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Food-borne outbreaks, distributions, virulence, and antibiotic resistance profiles of *Vibrio parahaemolyticus* in Korea from 2003 to 2016: a review

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Abstract

Background: *Vibrio parahaemolyticus* is one of the most common causes of seafood-borne illnesses in Korea, either directly or indirectly, by consuming infected seafood. Many studies have demonstrated the antibiotic susceptibility profile of *V. parahaemolyticus*. This strain has developed multiple antibiotic resistance, which has raised serious public health and economic concerns. This article reviews the food-borne outbreaks, distributions, virulence, and antibiotic resistance profiles of *V. parahaemolyticus* in Korea during 2003–2016.

Main body: *V. parahaemolyticus* infections appeared to be seasonally dependent, because 69.7% of patient infections occurred in both August and September during 2003–2016. In addition, the occurrence of *V. parahaemolyticus* in marine environments varies seasonally but is particularly high in July, August, and September. *V. parahaemolyticus* isolated from aquaculture sources on the Korean coast varied in association with virulence genes, some did not possess either the *tdh* (thermostable direct hemolysin) or *trh* (*tdh*-related hemolysin) genes, and a few were positive for only the *trh* gene or both genes. The high percentage of ampicillin resistance against *V. parahaemolyticus* in the aquatic environment suggests that ampicillin cannot be used to effectively treat infections caused by this organism.

Short conclusion: This study shows that the observed high percentage of multiple antibiotic resistance to *V. parahaemolyticus* is due to conventionally used antibiotics. Therefore, monitoring the antimicrobial resistance patterns at a national level and other solutions are needed to control aquaculture infections, ensure seafood safety, and avoid threats to public health caused by massive misuse of antibiotics.

Keywords: *Vibrio parahaemolyticus*, Food-borne outbreak, Virulence, Antibiotic resistance, Korea

Background

Vibrio parahaemolyticus is a naturally occurring bacterium in estuarine and marine environments and the leading cause of seafood-borne illness in many countries including Korea (Oh et al. 2011; Haendiges et al. 2014; Elmahdi et al. 2016). *V. parahaemolyticus* is one of the most common causes of seafood-associated bacterial gastroenteritis in Korea, either directly or indirectly, by consuming infected seafood (Kang et al. 2016; Yang et al. 2017).

Fortunately, the majority of environmental *V. parahaemolyticus* strains are not pathogenic (Han et al. 2007; Elmahdi et al. 2016). In addition, very few *V. parahaemolyticus* isolates from aquaculture sources in Korea express the virulence genes *tdh* (thermostable direct hemolysin) and *trh* (*tdh*-related hemolysin) (Oh et al. 2011; Yu et al. 2014; Park et al. 2016; Yang et al. 2017). Nevertheless, according to the food poisoning statistics from 2003 to 2016 (KMFDS (Korea Ministry of Food and Drug Safety) 2017), this strain caused infections in 4256 patients, including 2876 patients during 2003–2007, 986 during 2008–2012, and 394 during 2013–2016.

Since the discovery of penicillin in the 1920s, hundreds of antibiotic agents have been developed and

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applied for clinical use or animal treatment (Aarestrup and Wegener 1999). *Vibrio* species are usually susceptible to most veterinary and human antimicrobials (Oliver 2006). However, several studies have reported that antibiotic resistance has emerged and evolved in many bacterial genera including *Vibrio* spp. during the past few decades due to excessive use of antibiotics in human, agriculture, and aquaculture systems (Mazel and Davies 1999; Cabello 2006). As a result of the misuse of antibiotics to control infections during aquaculture production, *V. parahaemolyticus* exhibits multiple antibiotic resistance, which has increased concerns about public health and the economic threat of this bacterium (Lesmana et al. 2001; Ottaviani et al. 2013; Al-Othrubi et al. 2014; Shaw et al. 2014; Kim et al. 2016a, b; Kang et al. 2017). Elmahdi et al. (2016) reported that both environmental and clinical isolates of *V. parahaemolyticus* show similar antibiotic resistance profiles. Antibiotic resistance within a wide range of infectious agents is a growing public health threat of broad concern to multiple countries and sectors (WHO (World Health Organization) 2014).

In Korea, the occurrence, presences of virulence genes, and multiple antibiotic resistance of *V. parahaemolyticus* in seafood and aquatic environments are particularly concerning in fish and shellfish farming and human health.

Food-borne outbreaks caused by *V. parahaemolyticus* in Korea

V. parahaemolyticus is one of the most common causes of seafood-borne illnesses in Korea. According to the food poisoning statistics from 2003 to 2016 (KMFDS (Korea Ministry of Food and Drug Safety) 2017), 225 cases and 4256 patients were reported in outbreaks caused by *V. parahaemolyticus*, accounting for 5.8% of total outbreaks and 4.1% of total patients, respectively, based on all food-borne illnesses occurring in Korea. This outbreak was ranked fourth in Korea.

