A Review of the Distribution, Pathogenesis, Virulence Determinants, Epidemiology, and Antibiotic Resistance of *Vibrio Parahaemolyticus*

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ABSTRACT

Vibrio parahaemolyticus is a halophilic, Gram-negative microorganism that creates capsules with somatic (O) and capsular (K) antigens, intake of raw or undercooked seafood spreads virulent *V. parahaemolyticus* strains that result in severe gastrointestinal illness. *V. parahaemolyticus* can attach to a variety of host cells, comprising fibroblasts, epithelial cells, and macrophages. In addition to the ability of each clinical strain of *V. parahaemolyticus* to generate thermostable direct hemolysin (TDH), a substance that has the ability to lyse red blood cells on Wagatsuma blood agar. Among the key factor contributing to the formation as well as the widespread adoption of multidrug resistance (MDR) in *V. parahaemolyticus* isolates is most likely the wide utilize and abuse of prophylactic antibiotics in aquaculture for the bacterial infection reduction and the quick extension of infection. To summarize an important public health concern is the persistent rise in antibiotic- and drug-resistant strains of *V. parahaemolyticus*. However, it is crucial to learn more about current antimicrobial trends.

Keywords: Type III secretion systems, pathogenesis, *Vibrio Parahaemolyticus*, virulence determinants

1. Introduction

Pathogenic bacteria could potentially cause disease outbreaks depending on the environment, their presence in the world's marine ecosystem raises concerns about the safety of human food[1]; A excellent example is *Vibrio parahaemolyticus* a halophilic, G-ve microorganism that creates capsules with unique somatic (O) and capsular (K) antigens[1]. It frequently swims freely, is linked to underwater objects, and frequently associates with different kinds of shellfish[1, 2]. Tsunesaburo Fujino made the initial identification of *Vibrio parahaemolyticus* as a cause of foodborne illness in 1950 as a result of a large outbreak in Japan caused by shirasu consumption that resulted in 272 illnesses and 20 fatalities [3]. Intake of raw or undercooked seafood spreads virulent *V. parahaemolyticus* strains that cause severe gastroenteritis. *V. parahaemolyticus* occasionally causes septicemia, ear infections, or wound infections that can be lethal to humans with underlying medical disorders[4]. The twin flagella system that *V. parahaemolyticus* has allows it to adapt to various environments. The lateral flagella are involved in biofilm, while the polar flagella aid in mobility[5]. When *V. parahaemolyticus* attaches to the fibronectin and phosphatidic acid on the host cell, it secrets various materials like toxins into the cytoplasm of the host cell's, which causes infection and a potentially fatal

illness[6]. Since its discovery, 20–30% of instances of food poisoning in Japan have been attributed to *V. parahaemolyticus* and many Asian nations are caused by seafood, the main factor causing gastroenteritis in people linked to seafood eating in the United States has also been identified as *V. parahaemolyticus* [7]. This study's goal was to give an updated evaluation of *V. parahaemolyticus's* pathogenicity factors and geographic distribution in order to improve knowledge of the disease's importance and host-pathogen interactions.

2. Pathogenesis of *Vibrio Parahaemolyticus*

Many unique virulence elements, like adhesins, thermostable direct hemolysin (TDH), and TDH related hemolysin (TRH), and moreover two type III secretion systems, T3SS1 and T3SS2, were found in various *Vibrio parahaemolyticus* strains[8]. Numerous virulence components of the T3SS1 cause the lysis of a host cell that is infected, allowing for the nutrition essentials released, Additionally, *V. parahaemolyticus* strains develop the genes for TDH and TRH, that generates range of strains with different levels in terms of pathogenicity. Additionally to *T3SSs* and *TDH* genes, *V. parahaemolyticus* has the ability to develop capsules as well as two distinct flagella with different functions for swimming and swarming. Each of these elements probably going to assist the strains in colonizing a human host and surviving in the environment [5]. Apart from the virulence gene, which makes V. parahaemolyticus more pathogenic, the ability of the pathogen to move freely and thrive in its surroundings as well as a human host is made possible by the presence of the flagella for movement [5].

