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Review Article

Bacterial Zoonoses of Fishes: A One Health Assessment of the Evidence

Nebiyu Kassa Kerigano*
Animal Health Institute (AHI), Sebeta, Ethiopia

***Corresponding author:** **Nebiyu Kassa Kerigano**
Animal Health Institute (AHI), Sebeta, Ethiopia.
Email: neby.etu@gmail.com; k.nebiyu@ahi.gov.et

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Abstract

Aquaculture and fishery production has rapidly increased for the last four decades and is considered a key solution to meet the world food demand. Fish is considered one of the most nutritive and highly desirable food-stuffs and 16% of the animal protein consumed globally is derived from fish and more than a billion persons depend on fish as the main source of protein. The aquatic environment is rich in pathogenic microorganisms and the aquatic animals including fish are obliviously prone to the invasion of micro-organisms organisms. Fish and fish products are often associated with human disease, especially when raw or undercooked products are consumed. Human infections caused by pathogens transmitted from fish or the aquatic environment are quite common and depend on the season, patients' contact with fish and related environment, dietary habits, and the immune system status of the exposed individual. They are often facultatively pathogenic for both fish and human beings and may be isolated from fish without apparent symptoms of the disease but they are pathogenic to humans. The infection source may be fish kept for both for food and as a hobby. The following bacteria have been recorded as most prevalent infections and intoxications: Mycobacterium spp., Streptococcus iniae, V. alginolyticus, V. vulnificus, V. parahaemolyticus, V. cholerae, Escherichia coli, Aeromonas spp., Salmonella spp., Staphylococcus aureus, Listeria monocytogenes, Clostridium botulinum, C. perfringens, and Edwardsiella tarda. Pathogens via contaminated fish and fish products may enter the food chain and processing of fish may lead to cross-contamination of premises, equipment, and end-product may facilitate the distribution of pathogenic bacteria. Therefore, good hygienic practice is a measure to avoid contamination and provide the safety of fish and fish products and avoid consumption of raw fish.

Keywords: Epidemiology; Aquaculture; Fish; Bacteria; Zoonosis

Introduction

Aquaculture production has rapidly increased for the last four decades and is considered a key solution to meet the world food demand [5]. Fish is considered one of the most nutritive and highly desirable foodstuffs [25]. Actually, about 16% of the animal protein consumed globally is derived from fish, and more than a billion persons depend on fish as the main source of protein [3]. As fish meat has excellent nutritional value being rich in proteins, vitamins and unsaturated fatty acids [59]; it is also extremely perishable and requires safe consumption, adequate sanitary conditions from the moment of catch, through preparation, sale and consumption [41].

The aquatic environment is rich in pathogenic microorganisms and the aquatic animals including fish are obliviously prone to the invasion of these organisms with many of them are pathogenic [10]. Infectious diseases are emerging globally at an unprecedented rate while global food demand is projected to increase sharply by 2100 [51]. Fish and fish products are often associated with human disease, especially when raw or undercooked fish and fish products are consumed. The presence of different bacteria species including human pathogenic bacteria in fish can be linked to direct contact with a contaminated water environment and ingestion of bacteria from sediments or

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contaminated feed [28]. Ornamental aquarium pet fish can also carry pathogenic agents of bacterial that may have zoonotic features, endangering the individuals who handle the animals [44].

As per Farzadnia and Naeemipour, (2019) zoonotic bacteria from fish transmitted to humans via various routes, with 64% transmitted from fish species via the oral route through the consumption of untreated food, 23% transmitted through skin contact and cutaneous ulcers, and 19% transmitted through water contaminated with these bacteria. Due to the increased production and consumption of aquatic animals by humans the risk of developing zoonotic diseases is increasing worldwide [7].