This strain caused illness in 4256 patients from 2003 to 2016, including 2876 (300–732) patients during 2003–2007, 986 (106–329) during 2008–2012, and 394 (25–251) during 2013–2016 (see Fig. 1a). According to these data, the outbreaks associated with *V. parahaemolyticus* have been decreasing recently. In particular, the patient numbers caused by *V. parahaemolyticus* were remarkably low during 2013–2015 due to the decreases in the outbreak cases. It is assumed in the results that the Korean government further strengthens the publicity activities to reduce the seafood-borne outbreaks, especially during summer season. The rates of seafood-borne infections associated with *V. parahaemolyticus* increase during summer, especially between August and September, leading to 1355 patient infections (31.8%) and 1612 patient infections (37.9%), respectively (see Fig. 1b). In addition, according to the originating facility, the patient infection
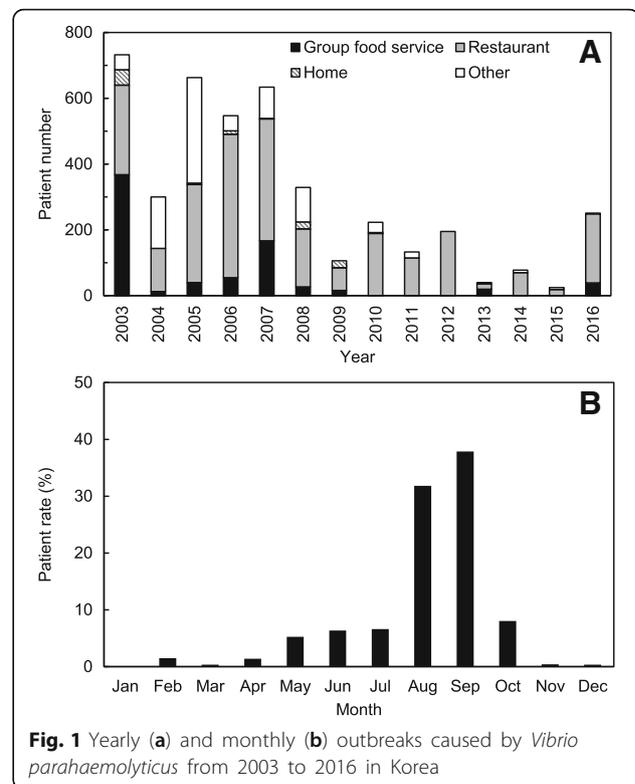

Fig. 1 Yearly (**a**) and monthly (**b**) outbreaks caused by *Vibrio parahaemolyticus* from 2003 to 2016 in Korea

rate caused by *V. parahaemolyticus* was highest at restaurants (average 60.3%) with a range of 37.2–100.0% during 2003–2016 in Korea (Fig. 1a).

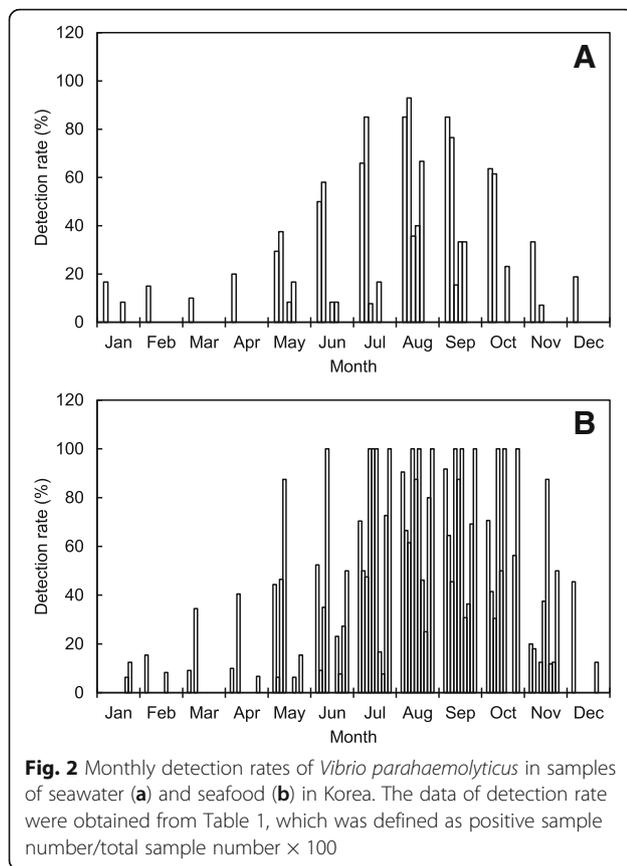## Distribution of *V. parahaemolyticus* isolates on the Korean coast