2.1. Fixation of the pathogen to the host cell

A critical stage in the progression of disease is the bacteria's capacity to integrate itself into the host cell. *V. parahaemolyticus* can attach to a variety of host cells, including fibroblasts, epithelial cells, and macrophages [9]. To make contact with the host cell and secrete effectors and toxin proteins, bacteria secrete adhesion factors when they are infected. A unique adhesion known as MAM7 "Multivalent Adhesion Molecule 7" is preserved in numerous G-ve microorganisms, at its N terminus, MAM7 has a 44-amino-acid hydrophobic stretch, which is necessary for the protein's accurate localization and anchoring in the outer membrane. MAM7 also has seven Mammalian Cell Entry (MCE) domains [4]. If one of the surface receptors is inhibited when MAM7 binds to fibronectin and PA, an blockage may develop throughout the attachment of MAM7 to the host cell. Additionally, MAM7 plays a crucial role in T3SS- cell death mediated in some cell types as well as primary host binding once the disease has already manifested. This knowledge of MAM7 sheds light on the interaction between the host cell and the bacteria [10] .

2.2 Iron acquisition

Iron is a component of numerous molecular structures in people, including transferrin and hemoglobin. *V. parahaemolyticus* uses heme as a direct source of iron during infection and produces siderophores as a means of acquiring iron[11]. Siderophores are substances which possess a strong affinity for iron and a low molecular weight. They can collect extracellular iron, free it from transferrin and lactoferrin, and help the bacteria take it up[12]. Vibrioferrin, a siderophore produced by *V. parahaemolyticus*, is made of proteins from the pvsABCDE operon. The ferric-charged vibrioferrin is noticed by a PvuA1 and PvuA2 protein outer membrane receptor[13]. It has been discovered that the existence of ferric Fe in media increases the virulent *V. parahaemolyticus* strains' in vitro adhesion intensities to human fetal intestine (HFI) cells[14]. A recent study, it was shown that metal ions had distinct effects on how *V. parahaemolyticus* behaves and expresses its genes. In addition to high-calcium and low-iron growing conditions encouraged *V. parahaemolyticus* to produce swarming and T3SS regulons[6]. It has been proven that an excess of iron in people makes viruses more virulent in vivo. Iron overload conditions are typical in people with hemochromatosis and liver disorders, for instance. These ailments are known to put patients at risk for recurrent infections, septicemia, and high mortality from bacteria like *V. vulnificus*[15].

2.3. Toxins produced by *V. parahaemolyticus*

The capability of each clinical strain of *V. parahaemolyticus* to generate thermostable direct hemolysin (TDH), a substance that has the ability to RBC on Wagatsuma blood agar, is typically used to distinguish them from environmental strains. This Wagatsuma agar hemolysis is also known as the Kanagawa phenomenon[16]. TDH is made up of quadruple-soluble monomers, each of which forms a central pore through which tiny molecules can diffuse, according to molecular epidemiological research, Vibrio parahaemolyticus KP-negative bacteria lack the *tdh* gene's distinctive features but still produce the *trh* gene. According to a study, a strain of *V. parahaemolyticus* that expresses the *trh* gene and is KP-negative was isolated from an outbreak of gastrointestinal illness that happened in the Maldives 1985, because of its similar function to that of the *tdh* gene in pathogenesis, the *trh* gene is regarded as a component of the pathogen's virulence[17].

2.4. Type III secretion systems

Type III secretion systems consider as mechanisms in bacteria that resembles needles and is accustomed to directly inject bacterial protein effectors in to eukaryotic cells' membrane and cytoplasm without coming into contact with the external environment[18]. On chromosome, T3SS1 is encoded by almost all ecological and medical strains of *V. parahaemolyticus*. The *T3SS1* gene cluster's sequence similarity to that of Yersinia spp. and other vibrios implies that it was obtained during evolution and has been preserved[1]. T3SS1 starts a chain of processes that include blebbing membranes, cell rounding, and autophagy, and ultimately cell lysis during tissue cell infection. Three primary receptors from the T3SS1 gene, VopQ (VP1680), VPA0450, and VopS (VP1686), carry out this full reproducible chain of events. Upon POR3 infection or VopQ transfection into Hela cells, Pi3-kinase independent autophagy is triggered, which precludes phagocytosis of the infecting bacteria[19]. VPA0450 interferes with the human membrane's inner surface which has cytoskeletal binding sites. The ensuing plasma membrane blebbing jeopardizes the integrity of the membrane, promotes cell lysis, and contributes to cytotoxicity. Finally, VopR localizes to the cellular membrane by attaching to the phosphoinositide on the host cell. By encouraging the refolding of T3SS modifying proteins following their introduction into host cells, it may also add to the infection of *V. parahaemolyticus*[20].