Bacterial zoonosis of fishes has received increasing attention as new bacterial pathogens that have been identified and improved microbiological and molecular methods have enabled identification of fish pathogens in human hosts. Many bacteria generally considered as fish zoonosis are facultative pathogens with an environmental niche and often it is not possible to differentiate between infections-in-common and strict zoonosis as a result to some degree obscures the biology and true epidemiological connections of an infectious association. Most of the existing literature is limited to phenotypic/biochemical descriptions of isolates from fishes and humans, and there is a paucity of information as to whether infections in fishes and humans are caused by the same strains, serotypes, or in some cases, species of bacteria. Use of molecular techniques has improved our ability to determine whether human infections have arisen directly from infected fishes, environmental sources, or through exposure to transiently colonized or contaminated fish products [25].

The microbiota of fish is very diverse, its composition and amount can be influenced by many different factors, such as microbial population of water and bottom mud, water source type, fish species and the conditions of their habitat [45].

Human infections caused by pathogens transmitted from fish or the aquatic environment are quite common depending on the season, patients' contact with fish and related environment, dietary habits and the immune system status of the exposed individual [57]. They are often bacterial species facultatively pathogenic for both fish and man and may be isolated from fish without apparent symptoms of disease. The infection source may be fish kept either for food or as a hobby [53]. Therefore, the objective of this paper is to elaborate the epidemiology of significant bacterial causative agents of human diseases transmitted from fish and exploring evidence for linkages between fish and human infections determination of infection.

Potential Agents of Fish-Borne Zoonosis

Mycobacterium spp.

Mycobacteriosis is particularly significant among infections transmissible from fish to human beings (Broutin *et al.*, 2012). Mycobacteriosis affects a wide range of fish species worldwide and most frequently manifests as chronic progressive granulomatous inflammation in viscera and muscles, as well as ulcerative skin lesions spread all over the world (Pate *et al.*, 2019). Infection from fish with NTM is a public health increasing concern due to their best-known zoonotic capability. The rise of PNTM may be partially associated to the advancement of detection methods of mycobacteria (Chin, 2020). Human infections with fish-pathogenic mycobacteria are generally contracted through exposure of wounds and skin abrasions to contaminated water (Nascimento *et al.*, 2016).

The significance of fish mycobacteriosis as zoonosis is evident from case reports published in scientific papers causing cellulitis, skin tuberculosis, and foreign body reaction in humans. Ninety-nine publications dealing with the infection of 652 cases of human beings with *M. marinum* appeared between 1966 and 1996. Of 193 infections with known exposures, 49% were associated with aquarium environment, 27% with injury by aquarium fish and 9% with injury during bathing in brackish water (Hikima *et al.*, 2016). Among *M. marinum* causes granulomatous inflammation of the skin and occasionally deeper tissues in humans known as 'fisherman's finger', 'fish tank granuloma, 'fish-fanciers finger', the so-called 'fish finger's fancier' or swimming pool granuloma in humans, depending on where the infection was contracted (Hashish *et al.*, 2018). while *M. ulcerans* causes Buruli ulcer [58]. Other NTM infection in some cases can result in tenosynovitis, arthritis and osteomyelitis (Ranger *et al.*, 2006). Like *M. fortuitum, M. chelonae and M peregrinum* are opportunistic pathogens of fish and humans results ulcerative lessions especially in immuno-compromised individuals (Gcebe, Michel and Hlokwe, 2018). Both localized and 'sporotrichoid' forms of the diseases are described; the former presents with nodular or ulcerated lesions while the latter is associated with lymphatic spread (Hashish *et al.*, 2018). In addition to their direct effects *M. marinum* and other non-tuberculous mycobacteria (NTM) can induce cross-reactivity to skin tests based on purified protein derivative (PPD) of *M. tuberculosis* and *M. avium* (Hashish *et al.*, 2018).

Streptococcus Spp.