Distribution of *V. parahaemolyticus* in seawater

Table 1 and Fig. 2 summarize the distribution of *V. parahaemolyticus* isolated in seawater samples collected from the Korean coast, as reported in many studies. Presumptive strains of *V. parahaemolyticus* in the samples were isolated using the plates of thiosulfate citrate bile salt and then confirmed using the VITEK, API 20E, or polymerase chain reaction (PCR) systems. In some reported results, *V. parahaemolyticus* was enumerated by the most probable number method. Han et al. (2012) investigated the abundance of *V. parahaemolyticus* in 281 seawater samples collected from the west coast of Korea (Kyunggi province and Incheon city). According to their results, the level of *V. parahaemolyticus* was high in summer, especially in August (92.9%) followed by July (85.0%) and September (76.5%). Park et al. (2016) compared the distribution of *V. parahaemolyticus* in seawater samples ($n = 429$) collected from the same shellfish farms at each site along the south coast of Korea during 2013–2015. They reported that the detection rate of *V. parahaemolyticus* was also highest in August of each year; however, the strain was barely

Table 1 Seasonal distribution of *Vibrio parahaemolyticus* isolated from samples of seawater, fish, and shellfish in Korea

Samples	Type (number)	Positive number	Detection rate (%) (positive/total number)								References
Site (year)			Dec~Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	
Seawater											
Coast in Kyunggi and Incheon	Seawater (281)	174	42.3[a]	37.5[a]	58.0[a]	85.0[a]	92.9[a]	76.5[a]	61.5[a]	–	Han et al. 2012
Shellfish farms in south coast (2013)	Seawater (152)	9	0.0 (0/59)	0.0 (0/13)	0.0 (0/13)	7.7 (1/13)	35.7 (5/14)	15.4 (2/13)	0.0 (0/13)	7.1 (1/14)	Park et al. 2016
Shellfish farms in south coast (2014)	Seawater (143)	10	0.0 (0/61)	8.3 (1/12)	8.3 (1/12)	0.0 (0/12)	40.0 (4/10)	33.3 (4/12)	0.0 (0/12)	0.0 (0/12)	Park et al. 2016
Shellfish farms in south coast (2015)	Seawater (134)	21	2.1 (1/48)	16.7 (2/12)	8.3 (1/12)	16.7 (2/12)	66.7 (8/12)	33.3 (4/12)	23.1 (3/13)	0.0 (0/13)	Park et al. 2016
Fish and shellfish											
Seafood markets in Busan and Gyeong Nam (2004)	Sea foods (213)	65	0[a]	6.3[a]	9.1[a]	50.0[a]	66.5[a]	64.5[a]	41.5[a]	18.0[a]	Kim et al. 2005
Seafood markets in Kyunggi and Incheon	Fish and shellfish (685)	286	37.5[a]	46.5[a]	35.0[a]	47.5[a]	61.5[a]	45.5[a]	30.5[a]	–	Han et al. 2012
Seafood markets in Seoul (2005)	Oyster (72)	48	0.0 (0/16)	87.5 (7/8)	100 (8/8)	100 (8/8)	100 (8/8)	100 (8/8)	100 (8/8)	12.5 (1/8)	Lee et al. 2008
Shellfish farms in Geoje and Tongyeong Coast (2011)	Oyster (40)	29	–	–	–	100 (8/8)	87.5 (7/8)	87.5 (7/8)	50.0 (4/8)	37.5 (3/8)	Yu et al. 2014
Gomso Bay (2011)	Shellfish (40)	39	–	–	–	100 (8/8)	100 (8/8)	100 (8/8)	100 (8/8)	87.5 (7/8)	Yu et al. 2014
Shellfish farms in south coast (2013)	Shellfish (169)	19	1.4 (1/73)	6.3 (1/16)	23.1 (3/13)	16.7 (2/12)	46.2 (6/13)	30.8 (4/13)	0.0 (0/16)	11.8 (2/17)	Park et al. 2016
Shellfish farms in south coast (2014)	Shellfish (161)	14	3.8 (3/79)	0.0 (0/12)	7.7 (1/13)	7.7 (1/13)	25.0 (3/12)	36.4 (4/11)	0.0 (0/10)	12.5 (2/16)	Park et al. 2016
Shellfish farms in south coast (2015)	Shellfish (151)	50	4.8 (3/62)	15.4 (2/13)	27.3 (3/11)	72.7 (8/11)	80.0 (8/10)	69.2 (9/13)	56.3 (9/16)	50.0 (8/16)	Park et al. 2016
Shellfish farms in Incheon Coast (2014–2015)	Oyster (96)	36	0.0 (0/40)	0.0 (0/8)	50 (4/8)	100 (8/8)	100 (8/8)	100 (8/8)	100 (8/8)	0.0 (0/8)	Kim et al. 2016a

[a]Detection rate was assumed based on the figures in references Kim et al. 2005; Han et al. 2012

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Fig. 2 Monthly detection rates of *Vibrio parahaemolyticus* in samples of seawater (**a**) and seafood (**b**) in Korea. The data of detection rate were obtained from Table 1, which was defined as positive sample number/total sample number × 100

detectable from November to April of the following year. In addition, Yang et al. (2017) reported that *V. parahaemolyticus* was detectable in 9.7 and 32.9% of the *Vibrio* sp. isolates obtained from seawater and zooplankton samples in the Geoje coastal area of Korea during September 2016. *V. parahaemolyticus* was detected more frequently in mesozooplankton samples than in seawater samples.

