disc diffusion method for their susceptibility to 11 antibiotic agents representing 10 antibiotic drug classes. The results showed a high incidence of resistance to ampicillin (45.2%) and to the tetracycline class (38.7%). Also among these isolates, 61.3% showed resistance to at least one of the 11 tested antibiotics. The occurrence of simultaneous resistance to multiple antibiotic-drugs was observed in 29% of *Vibrio* isolates. Florfenicol and nitrofurantoin were 100% effective against all *Vibrio* isolates (Reboucas *et al.*, 2011).

2.4. China

Pan *et al.* (2013) tested the antibiotic susceptibilities of the *V. vulnificus* strains isolated from retail shrimps in Hangzhou, People's Republic of China to 21 antibiotics. Some strains showed resistance or intermediate resistance to cefepime (3.03%), tetracycline (6.06%), aztreonam (24.24%), streptomycin (45.45%), gentamicin (93.94%), tobramycin (100%), and cefazolin (100%). In 2009, Liu *et al.* studied 38 strains of *V. parahaemolyticus* isolated from seafood in Hebei province of China. Resistance to 13 antibiotics was determined using broth microdilution methods. All these strains were typed by Pulsed Field Gel Electrophoresis (PFGE) technique and grouped into 5 types with 71% pattern similarity.

All type E strains were isolated from the same geographical region and simultaneous resistance to ampicillin, sulfisoxazole, streptonigrin and vancomycin, suggesting a good correlation among antibiotic susceptibility test, PFGE profiles and geographic distribution.

2.5. India

Six potentially pathogenic *Vibrio* strains, including 68% *V. parahaemolyticus* and 2% *V. vulnificus* were isolated from four retail markets in Cochin, India. Isolates were tested for their susceptibility to various antibiotics. The highest incidence of antibiotic resistance was reported against ampicillin, colistin and cephalothin (100%) followed by amoxycilin, carbencillin, and ceftazidime ($\geq 95\%$). All *V. parahaemolyticus* and *V. vulnificus* strains were susceptible to chloramphenicol, tetracycline and nalidixic acid. Multiple drug resistance was prevalent among the isolates (Sudha *et al.*, 2014).

In a previous study, similar results were obtained by Vaseeharan *et al.* (2005) in isolates from shrimp culture hatcheries and ponds in India, where 100% of *V. parahaemolyticus* and *V. vulnificus* isolates were resistant to ampicillin and 80% of *V. parahaemolyticus* strains were resistant to furazolidone, neomycin B and penicillin G.

2.6. Some South Asian Countries

Tendencia and De la Pena, (2001) compared the incidence of antibiotic resistance of the *Vibrio* bacteria including *V. vulnificus* isolated from cultured shrimp, water and sediment from the ponds treated with antibiotics and cultured shrimp from ponds that have not used any antibiotics in the Philippines. Multiple-resistances to at least two antibiotics were highest in ponds that used antibiotics while the lowest incidence of resistance was observed in ponds that had not used any antibiotics.

Al-Othrubí *et al.* (2014) conducted a study to determine the antibiotic resistance profile of 65 *V. parahaemolyticus* isolates from cockles and shrimp collected from different markets in Malaysia. These isolates showed high resistance to ampicillin (63.1%) and cefalexin (35.4%). However, 97% of these isolates were susceptible to tetracycline and 49.3% to ciprofloxacin. They also found highest resistance to ampicillin, cephalixin and ciprofloxacin in isolates from retail cockles compared to isolates from shrimp.

Similarly, in Thailand, Yano *et al.* (2014) reported high resistance to ampicillin (72%) of *V. parahaemolyticus* strains isolated from inland ponds' shrimp, and 20% of *V. vulnificus* isolates showed resistance to nalidixic acid. Both *Vibrio* spp. were susceptible to most tested antibiotics.

The study on the antibiotic resistance profiles of clinical *V. parahaemolyticus* in Indonesia showed a 98% resistance rate to ampicillin while all isolates (100%) were sensitive to chloramphenicol, tetracycline, trimethoprim-sulfamethoxazole, gentamicin, and ciprofloxacin (Lesmana *et al.*, 2001).