Streptococcosis is an important disease in fish and exceptionally wide and taxonomically diverse host range transmission from fish to human (Richards *et al.*, 2019). The major cause of economic losses from streptococcus's in aquaculture and wild fish populations are *Streptococcus iniae* and *Streptococcus agalactiae* (Laith *et al.*, 2017). Both of these pathogens can also cause disease in humans and the aquatic habitat and can act as a reservoir for human infection (Sentani *et al.*, 2014). In the last 40 years, *S. iniae* has emerged as a major finfish pathogen with a host range of over 27 species of fish from both freshwater and marine environments. *Strep. iniae* causes meningoencephalitis and death in cultured fish species (Tavares *et al.*, 2019). In almost all cases, infection results in high morbidity and mortality but may also be an emerging human pathogen associated with injury while preparing fresh aqua cultured fish. One study established a link between frequent consumption of fish and increased risk of colonization by streptococcal infection [29]. Infection in humans is usually a result of handling of contaminated fish and sustaining an injury, allowing access of the pathogen to the underlying dermis layer, most often of the hand. The resulting infection manifests as bacteremic cellulitis with the rare complications of endocarditis, meningitis, systemic arthritis, sepsis and toxic shock in immunocompromised individuals may die as a result (Li *et al.*, 2019). Microbiol *et al.*, [28] identified zoonotic infection with *S. iniae* in a disease outbreak in Toronto, Canada, involving nine humans with cellulitis related to handling raw fish (tilapia); one patient also had endocarditis, meningitis and arthritis. The PFGE pattern demonstrated an identical strain of *S. iniae* in all nine human patients all matching isolates from tilapia in local fish markets. Two additional human cases were identified retrospectively in Texas, USA, in 1991 and Ottawa, Canada, in 1994 [42]. Zoonotic infections with S. iniae have been reported in Southeast Asia, Canada and Hong Kong, and are primarily associated with processing and handling live fishes [29].

Streptococcus agalactiae, better known as Group B Streptococcus, (GBS) is a Gram-positive pathogen responsible for human and agricultural disease. Of all the streptococcal species, *S. agalactiae* appears to have the broadest host range for pathogenesis, having been isolated from both cold-blooded aquatic organisms and warm-blooded terrestrial animals [30]. A major outbreak of Group B Streptococcus (GBS) infection associated with consumption of a Chinese-style raw fish dish (yusheng) occurred in Singapore during 2015 and involved 238 persons during the first half of the year [18]. Persons with severe clinical cases had meningoencephalitis, bacteremia, and septic arthritis GBS, or Streptococcus agalactiae, was identified as the causative agent [15]. Recent genomic analysis revealed that Streptococcus agalactiae, increasing the risk of foodborne and zoonotic infections, tilapia derived infection with virulence and pathologic characteristics similar isolate to human case strains that caused pneumonia and meningitis in humans (V *et al.*, 2020).

Escherichia Coli

The contamination of food of fish origin with pathogenic E. coli probably occurs during handling of fish and during the production process. An outbreak of diarrheal illness caused by ingestion of food contaminated with enterotoxigenic *E. coli* was described in Japan. The illness was strongly associated with eating tuna paste. Brazilian authors Magana-Arachchi and RP Wanigatunge, [37] isolated 18 enterotoxigenic strains of E. coli (ETEC) from 3 of 24 samples of fresh fish originating from Brazilian markets. An outbreak caused by salted salmon roe contaminated probably during the production process with enterohaemorrhagic *E. coli* (EHEC) O157:H7 occurred in Japan in 1998 [36]. The roe was stored frozen for 9 months but it appears that O157:H7 could survive freezing and a high concentration of NaCl and retained its pathogenicity for humans [4]. In Italian Sardinian shellfish farming confirmed the presence of *E. coli* from fish ready for consumption and during the study 3.8% (49 samples positive/1266 samples analyzed) [11].

Shiga toxin-producing *E. coli* O157:H7 is considered as food and water-borne pathogen that causes diarrhea, hemorrhagic colitis, and Hemolytic Uremic Syndrome (HUS) in humans Isolated from fishes in both sporadic cases and outbreaks in [37]. Several studies have analyzed the presence of STEC and EPEC in fish as well as detected their virulence and antibiotic-resistant profile and analyzed their genetic similarity looking humans and other mammals so that fishes contributed to human infections [13].