These results indicate that *V. parahaemolyticus* occurs at high levels during summer to early autumn in seawaters off the Korean coast, especially in July, August, and September. However, the strain was often detected very little during winter to early spring when the water temperature is low in the seawaters off the Korean coast (Table 1 and Fig. 2). Na et al. (2016) investigated the prevalence of pathogenic *Vibrio* species, including *V. parahaemolyticus* isolated from 2220 seawater samples during 2013–2015 in Korea and their relationship with marine environmental factors. According to their results, among the environmental factors, the correlation between seawater temperature and *V. parahaemolyticus* strains was the highest ($R^2 = 0.90$).

Distribution of *V. parahaemolyticus* in fish and shellfish

Various studies have investigated the distribution of *V. parahaemolyticus* isolated in samples of shellfish and

fish collected from the Korean coast (Table 1 and Fig. 1). Kim et al. (2005) investigated the abundance of *V. parahaemolyticus* in 213 seafood samples, including sliced raw fish and living marine invertebrates (oysters, ascidians, and sea cucumbers) collected from seafood markets and restaurants in Busan city and Kyeongnam province of Korea. According to their results, *V. parahaemolyticus* was detected at a range of 41.5–66.5% from July to October, but its incidence was < 20% during the other months. The strain isolation rate (49.2%) in raw marine invertebrates including shellfish was higher (28.9%) than that in sliced raw fish. Another study was conducted in samples ($n = 685$) of fish and shellfish collected from retail seafood markets in Kyunggi province and Incheon city, Korea. In that study, the monthly detection rate of *V. parahaemolyticus* ranged from 30.5 to 61.5%; the highest level was found in August (Han et al. 2012).

In addition, most shellfish samples (including oysters) collected from seafood markets and shellfish farms in Korea also contain relatively high levels of *V. parahaemolyticus* during summer and early autumn (Lee et al. 2008; Yu et al. 2014; Kim et al. 2016a; Park et al. 2016). However, *V. parahaemolyticus* was often detected at very low rates during winter and early spring in low water temperatures off the Korean coast.

These results show that the seasonal variation and cycle are correlated with water temperature, which is a major factor affecting the abundance of *V. parahaemolyticus* (Sudha et al. 2014). Some previous studies have reported a positive correlation between water temperature and *V. parahaemolyticus* counts (DePaola et al. 2003). The outbreaks associated with *V. parahaemolyticus* in Korea appear to be seasonally dependent because 31.8 and 37.9% of patient infections occurred in August and September during 2003–2016, respectively (Fig. 1b). The Korean results also show seasonal variations in the occurrence of *V. parahaemolyticus* in the samples of seawater, fish, and shellfish (Table 1 and Fig. 2).

Virulence genes of *V. parahaemolyticus* isolates in Korea

Virulence of *V. parahaemolyticus* has been attributed to the presence of the *tdh* and *trh* toxic genes using the PCR (Nishibuchi et al. 1985). The *tdh* and *trh* genes are widely considered predominant indicators of virulence in *V. parahaemolyticus* (Su and Liu 2007; Shimohata and Takahashi 2010). Honda and Iida (1993) reported that only 1–2% of environmental *V. parahaemolyticus* strains normally produce the *tdh* gene.

In this article, some *V. parahaemolyticus* isolates were investigated for the presence of virulence genes (*tdh* and *trh*) by PCR system. The expected size of the amplified DNA was 251 bp for the *tdh* gene and 250 bp for the *trh* gene, respectively. Oh et al. (2009) conducted a study to

Table 2 Summary of antibiotic resistance profiles of *Vibrio parahaemolyticus* isolated from samples of seawater, fish, and shellfish in Korea

