Zoonotic Risks of Anisakiasis from Seafood Consumption: An Emerging Public Health Concern

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Abstract

Seafood is a vital source of nutrition globally, rich in high-quality proteins, essential fatty acids, minerals, and vitamins. However, it also possesses potential pathogens responsible for foodborne zoonoses. Anisakiasis, an emerging parasitic disease, is a public health concern resulting from the consumption of raw and undercooked seafood especially fish, infected with *Anisakis* larvae. The growing popularity of raw seafood meals such as sushi, sashimi, ceviches, etc. has led to an increase in Anisakiasis incidents. This chapter presents a comprehensive overview of Anisakiasis by exploring its biological, clinical, and epidemiological aspects and reviewing current diagnostic and preventive strategies. Consumption of infected fish can cause gastrointestinal symptoms and food allergic reactions including anaphylaxis, angioedema, and urticaria as a result of thermostable *Anisakis* allergens. Diagnoses often involve endoscopy, serological tests, or imaging techniques whereas prevention relies on proper fish handling, including proper cooking and freezing of fish to kill the larvae. Improved diagnoses and strict food safety protocols are needed. More study into parasite biology and host interactions is required to establish effective management techniques and reduce the burden of this zoonotic disease.

Keywords: Anisakiasis, Seafood, Foodborne, Parasite, Zoonotic disease

Cite this Article as: Munir A, Hussain AK and Tariq L, 2025. Zoonotic risks of anisakiasis from seafood consumption: an emerging public health concern. In: Abbas RZ, Akhtar T and Arshad J (eds), One Health in a Changing World: Climate, Disease, Policy, and Innovation. Unique Scientific Publishers, Faisalabad, Pakistan, pp: 164-169. https://doi.org/10.47278/book.HH/2025.127

A Publication of Unique Scientific Publishers

Chapter No: 25-023

Received: 25-Feb-2025
Revised: 15-Apr-2025
Accepted: 18-Apr-2025

Introduction

Anisakiasis is a foodborne zoonotic disease that is caused by nematodes belonging to the genus *Anisakis,* affecting various marine animals and humans (Smaldone et al., 2020). Of the existing 9 confirmed species of the genus *Anisakis*, *A. simplex s.s.* and *A. pegreffii* are most commonly reported and of major public health importance since they are known to cause Anisakiasis (Mattiucci et al., 2018). The complex life cycle of these parasitic nematodes of the *Anisakidae* family uses marine mammals as their final definitive hosts. These nematodes use several crustaceans, cephalopods, and fish species as intermediate or paratenic hosts and humans are accidental hosts (Mattiucci & Amelio, 2014). Humans contract the infection by consuming raw or undercooked seafood like marine fish or squid contaminated with the third larval stage (L3) of *Anisakis* species (Chai et al., 2005). Although once considered rare, Anisakiasis has become a recognized public health issue due to the increasing global popularity of raw and minimally processed seafood dishes such as sushi, sashimi, ceviche, and others (Wolfe et al., 2007). The infections can be both cutaneous and systemic (Ivanovic et al., 2017) causing respiratory symptoms, fever, vomiting, abdominal pain, diarrhea, constipation, nausea, etc. (Fazii et al., 2006). *Anisakis simplex* can also produce allergic reactions in the human body (Audicana & Kennedy, 2008) like anaphylaxis, angioedema, and urticaria (Daschner et al., 2012). This chapter aims to provide a comprehensive overview of Anisakiasis by discussing the lifecycle of the *Anisakis* parasite, transmission, risk factors, epidemiology, clinical manifestations and diagnoses of the disease in humans.

Transmission of Anisakiasis to Humans

Fish infected with *Anisakis spp.* may be consumed by humans either directly or indirectly, through natural or accidental means (Shamsi et al., 2019). The transmission of the *Anisakis* nematode occurs not only through the consumption of food but also through the direct transfer of infected larvae to the human body. In humans, *Anisakis* larvae reside in the gastric and intestinal linings of the host and are transmitted through the consumption of raw or undercooked seafood (e.g. ceviche, sushi, herring roe, sashimi, lomi-lomi, gravlax) as well as contaminated preserved seafood, grilled, marinated, salted, baked, pickled, and smoky fish which doesn't kill the *Anisakis* larvae (Sohn & Murrell, 2011) resulting into allergic reactions in the human body (Audicana & Kennedy, 2008).