2.7. Other Countries

Raissy *et al.* (2012) conducted a study in Iran, to evaluate the antibiotic resistance and the presence of antibiotic resistance genes in 6 *Vibrio* spp. including *V. parahaemolyticus* and *V. vulnificus* isolated from Persian Gulf. The results revealed that all isolates expressed resistance to multiple antibiotics. Ninety seven percent (97%) were resistant to ampicillin, 83.3% to gentamycin and 77.7% to penicillin, and 27.7% of the *Vibrio* strains contained one to three of the antibiotic resistance genes.

Okoh and Igbinosa (2010) conducted the antibiotic resistance study of some *Vibrio* spp. including 18 *V. vulnificus* and 12 *V. parahaemolyticus* isolates from wastewater in a

rural community of South Africa. They used the disk diffusion method and Polymerase Chain Reaction (PCR) to characterize and evaluate the presence of established antibiotic resistance genes. The results indicated that all *Vibrio* strains were resistant to penicillin and sulfamethoxazole, but sensitive to imipenem, meropenem and norfloxacin. Ninety two percent (92%) of *V. vulnificus* and 82% of *V. parahaemolyticus* strains were resistant to cephalothin. The antibiotic resistance genes were detected in several isolates. Some of these genes were only recently described from clinical isolates, indicating genetic exchange between clinical and environmental *Vibrio* spp. The characterized *Vibrio* spp. contained one to six of antibiotic resistance of SXT-like element.

Finally in Australia, 46 out of 62 *Vibrio* isolated from aquaculture sources were resistant to at least one antibiotic. Twenty five (40%) of the isolates were resistant to ampicillin, 28 (45%) to amoxicillin, 21(34%) to cephalexin and erythromycin, 9 (14%) to cephalothin, tetracycline 3 (5%), and oxytetracycline 4 (6.5%). All the strains were susceptible to ceftiofur, cefoperazone, chloramphenicol, florfenicol, oxolinic acid, ciprofloxacin, trimethoprim, sulfamethoxazole or trimethoprim-sulfamethoxazole (Akinbowale *et al.*, 2006).

3. TREATMENT OF *V. VULNIFICUS* AND *V. PARAHAEMOLYTICUS* INFECTIONS USING ANTIBIOTICS AND OTHER ALTERNATIVE METHODS

The fatality rate for patients with septicemia has been shown to increase with greater delays between the onset of illness and initiation of antibiotic treatment (Klontz *et al.*, 1988).

Tetracycline has been recommended as the antibiotic of choice for treatment of severe *Vibrio* infections (Morris and Tenny, 1985). The superiority of tetracycline is thought to be related to its ability to inhibit protein synthesis of the pathogenic extracellular

enzymes (e.g., proteases and lipases) (Fang, 1992). Unfortunately, recent studies (Labella *et al.*, 2013; Pan *et al.*, 2013) found that both *V. parahaemolyticus* and *V. vulnificus* developed resistance to tetracycline.

Alternative treatments were combinations of expanded-spectrum cephalosporins (e.g., ceftazidime) and doxycycline or just a fluoroquinolone (Tang *et al.*, 2002). However the multiple-antibiotic resistance displayed by pandemic *V. parahaemolyticus* strains, increase the concerns about possible antibiotic treatment failure.

Phage treatment has been proposed in the form of a novel alternative biocontrol agent for antibiotic resistant pathogens due to their bactericidal activity, host specificity, and safety for human applications (Brussow, 2005). Researchers isolated and characterized one lytic phage that infects *V. parahaemolyticus* pandemic strains to determine whether this phage could be suitable for therapeutic use in a mouse model of a multiple-antibiotic-resistant *V. parahaemolyticus* pandemic strain. They observed that phage-treated mice displayed protection from a *V. parahaemolyticus* infection and survived lethal oral and intraperitoneal bacterial challenges (Jun *et al.*, 2014). Also Lee *et al.* (2014) found that the SSP002 Phage significantly protects mice from infection by *V. vulnificus* for up to 2 months, suggesting that this phage may be a good candidate for the development of biocontrol agents against *V. vulnificus* infection. Defoirdt *et al.* (2007) stated that using new strategies (e.g. the application of probiotics and phage therapy) to control infections in aquaculture is urgently needed to avoid the massive misuse of antibiotics which pose important threats to public health.

4. CONCLUSION

Traditionally, *V. vulnificus* and *V. parahaemolyticus* were susceptible to the majority of antibiotic agents. However, several recent studies have reported that *V. vulnificus* and *V. parahaemolyticus* showed a multiple antibiotic resistance or intermediate sensitivity test reaction to one or more antibiotic agents.