Samples / Site (year)	Type (number)	Number of isolates	Virulence genes (%)	Resistant (%)[a] / Antimicrobials used	Three or more of antimicrobials	References
Water						
Fish farms in south coast (2004)	Seawater (60)	145	–	AM (98.0), OA (30.6), AN (26.5), AMC (20.4), TE (12.2), CIP (6.1), D (4.1), CEP (2.0), CTX and SXT (0.0)	15.2 (22/145)	Son et al. 2005
Coast in Geoje, Tongyeong, and Goseong (2005)	Brackish water (27)	177	*tdh* (13), *trh* (0)	AM (85.9), RA (26.6), AN (16.4), S (13.6), TMP (13.0), E (3.4), GM (1.1), AMC, TE, CIP, CEP, CTX, SXT, C, and NA (0.0)	20.3 (36/177)	Oh et al. 2009
West coast (2006)	Seawater (22)	21	–	AM (100), CF (85.7), AN (81.0), FOX (38.1), GM (9.5), AMC (4.8), CIP, CTX, SXT, and C (0.0)	–	Lee et al. 2009
Shellfish farms in Gomso Bay (2008)	Seawater (–)	28	*tdh* (0), *trh* (0)	–	–	Lee and Park 2010
Shellfish farms in Wando Coast (2011–2012)	Seawater (–)	67	*tdh* (0), *trh*(0)	AM (100), OX (100), VA (64.2), S (56.7), AN (31.3), K (22.4) CF (20.9), E (10.4), CIP (4.5), TE (3.0), SXT, TMP, GM, C, and NA (0.0)	88.1 (59/67)	Kim et al. 2014
Shellfish farms in south coast (2013–2015)	Seawater (429)	37	*tdh* (0), *trh* (0	–	–	Park et al. 2016
Shellfish farms in Gomso Bay (2014–2015)	Seawater (100)	79	*tdh* (0), *trh* (0)	OX (100), VA (100), P (100), AM (96.2), E (10.1), S (7.6), FOX (6.3), AN (2.5), CF (2.5), TE, CIP, CEP, CTX, SXT, RA, TMP, GM, C, NA, K, CTT, and CZ (0.0)	100 (79/79)	Kim et al. 2016b
Fish						
Fish farms in south coast (2004)	Fish (66)	49	–	AM (97.9), OA (24.1), AN (17.2), TE (4.8), D (4.1), CIP (2.8), AMC (1.4), CTX and SXT (0.7), CEP (0.0)	38.8 (16/49)	Son et al. 2005
Fish farms in south coast (2005–2007)	Fish (180)	218	*tdh* (5.5), *trh* (0.5)	AM (57.8), RA (11.9), S (8.7), TMP (6.4), TE and C (3.7), AN and NA (2.8), GM (1.8), CEP and SXT (1.4), CTX and E (0.9), CIP (0.5), AMC (0.0)	10.1 (22/218)	Oh et al. 2011
Shellfish						
Shellfish farms in Geoje and Tongyeong Coast (2011)	Oyster (40)	129	*tdh* (0), *trh* (0)	AM (79.1), TMP (3.1), S (1.6), CTX, SXT, RA, GM, and NA (0.8), AN, AMC, TE, CIP, CEP, E, and C (0.0)	1.6 (2/129)	Yu et al. 2014
Shellfish farms in Gomso Bay (2011)	Short neck clam (40)	307	*tdh* (0), *trh* (0)	AM (61.0), TMP (5.2), S (2.9), RA (2.3), GM and NA (1.0), C (0.3), AN, AMC, TE, CIP, CEP, CTX, SXT, and E (0.0)	3.6 (11/307)	Yu et al. 2014
Shellfish farms in south coast (2013–2015)	Shellfish (481)	84	*tdh* (2.4), *trh* (9.5)	–	–	Park et al. 2016
Shellfish farms in Incheon Coast (2014)	Oyster (15)	71	*tdh* (0.0), *trh* (53.5)	AM (100), S (50.7), CF (52.2), RA (50.7), GM (2.9), E (15.5), CIP (2.8), TE, CEP, CTX, SXT, C, and NA (0.0)	87.3 (62/71)	Kang et al. 2016
Shellfish farms in Incheon Coast (2014–2015)	Oyster (96)	115	*tdh* (0.0), *trh* (9.6)	AM (94.8), S (60.0), CF (53.9), RA (47.8), E (13.9), GM (7.0), CIP (4.4), CEP(3.5), NA (1.7), TE (0.9), K (0.4), CTX, SXT, C, and CTT (0.0)	46.1 (53/115)	Kim et al. 2016a

Table 2 Summary of antibiotic resistance profiles of *Vibrio parahaemolyticus* isolated from samples of seawater, fish, and shellfish in Korea (*Continued*)