Aeromonas spp.

Aeromonas species are known as causative agents of a wide spectrum of diseases in man and animals [31. Among Aeromonas spp. that has been recognized as potential foodborne pathogens for more than 20 years *A.hydrophila* is a very typical pathogen of human-animal-fish comorbidity [35]. In the last two to three decades *Aeromonas hydrophila* is an important emerging zoonotic pathogen of aquatic origin in humans [47]. And causes gastroenteritis, necrotizing fasciitis, septicemia and meningitis [8]. However, another Aeromonas spp, more recently *A. veroni* have increasingly been infecting fish, with many similar symptoms and histological lesions compared to *A. hydrophila* [16].

Since 2009, a clonal group of *A. hydrophila* strains (referred to as virulent *A. hydrophila* or vAh) The Aquatic Diagnostic Laboratory at Mississippi State University has reported a continued increase of vAh for the past 5 years [2]. Aeromonas spp. infections arising from wound exposure have been associated with handling seafood, particularly opening fishes and they are the most common zoonotic bacterium isolated from ornamental fishes [50]. In Southern Taiwan 2011, from 47 clinical isolates the infection sources of Aeromonas bacteremia were identified in 15 patients and which is all patients were hospitalized and received antimicrobial therapy and four died in the hospital resulting in an in-hospital mortality rate of 13.8% associated with consumption of frozen fish in market-sold sushi products containing raw fish [60]. Moreover, Aeromonas species have been isolated from stool samples obtained from persons with diarrhea [17,34].

The epidemiological results so far are very questionable the organism is very frequently present in many food products, including raw vegetables [49]. The same Aeromonas species (primarily A. hydrophila HG1, A. veronii biovar sobria HG8/10, and A. caviae HG4) can cause self-limiting diarrhoea, particularly in children [1]. Up to 8.1% of cases of acute enteric diseases in 458 patients in Russia were caused by Aeromonas spp. In other study Aeromonas spp. isolated with the same pathogenicity factors were observed isolated from river water, from fish, raw meat, and from patients with diarrhea in the Volga Delta [63].

Staphylococcus Spp.

Staphylococcus Spp. are gram-positive cocci that cause disease in many species of animals. However, in fish, this bacterium is rarely a primary cause of disease but can be cultured from samples of aquarium and pond water [40]. The greatest source for illness associated with Staphylococcus spp. is ingestion of enterotoxin produced by the bacteria during improper food handling and preparation. Staphylococcus spp. specifically *S. epidermidis* and *S. aureus* have been isolated from cultured fishes during disease outbreaks [27]. Enterotoxins produced by *Staph. aureus* is another serious cause of gastroenteritis after consumption of fish and related products. In the southern area of Brazil, *Staph. aureus* was isolated from 20% of 175 examined samples of fresh fish and fish fillets (Cynoscion leiarchus). However, only nine of 109 *Staph. aureus* isolates produced enterotoxins including enterotoxin A (n = 4), D (n = 1), and AB (n = 4) [55].

Listeria Monocytogenes

Listeria monocytogenes is widely distributed in the general environment including fresh water, coastal water and live fish. Contamination or recontamination of fish may also take place during processing [4]. The outbreak of listeriosis related to vacuum packed gravad and cold-smoked fish was described in at least eight human cases for 11 months in Sweden [28]. Cold-smoked and gravad rain- bow trout (Oncorhynchus mykiss) and salmon (Salmo salar) have been focused on during recent years as potential sources of infection with *L. monocytogenes.* Investigations have shown that up to 10% of retail vacuum-packaged products contain *L. monocytogenes* [45].