Life Cycle of *Anisakis Species*

Anisakis nematodes can infest aquatic species at various stages, from an egg to an adult capable of reproduction (Di Azevedo et al., 2017). To comprehend the parasite's life cycle it is crucial to understand that there are four larval stages (L4) (Ugland et al., 2004). The adult *Anisakis* inhabit the gastric chambers of the definitive hosts which are marine mammals (such as dolphins, whales, seals, etc), where females lay eggs that are later expelled through feces (Figure 1). Once matured these embryonated eggs (L1) hatch into the aquatic environment, where they progress into L2 larval stages (Castellanos et al., 2017). The L2 larvae will become integrated with small crustaceans, copepods, krill, and plankton (Gregori et al., 2015). The L2 larvae are ingested by crustaceans, where they grow inside their hemocoel, until it achieves an appropriate size to molt into the L3 stage, unless the crustaceans are eaten by fish (Anderson, 2000). When marine fish ingest intermediate hosts, they serve as paratenic hosts or carriers of the L3 stage (Figure 1) (Castellanos et al., 2017), The larvae become lodged in the gastrointestinal tract and move toward the coelomic cavity; Once there, they encyst in internal tissues such as epiaxial muscle, kidney, and liver (Reyes et al., 2020) or attach to the serosal surfaces of internal tissues, triggering an inflammatory reaction (Ferrantelli et al., 2015). The parasite's life cycle is completed when a marine mammal consumes fish infected with L3, allowing the larvae to develop into the L4 stage, or mature into the adult form. In birds, upon consuming infected fish, the L3 larvae are released during digestion, allowing the parasite to undergo its final molt into the L4 stage and continue its life cycle (Nemeth et al., 2012). It is crucial to note that L3 larvae cannot develop into the L4 stage in fish or humans, preventing any parasitic reproduction in these hosts. Humans become accidental hosts of *Anisakis* nematode when they eat raw or undercooked fish or squid containing L3 larvae (Fig. 1). These larvae can adhere to the human gastrointestinal tract, causing either gastric or intestinal *Anisakiasis* (Valles et al., 2017).