Samples		Number of isolates	Virulence genes (%)	Resistant (%)[a]		References
Site (year)	Type (number)			Antimicrobials used	Three or more of antimicrobials	
Shellfish farms in Incheon Coast (2015)	Oyster (16)	44	tdh (0.0), trh (9.1)	AM (86.4), S (75.0), CF (56.8), RA (43.2), GM (13.6), E (11.4), CIP (6.8), NA (4.5), TE (2.3), CEP, CTX, SXT, and C (0.0)	77.3 (25/44)	Kang et al. 2017
Other						
Seafood markets in Busan and Gyeong Nam (2004)	Seafood (213)	65	–	AM (96.9), AN (29.2), TE (27.7), CTX (9.2), AMC, CIP, CEP, and SXT (0.0)	–	Kim et al. 2005
Coast and seafood markets in Kyunggi and Incheon	Seawater (281) Fish and shellfish (685)	716	–	VA(97.3), AM (87.3), CF (48.8), RA (46.1), E (28.7), NA(16.5), TE (13.5), CTX, SXT, GM, C, K, and NN (<10)	68.7 (492/716)	Han et al. 2012
Geoje Coast (2016)	Zooplank-ton (14) Seawater (14)	24 6	tdh (0.0), trh (0.0) tdh (0.0), trh (0.0)	AM (100), PIP (90.0), RA (73.3), CF (73.4), CZ (66.7), TMP (10), AN (6.7), CIP and SXT (3.3), TE, AMC, CEP, CTX, S, GM, C, NA, and CTT (0.0)	93.3 (28/30)	Yang et al. 2017

AM ampicillin, OA oxolinic acid, AN amikacin, AMC amoxicillin/clavulanic acid, TE tetracycline, CIP ciprofloxacin, D doxycycline, CEP cefepime, CTX cefotaxime, SXT sulfamethoxazole–trimethoprim, RA rifampin, S streptomycin, TMP trimethoprim, E erythromycin, GM gentamicin, C chloramphenicol, NA nalidixic acid, CF cephalothin, FOX cefoxitin, OX oxacillin, VA vancomycin, K kanamycin, P penicillin, CTT cefotetan, CZ cefazolin, NN tobramycin, PIP piperacillin

[a]Resistance was classified according to guidelines of the Clinical and Laboratory Standards Institute (CLSI)

investigate the presence of the *tdh* and *trh* toxic genes in *V. parahaemolyticus* isolated from brackish water samples collected off the south coast of Korea, such as Geoje city, Tongyeong city, and Goseong Gun (Table 2). According to their results, 23 of 177 isolates were positive for the *tdh* gene, whereas all strains tested negative for the *trh* gene. On the other hand, many studies have shown that all *V. parahaemolyticus* stains isolated from seawater samples collected from the Korean coast were negative for the *tdh* and *trh* virulence genes (Lee and Park 2010; Kim et al. 2014, 2016a, b; Park et al. 2016). Yang et al. (2017) reported that all 30 *V. parahaemolyticus* strains and mesozooplankton samples isolated from seawater were negative for the *tdh* and *trh* virulence genes. Therefore, these reports indicate that all *V. parahaemolyticus* stains isolated from seawater samples collected off the Korean coast are negative for the *tdh* and *trh* virulence genes; however, the *tdh* gene was detected in 13.0% of isolates from brackish water samples collected from sites located in the mouths of streams (Table 2).

In addition, Oh et al. (2011) carried out a study to determine the virulence genes of 215 *V. parahaemolyticus* isolates from farmed fish in Korea. Of them, 12 (5.5%) and 1 (0.5%) strains were positive for the *tdh* and *trh* genes, respectively. Finally, according to various shellfish studies of Korean coastal shellfish farms, some *V. parahaemolyticus* isolates do not possess the *tdh* and *trh* genes (Yu et al. 2014), and a few were positive for only the *trh* gene with a range of 9.1–53.5% (Kang et al. 2016, 2017; Kim et al. 2016a, b). Another Korean study reported that 2 (2.4%) and 8 (9.5%) of 84 strains isolated from shellfish samples were positive for the *tdh* and *trh* genes, respectively (Park et al. 2016). Therefore, some *V. parahaemolyticus* isolates from cultured shellfish and fish do rarely possess both genes, and a few were positive for only the *trh* gene (Table 2).

Antibiotic resistance profiles of *V. parahaemolyticus* isolates in Korea
Antibiotic resistance profiles of *V. parahaemolyticus* in seawater
Pathogenic bacteria with antimicrobial resistance genes are often released with wastewater discharge into the aquatic environment (Baquero et al. 2008), indicating that naturally occurring aquatic bacteria including *V. parahaemolyticus* are capable of serving as reservoirs for resistance genes. Many studies have investigated antibiotic resistance of *V. parahaemolyticus* in water samples from the Korean coast (Table 2). The recommended antibiotics to treat *V. parahaemolyticus* illnesses are tetracycline or ciprofloxacin (CDC (Centers for Disease Control and Prevention) 2013). Some Korean studies that were carried out to characterize the antibiotic susceptibility profile of *V. parahaemolyticus* isolates in

seawater samples indicated that 3.0–12.2% of isolates were resistant to tetracycline and ciprofloxacin (Son et al. 2005; Kim et al. 2014).