L. monocytogenes is one of the most important causes of death from food-borne infections in developed countries (Jami et al., 2014; Wan Norhana et al., 2010). Listeriosis outbreaks have been associated with the consumption of mussels and smoked mussels, smoked cod roe, and undercooked fish. Another study reported a prevalence of 6.1% of *L. monocytogenes* in RTE crabmeat samples collected monthly from some processing plants during the plant operating season in the U.S. [4]. Consumption of raw fish is the major sources of infection. Human listeriosis is associated with serious invasive illness, particularly in elderly and immunocompromised patients, pregnant women, newborns and infants [27].

Clostridium Spp.

Clostridium spp. contribute to the resident intestinal bacteria in many fish species and rarely cause disease in fish. For humans, the primary risk of illness associated with Clostridium organisms from fish species is through ingestion of preformed toxin produced by vegetative cells in improperly handled fish products [19].

Clostridium botulinum is commensal in the intestines of marine and freshwater fish species worldwide and can also be found in environmental sediments and decaying organic matter. The main habitat of clostridia is the soil but they are also found in sewage, rivers, lakes, sea water, fresh meat, and fish [58]. A potent paralytic neurotoxin is produced by this bacterium that induces descending paralyses in human beings [48]. Of the seven recognized botulinum toxin types (A-G), type E is involved in most cases of human disease related to fish consumption, although types A and B are occasionally implicated [26]. Disease in fishes due to *C. botulinum* is uncommon and occurs when fishes feed on decaying carcasses that have become anaerobic and thus support growth of the bacterium. The disease is known as 'bankruptcy disease' in earthen pond culture of salmonids [48]. and has also been documented as 'visceral toxicosis' of catfish in south eastern USA [19]. Human botulism has been associated with consumption of contaminated fish products, notably smoked fish in arctic and northern temperate regions. PFGE has demonstrated links between food and *C. botulinum* genotypes involved in individual outbreaks [23].

Edwardsiella spp.

The three species recognized in the genus Edwardsiella are Edwardsiella ictaluri, Edwardsiella tarda and Edwardsiella hoshinae. E. ictaluri is a serious pathogen of catfishes causing enteric septicemia [28], but is not known to infect humans. *E. hoshinae* is typically isolated from reptiles and birds and although it has been isolated from human feces its role as an animal or human pathogen is questionable [39]. E. tarda is the only zoonotic Edwardsiella spp. characterized primarily by bacterial gastroenteritis, although wound infections and systemic conditions, such as septicemia and meningitis, are also observed as are extra intestinal infections [9].

A case report of E. tarda infection that presented as multiple liver abscesses leading to fulminant septic shock in a previously healthy 37-year-old south east Asian woman [9]. Case history reveals the patient had frequently eaten raw fish. Another case history with a 65-year-old Japanese woman was admitted to hospital with a fever, lumbago, and right groin pain that had persisted for 2 weeks. A dietary history revealed that she had frequently eaten sashimi (sliced raw fish) and grilled eel, including within a few days prior to the onset of symptoms [52]. The highest potential for infection to a human is through a puncture wound received during handling or examination of fish, followed by contamination of existing cuts and abrasions [54].

Salmonella Spp.

Salmonella spp. commonly been isolated from contaminated aquarium and tanks and polluted ponds and salt water (Fern and Jos, 2020). Salmonella spp. are not known to be pathogenic to fish but can be associated with human disease. Salmonella spp. is one of the leading causes of foodborne illnesses in the United States contributing to at least 1.4 million cases annually, the most common causal agents of outbreaks in shellfish [22].

Recently Food and Drug Administration (FDA) in USA inspected the safety of shrimp products, out of inspected 58% of total seafood products (shrimps and prawns) identified as being contaminated with Salmonella spp. [42]. Salmonella enterica subsp. enterica serovar Enteritidis is the most frequently isolated serovar from humans all over the world [37]. According to various reports, S. enterica serovar Albany, ser. Agona, ser. Corvallis, ser. Stanley, ser. Bovismorbificans, and ser. Typhimurium were present in fish, fishery products, and aquaculture environments. Niquice *et al.*, [42] described the presence of *S. enterica serovar Albany, ser. Agona*, and *ser. Stanley* in catfish fed offal and *ser. Corvallis* in tilapia fed spoiled eggs.