Considering few recent studies have investigated the antibiotic susceptibility of these two species, research is needed to test first-line drugs if they remain highly effective against both *V. parahaemolyticus* and *V. vulnificus*. Also, the observed high percentage of ampicillin-resistance to *V. parahaemolyticus* suggests the exclusion of ampicillin as an effective treatment of infections caused by this organism. Monitoring the hygiene status of seafood and using new strategies other than antibiotics (e.g. probiotics and phage therapy) to control infections in aquaculture are urgently needed to avoid threats to public health caused by massive misuse of antibiotics.

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294 Table: Summary of geographical antibiotic resistance profiles of *Vibrio parahaemolyticus* and *V. vulnificus*

Country	Samples		Species	Pathogenic genotype (%)	Resistance (%)	Intermediate (%)	Susceptible (%)	References
	Site	Type						
U.S.A.	Louisiana Gulf Coast and retail seafood market	Oysters	<i>V. vulnificus</i>				*Cefotaxime, *ceftazidime, chloramphenicol, *ciprofloxacin, *gentamicin, imipenem and *tetracycline (100)	Han <i>et al.</i> , 2007
			<i>V. Parahaemolyticus</i>	tdh and trh (0)	Ampicillin (57)	Ampicillin (24)		
	ACE Basin, Beaufort, South Carolina; Shipyard Creek, Charleston, South Carolina and LCP, Brunswick, Georgia	Water, sediment and blood (clinical primary septicemia isolates)	<i>V. vulnificus</i>	**C (14.6)	*Doxycycline, *tetracycline, *aminoglycosides, and *cephalosporins (17.3), *apramycin (99), nalidix acid (7.3), azithromycin (3.3), chloramphenicol, *quinolones, macrolides and carbapenams (< 1)		Imipenem, erythromycin and *ciprofloxacin (100)	Baker-Austin <i>et al.</i> , 2009
	Maryland Coastal Bay and Chesapeake Bay	Water	<i>V. vulnificus</i>	**C (2.5)	*Apramycin (1), *streptomycin (4)	Chloramphenicol (78), *ceftazidime (1), *amikacin (1), *streptomycin (17)	*Gentamicin (100%)	Shaw <i>et al.</i> , 2014

			<i>V. Parahaemolyticus</i>	**tdh (1.3) and trh (1.3)	Penicillins (68), ampicillin (53), piperacillin (4) and *streptomycin (4)	Chloramphenicol (96), ampicillin (25), cephalotin (17), penicillin (16) and cefuroxime sodium (14)		
Italy	La Maddalene and Tavolara islands and Alghero gulf	Water	<i>V. vulnificus</i> and <i>V. Parahaemolyticus</i>		Ampicillin (80)		Flumequine (99.7)	Zanetti <i>et al.</i> , 2001
	Adriatic Sea fish farm	Water and sediment	Marine bacteria including <i>Vibrio spp.</i>		Tetracycline (17) trimethoprim-sulfadiazine (7) trimethoprim (2)			Labella <i>et al.</i> , 2013
	Italy Coastal water, Adriatic Sea	Shellfish (bivalves) and clinical samples (stools)	<i>V. Parahaemolyticus</i>	**tdh (6.5) and trh (24.3)	Ampicillin and amoxicillin (100)	*Tetracycline (11.2), oxitetracycline (8.4), *trimethoprim/sulfanethoxazole (3.7)	Chloramphenicol and *doxycycline (100)	Ottaviani <i>et al.</i> , 2013
		Fresh and frozen seafood	<i>Vibrio spp.</i> Including <i>V. vulnificus</i> and		Lincomycin (100)		Chloramphenicol, imipenem and meropenem (100)	Ottaviani <i>et al.</i> , 2001