A study was carried out in 2004 on the antibiotic resistance of 145 *V. parahaemolyticus* isolates collected from seawater samples at fish farms on the south coast of Korea (Son et al. 2005). *Vibrio* spp. were resistant to the majority of antibiotics tested (2.0–98%), except for cefotaxime and sulfamethoxazole-trimethoprim, with the highest resistance found for ampicillin. About 15 of the isolates were resistant to three or more antibiotic agents, including tetracycline or ciprofloxacin, which are usually prescribed for *V. parahaemolyticus* infections.

Oh et al. (2009) investigated the antibiotic susceptibility of *V. parahaemolyticus* by analyzing the toxigenic and non-toxigenic strains isolated from brackish water samples on the south coast of Korea, such as in Geoje city, Tongyeong city, and Goseong Gun, to 15 antibiotics. A total of 177 *V. parahaemolyticus* strains were analyzed including 13% of the isolates with the *tdh* gene. No significant difference was observed in the distribution of multiple resistances with respect to pathogenic potential, and 20.3% of all strains were resistant to three or more classes of antibiotics. Some strains were resistant to ampicillin (85.9%), rifampin (26.6%), amikacin (16.4%), streptomycin (13.6%), trimethoprim (13.0%), erythromycin (3.4%), and gentamicin (1.1%).

Another study was conducted to investigate the susceptibility patterns to different antibiotic agents of 67 *V. parahaemolyticus* isolates in seawater samples from shellfish farms on the Wando coast of Korea. All isolates (100%) were resistant to ampicillin and oxolinic acid, and 88.1% of all strains were resistant to three or more classes of antibiotics. However, all isolates were sensitive to sulfamethoxazole-trimethoprim, trimethoprim, gentamicin, chloramphenicol, and nalidixic acid (Kim et al. 2014).

Similarly, Kim et al. (2016a, b) reported that all *V. parahaemolyticus* strains (79 isolates), isolated in seawater samples from shellfish farms in Gomso Bay, Korea, were resistant to oxolinic acid, vancomycin, and penicillin, and 96.2% of all isolates also demonstrated resistance to ampicillin. Unexpectedly, all isolates were resistant to three or more classes of antibiotics.

These reports indicate that *V. parahaemolyticus* isolates collected from water samples on the Korean coast show very high resistance to ampicillin, accounting for 85.9–100% (see Table 2). A very high ampicillin resistance rate was observed in *V. parahaemolyticus* in the USA as early as 1978, even before the recognition of *Vibrio vulnificus* as a food-borne pathogen (Blake et al. 1979).

Antibiotic resistance profiles *V. parahaemolyticus* in fish
Forty-nine isolates of *V. parahaemolyticus* were obtained from fish at different fish farms on the south coast of

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Korea and tested for their susceptibility to various antibiotics. The highest incidence of antibiotic resistance was reported against ampicillin (97.9%) followed by oxolinic acid (24.1%) and amikacin (17.2%). Among these isolates, 100 and 38.8% showed resistance to at least one and three of the ten tested antibiotics, respectively (Son et al. 2005). Oh et al. (2011) also investigated the antibiotic resistance of *V. parahaemolyticus* isolated from fish farms on the south coast of Korea, where 57% of all isolates were resistant to ampicillin, and 65.1% of the isolates were resistant to at least one of the 15 tested antibiotics.

Antibiotic resistance profiles of *V. parahaemolyticus* in shellfish

Yu et al. (2014) compared the incidence of antibiotic resistance of *V. parahaemolyticus* strains isolated from oysters and short-neck clams in each shellfish-growing area of the Korean coast. Of the 129 and 307 isolates from each shellfish species, 79.1 and 61.0% were resistant to ampicillin, respectively, which was the highest of the tested antibiotics. Multiple resistance to at least three antibiotics was relatively low with a range of 1.6–3.6%. Kang et al. (2016, 2017) and Kim et al. (2016a, b) conducted an antibiotic resistance study of *V. parahaemolyticus* isolates from oysters on shellfish farms located on the Incheon coast of Korea during 2014–2015. Their results indicate that the highest resistance in each study was against ampicillin (86.4–100%) followed by streptomycin (50.7–75.7%), cephalothin (52.2–56.8%), and rifampin (43.2–50.7%). Among these isolates, 46.1–87.3% were resistant to at least three of the tested antibiotics.

Antibiotic resistance profiles of *V. parahaemolyticus* in other samples

Kim et al. (2005) tested the antibiotic resistance of *V. parahaemolyticus* isolated in 213 seafood samples, including sliced raw fish and living marine invertebrates from different seafood markets and restaurants in Busan city and Kyeongnam province Korea. *V. parahaemolyticus* isolates were resistant to ampicillin (96.9%), amikacin (29.2%), and tetracycline (27.7%).