Vibrio spp.

Vibriosis is one of the most prevalent bacterial diseases affecting diverse fresh water and marine fish and shellfish [19]. Of the fish borne human pathogens that can be found in fresh water and seawater environments, Vibrios are the most predominant species [24]. Among Vibrio spp. that cause disease in fish and humans are, *Vibrio vulnificus, Vibrio cholera,* and *Vibrio parahemolyticus*, are associated with diseases in fishes and shellfishes and are also occasionally isolated from cases of human disease. MLST typing of fish isolates in Bangladeshi aquaculture demonstrated close similarity between identity of fish and clinical isolates of Vibrio spp. particularly gastroenteritis and wound infections [24]. The most common non-cholera human Vibriosis are caused by *Vibrio vulnificus* and *Vibrio parahemolyticus*. These infections are associated with gastroenteritis, septicemia and wound infections in humans, and are of particular concern because of their high case fatality rate (3.6%) relative to other enteric bacteria and another Vibrio species that is responsible for a great deal of morbidity and mortality worldwide associated with ingestion of raw fish and contaminated fish and water is *Vibrio cholera* [12].

Vibrio vulnificus is a highly invasive human pathogen and presents a food safety issue worldwide. Human infections caused by *V. vulnificus* are primarily caused by contaminated fish consumption or contaminated skin wounds, which can lead to septicemia, wound infections, and high hospitalization and fatality rates [14]. The current body of literature on genetic similarity between human and fish isolates of *V. vulnificus* is better developed than many other presumptive bacterial zoonosis of fishes and transmission between fishes and humans appears to be supported, although it is apparent that infections may also be contracted from environmental sources [55].

Vibrio cholerae is of paramount worldwide health significance, particularly strains which produce cholera toxin. V. cholerae have been implicated in human disease outbreaks associated with consumption of fish and V. cholerae has been reported in water used to house or transport ornamental fishes. However, V. cholerae is rarely reported as a disease agent in fishes and its role as a fish-borne zoonotic is considered as reservoirs [62].

The first outbreak of fish borne disease due to consumption of *V. parahaemolyticus* contaminated sardine was reported in Japan in 1950 (Odeyemi, 2016). In this outbreak, 20 people were reported dead while over 270 people were likewise hospitalized. [46,61]. RAPD profiling of *V. parahemolyticus* from fish in markets demonstrated connection with isolates from fish sources [33].

Conclusion and Recommendations

A variety of bacteria have been reported as potential fish-borne zoonotic agents and there is substantial epidemiological and molecular evidence for linkages between infections in both hosts. Epidemiological associations suggest zoonotic risks for other fish-associated bacteria however, some do not cause disease in fishes (e.g. E coli) and more work will be required to link human and fish infections. Other bacterial species either lack significant evidence for epidemiological connections between fishes and humans, have more plausible transmission routes not involving fishes, or are most likely to be transmitted through contamination of food. Further molecular studies examining isolates from fishes and human disease outbreaks would be fruitful in defining epidemiological connections and in determining the zoonotic risk from bacterial fish pathogens. Contamination of the natural habitat of fish may affect not only the health of fish stocks, but also raise public health concerns as fish and fish products can be a potential source of human pathogenic bacteria. Various factors such as human activity, contaminated water sources, and poor hygiene during capture, handling, and transportation of fish could affect the prevalence of bacteria in fish and surrounding water. The hazard of these microorganisms is increased with the specific abilities of these bacteria to survive in the environment. The emergence of bacteria discussed is also based on the fact that fish and fish products often miss the heat treatment procedure before consumption, which has dramatic effects on human health. Pathogens via contaminated fish and fish products may enter the food chain, and processing of fish may lead to cross-contamination of premises, equipment, and end-product, facilitating the distribution of pathogenic bacteria. However, Good Hygienic Practice is a measure to avoid contamination and provide the safety of fish and fish products and avoid consumption of raw fish.

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