3. The Establishment of a pandemic clone and the spread of *Vibrio parahaemolyticus*

In 1950, a case of acute gastroenteritis spread to Japan, infecting 272 people, 20 of whom died. Investigating the cause led to the initial isolation of the G-ve rods now identified as *V. parahaemolyticus*. In United States and Europe, *V. parahaemolyticus* epidemics date back to some of the earliest cases[21]. The most prevalent serovars of *V. parahaemolyticus* are O4:K68, O1:K25, and O1:KUT, which were found in 2007 were dubbed "serovariants" due to their similar genotypes and molecular profiles to the O3:K6[22].

V. parahaemolyticus has been obtained via environmental and clinical samples in India, a recent clinical trial found that, 13,617 patients declared to the infectious diseases Hospital in Kolkata between 2001 and 2012 yielded 178 *V. parahaemolyticus* strains. Additionally, diarrhea caused by *V. parahaemolyticus* were found in Kolkata, India's urban slums[23].

In the US, Pandemic strains of *V. parahaemolyticus* strains have also been isolated between 1979 and 1995, clinical *V. parahaemolyticus* from the U.S. Pacific Coast with the highest incidence were those with the O4:K12 serotype [24]. As showed Figure (1) a variety of ecological conditions, such as water temperature, oxygen in addition to salt content, interactions with plankton, and sediment content, organic substance in suspension, and marine creatures, affect the rate and dispersion of *V. parahaemolyticus* [25].

Figure 1. V. parahaemolyticus's global distribution is depicted on a world map.

4. Antibiotic resistance of *Vibrio parahaemolyticus*

Numerous medications, including the antibiotics amoxicillin, ampicillin, carbenicillin, ceftazidime, cephalothin, colistin, gentamicin, and tobramycin , were reported to be highly resistant to the vast the bulk of *V. parahaemolyticus* strains isolated from environmental and clinical specimens [26]. The key factor contributing to the formation and common use of multiple drug resistance (MDR) in *V. parahaemolyticus* is most likely the wide utilized and abuse of prophylactic antibiotics in fish farming for the bacterial infection avoidance and the quick extended of infection. Additionally, excessive antibiotic use in aquaculture leads to antibiotic remains in aquatic organisms like fish and expands the options of antibiotic-resistant bacteria and the propagation of genes for antibiotic resistance [27]. It should be highlighted that the plasmid contains the majority of the genetic elements that provide antibacterial resistance. Plasmids via vertical gene transfer can be pass to the coming the ear or traded with other bacteria via horizontal gene transfer, making the key mediators for the transfer of antibiotic resistance genes [28]. In 2005, a significant investigation on the antibacterial resistance of *V. parahaemolyticus* and *V. vulnificus* in the US, the majority of the antibacterial examined on the two Vibrio spp. were effective against them, with the exception of 95 (56%) ampicillin-resistant and 41 (24%) ampicillin-intermediate resistant strains of *V. parahaemolyticus*. When compared to *V. parahaemolyticus*, isolates of *V. vulnificus* had lower Minimum Inhibitory Concentrations (MICs) for cefotaxime, ciprofloxacin, and tetracycline [29]. An additional investigation was carried out in Italian fish farms near the Adriatic Sea to look for cases of natural marine bacterial strains that had developed multi-antibiotic resistance., such as Vibrio spp., because of the widespread use of antibacterial to prevent and cure infectious diseases in shellfish and fish. The most common patterns found in this investigation were resistance to tetracycline (18%), trimethoprim-sulfadiazine (8%) in addition to simply trimethoprim (2%)[30]. According to current studies, Carbapenems should only be used as a last resort to treat bacterial infections that are

resistant to multiple drugs as well as Gram-positive and Gram-negative illnesses [31]. However, the prevalence of carbapenem-resistant bacteria has increased. An important public health concern is the persistent rise in antibiotic- and drug-resistant strains of *V. parahaemolyticus*. However, it is crucial to learn more about current antimicrobial trends [32]

5. Conclusions and recommendations

an intricate network of genes orchestrates the host-pathogen interactions, according to research on the virulence factors used by *V. parahaemolyticus*, additional more studies are required to fill in any gaps in the current state of article. Since *V. parahaemolyticus* outbreaks continue to happen every year, it is clear that the infection cannot be controlled by the current preventive measures. Therefore, it is crucial to create a coordinated strategy to stop the spread of infections.

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