			<i>V. Parahaemolyticus</i>					
Brazil	Natal	Fresh and refrigerated Vannamei shrimp	<i>V. Parahaemolyticus</i>	tdh and trh (0)	Ampicillin (90), *amikacin (60)	*Amikacin (20)	Chloramphenicol (100)	De Melo <i>et al.</i> , 2011
	Ceara	Water and shrimp	<i>Vibrio spp.</i>		Ampicillin (45.2), *tetracycline (38.7)		Florfenicol and nitrofurantoin (100)	Reboucas <i>et al.</i> , 2011
China	Hangzhou	Shrimp	<i>V. vulnificus</i>	C (78.8)	Cefepime (3.03), *tetracycline (6.06), aztreonam (24.24), *streptomycin (45.45), *gentamicin (93.94), tobramycin (100), and cefazolin (100)			Pan <i>et al.</i> , 2013
	Hebbei Province	Clinical sample from septicemic patients	<i>V. vulnificus</i>	tdh (1.92) and trh (0.96)	Ampicillin, sulfisoxazole, streptonigrin and vancomycin (100)			Liu <i>et al.</i> , 2009
India	Cochin	Finfish from retail markets	<i>V. vulnificus</i> and <i>V. Parahaemolyticus</i>		Ampicillin and *streptomycin (89), carbencillin (83), cephalothin (80), colistin (77) and amoxycilin (63)	Ciprofloxacin (54) and *ceftazidime (26)	*Tetracycline and nalidixic acid (100), Chloramphenicol (97), trimethoprim (89), *ceftazidime (74) and *gentamicin (71)	Sudha <i>et al.</i> , 2014
	East Coast of India	Water, sediment and shrimp	<i>V. vulnificus</i>		Ampicillin (100), *ceftriaxone and penicillin G (71), furazolidone (57)	Nalidixic acid and polymyxin B (57)	Erythromycin (71)	Vaseeharan <i>et al.</i> , 2005

				<i>V. parahaemolyticus</i>		Ampicillin (100); furazolidone, neomycin B and penicillin G. (80)	Oxitetracycline (80), polymyxin B (67) chloramphenicol (60)		
Some South Asian Countries	Philippines	Ponds	Water, sediment and shrimp	<i>V. vulnificus</i>		Oxytetracycline (4.3), furazolidone (1.6), oxolinic acid (1) and chloramphenicol (0.66)			Tendencia and De la Pena, 2001
	Malaysia	Market	Cockles and shrimp	<i>V. parahaemolyticus</i>	tdh (12.31) and trh (40)	Ampicillin (63.1) and cefalexin (35.4)		*Tetracycline (97) and ciprofloxacin (49.3)	Al-Othrubai <i>et al.</i> , 2014
	Thailand	Inland ponds	Shrimp	<i>V. vulnificus</i>	C (40)	Nalidixic acid (20)			Yano <i>et al.</i> , 2014
				<i>V. parahaemolyticus</i>	tdh (1.43)	Ampicillin (72)			
	Indonesia	North Jakarta	Rectal swab	<i>V. parahaemolyticus</i>		Ampicillin (98), colistin (97), cephalothin (24), kanamycin (15)		Chloramphenicol, *tetracycline, trimethoprim-sulfamethoxazol, *gentamicin, and *ciprofloxacin (100)	Lesmana <i>et al.</i> , 2001
Iran		Persian Gulf	Fish, shrimp, lobster and crab	<i>V. vulnificus</i> and <i>V. Parahaemolyticus</i>		Ampicillin (97.2), *gentamycin (83.3) and penicillin (77.7)			Raissy <i>et al.</i> , 2012
South Africa		East of Alice Town in the	Waste water	<i>V. vulnificus</i>		Ampicillin and sulfamethoxazole (100)		Imipenem, meropenem and norfloxacin (100)	Okoh and Igbinosa, 2010

	Eastern of Cape Province				cephalothin (92)			
			<i>V. Parahaem olyticus</i>		Ampicillin and sulfamethoxazole (100), Cephalothin (82)			
Australia		Fresh and marine water, fishes, crustacean and environmen tal	<i>Vibrio spp.</i>		Ampicillin (40), amoxicillin (45), cephalexin and erythromycin (34), cephalothin (14), *tetracycline (5), and oxytetracycline (6.5)		Ceftiofur, cefoperazone, chloramphenicol, florfenicol, oxolinic acid, *ciprofloxacin, *trimethoprim, *sulfamethoxazole or *trimethoprim- sulfamethoxazole (100)	Akinbowale <i>et al.</i> , 2006

295 *CDC recommended; ** No difference was found between pathogenic and non-pathogenic regarding the number of resistant strains;
296 tdh= thermostable direct hemolysin, trh = tdh-related hemolysin; C=clinical genotype, E= environmental genotype

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