Han et al. (2012) determined the antibiotic resistance profile of 716 *V. parahaemolyticus* strains isolated from samples of seawater, fish, and shellfish on seven coastal areas of Kyunggi province and Incheon city, Korea. According to their results, 97.3 and 87.3% of the isolates showed very high resistance to vancomycin and ampicillin, respectively, followed by cephalothin (48.8%) and rifampin (46.1%). In addition, 68.7% of the isolates presented multiple resistance to at least 3 of the 13 antibiotics tested, including vancomycin and ampicillin. Two exhibited resistance to 11 antibiotics used in this study. However, about 92% of these isolates were highly

susceptible to sulfamethoxazole-trimethoprim and chloramphenicol. They also found high sensitivity to gentamicin (82.3%), tobramycin (74.8%), nalidixic acid (71.6%), tetracycline (69.4%), and cefotaxime (63.0%).

Yang et al. (2017) characterized the antimicrobial resistance profile of *V. parahaemolyticus* isolated from seawater and zooplankton samples in the Geoje coastal area Korea, which is an important area for coastal fisheries, the fishing industry, and tourism. All *V. parahaemolyticus* isolates were resistant to ampicillin, and 66.7–90.0% exhibited resistance to rifampin, cephalothin, cefazolin, and piperacillin. In addition, 93.3% of the isolates were resistant to three or more antimicrobial agents. This was the first antimicrobial susceptibility data of *V. parahaemolyticus* recovered from zooplankton samples in Korea.

Several studies have reported that *V. parahaemolyticus* isolates collected from samples of seawater, fish, shellfish, and zooplankton in Korea have a very high resistance to ampicillin of 57.8–100% (see Table 2). Similarly, a very high ampicillin resistance rate is also observed in *V. parahaemolyticus* isolated from marine environments and seafood in many countries, including the USA (Elmahdi et al. 2016).

Tetracycline has long been the most commonly used antibiotic in Korean fisheries, particularly to treat heavy infections caused by *Vibrio* species (Morris and Tenney 1985; Oh et al. 2011). The recommended antibiotics for treating *V. parahaemolyticus* illnesses are tetracycline and ciprofloxacin (CDC (Centers for Disease Control and Prevention) 2013; Elmahdi et al. 2016). Unfortunately, although a low percentage of tetracycline resistance to *V. parahaemolyticus* was observed, some *V. parahaemolyticus* isolates developed resistance to tetracycline (see Table 2).

In addition, many studies have reported high multiple antibiotic resistance in *V. parahaemolyticus* isolates from samples of water, fish, and shellfish on the Korean coast (Table 2).

Conclusions

V. parahaemolyticus is a naturally occurring bacterium in estuarine and marine environments and a leading cause of seafood-borne illness. Outbreaks associated with *V. parahaemolyticus* in Korea appear to be seasonally dependent because 69.7% of patient infections occurred in August and September during 2003–2016. In addition, the occurrence of *V. parahaemolyticus* increased during summer and early autumn in the samples of seawater, fish, and shellfish from the Korean coast, especially in July, August, and September.

All *V. parahaemolyticus* isolates in the seawater samples from the Korean coast were negative for the *tdh* and *trh* virulence genes; however, the *tdh* gene was detected in 13.0% of isolates from brackish water samples

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in the stream estuary areas. *V. parahaemolyticus* isolates from aquaculture production (shellfish and fish) showed various patterns associated with the virulence genes; some did not possess either the *tdh* or *trh* gene, whereas a few were positive for only the *trh* gene or both genes.

Our findings suggest that ampicillin has been excluded as a treatment option for infections caused by *V. parahaemolyticus*, because the strains from aquaculture sources (e.g., seawater, fish, shellfish, and zooplankton) in Korea have very high resistance to ampicillin, which ranged from 57.8 to100% of the isolates. In addition, multiple resistance to three or more antimicrobial agents were high with a range of 10.1–100% in *V. parahaemolyticus* isolates from samples of water, fish, and shellfish off the Korean coast, except two shellfish sampling areas (1.6–3.6%). These findings indicate that a high incidence of antimicrobial resistance of *V. parahaemolyticus* in marine environments is due to exposure to conventionally used antibiotics.

Therefore, monitoring the distribution and antimicrobial susceptibility of *V. parahaemolyticus* strains in seafood and marine environments, with surveys expanded to a national level, is needed to ensure seafood safety. Moreover, the development of new alternative methods (e.g., probiotics and natural antimicrobials) is urgently needed to reduce antibiotic use in fish and shellfish farming and to avoid threats to public health caused by massive misuse of antibiotics.

Abbreviations
tdh: Thermostable direct hemolysin; *trh*: *tdh*-related hemolysin; *V. parahaemolyticus*: Vibrio parahaemolyticus

Availability of data and materials
Not applicable.

Authors' contributions
KP and JSM designed this study, carried out the analysis of the antibiotic resistance data, and drafted the manuscript. JYK, ARR, SHK, and HJL carried out the data analysis of food-borne outbreaks, monthly distributions, and virulence genes, and polished the manuscript. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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