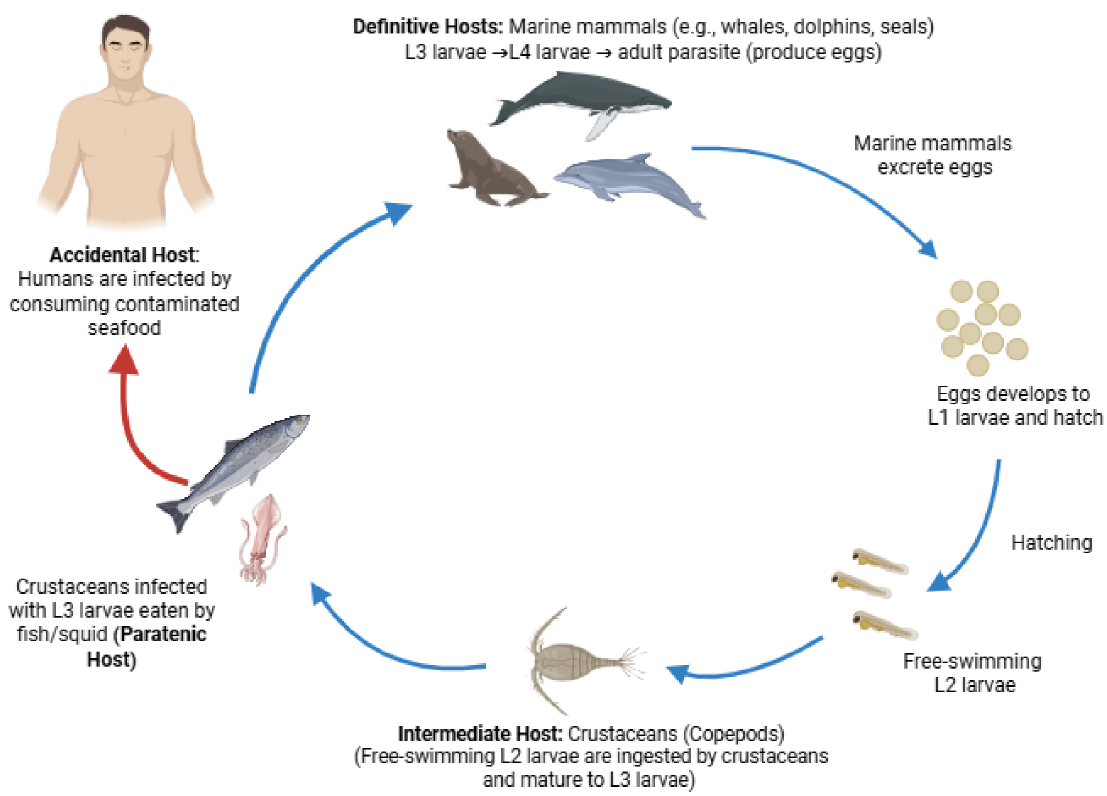

Fig. 1: The Lifecycle of Anisakiasis

Risk Factors of Anisakiasis

Exposure to Anisakiasis has been associated with an increased risk of various diseases, and recent research indicates that Anisakiasis infection may significantly elevate the risk of stomach and colon cancer (Garcia-Perez et al., 2015). Some risk factors for Anisakiasis are associated with fish characteristics (Meladineo et al., 2014) such as fish habits and habitat, fishing area, fish weight, seasonal changes and their impacts on fish infected larvae, fish gonad weight, consumption of infected skin cells, consumption of lower weighted fish, raw seafood, sushi, and Carpaccio (Abattouy et al., 2011). In regions with increased seafood consumption, the rising risk factors of Anisakiasis (Mladineo et al., 2014) may be linked to the methods of seafood storage and preparations, for example, *Anisakis spp.* are not killed by low temperature or improper cooking methods, such as those used for marinated, frozen, smoky, caned, and salted fish (Llarena-Reino et al., 2015). The infection can be transmitted through the handling of infected skin or wounds, corpses (such as slaughtered animals and aborted remains), as well as through processes like fishing, packing, shipping, transportation, and storage. Environmental factors such as temperature and seasonal changes including humidity, moisture, rainfall, and drought can also contribute to the spread of the Anisakiasis disease (Aguilar-Marcelino et al., 2022).

Epidemiology of Anisakiasis

Since Anisakiasis was first identified in 1960, every year thousands of cases of this zoonotic disease are reported worldwide, especially in developed countries with a large fishing industry, high fish consumption per capita, and culinary traditions that include dishes made with raw fish or squid. Before 2010, there were more than 20,000 cases of Anisakiasis documented worldwide (EFSA-BIOHAZ, 2010). Japan records the highest number of diagnosed cases, 2000–3000 cases each year (Yorimitsu et al., 2013), mainly because Japan has one of the highest levels of seafood consumption in the world and a long history of raw cuisine eating practices (Sugiyama et al., 2013). Anisakiasis has also been recorded in the United Kingdom, Taiwan, Spain, France, Italy, Malaysia, China, Korea, Germany, Norway, Denmark, Croatia, Egypt, Australia, the United States of America, South Africa, and Southern America, indicating that it occurs on all continents except Antarctica (Table 1) (Aibinu et al, 2019). A long history of consuming raw or undercooked fish such as traditional Japanese dishes 'sushi' and 'sashimi', 'marinated anchovies' in Spain (Herrador et al., 2018), 'ceviche' in South America (Eiras et al., 2018) has significantly increased the risks of Anisakiasis (Eiras et al., 2018). Recently research on Anisakiasis cases recorded in the European Union between 2000 and 2017 showed a total of 236 cases, with Spain having the greatest prevalence, followed by Italy (Serrano-Moliner et al., 2018). A popular dish in Spain, marinated anchovies in vinegar, was suggested as the major dietary source of Anisakiasis (Herrador et al., 2018). According to Sumner et al. (2015), 1259 tons of raw finfish are consumed in Australia each year, with 115.6 million servings utilized for sushi and sashimi dishes. While increased knowledge and awareness among healthcare professionals have led to more accurate diagnoses (Castán et al., 2002), some researchers remain concerned about the persistent issue of misdiagnosis. For instance, in Spain, Bao et al. (2017) used a quantitative risk assessment model and estimated approximately 8000 cases of Anisakiasis annually from anchovy consumption, Meanwhile, Herrador et al. (2019), analyzed hospitalized data and projected between 10,000 and 20,000 cases per year. Despite this, only about 500 cases are reported each year across Europe. Globally, the infection rate is estimated at 0.32 cases per 100,000 people, with Anisakiasis cases identified in over 20 countries (Adroher-Auroux & Benítez-Rodríguez, 2020).

Clinical Manifestations

Humans serve as accidental hosts for *Anisakis*, where the live L3 larvae, consumed through raw or improperly cooked fish or squid, often adhere to the gastric mucosa, and, in some cases, the intestinal mucosa (Adroher-Auroux & Benítez-Rodríguez, 2020). The kind of Anisakiasis that develops is determined by the larva's location along with the symptoms it is producing:

Gastric Anisakiasis: When the larva attaches to the gastroduodenal mucosa, it causes severe epigastric pain, often followed by symptoms like diarrhea, urticaria, vomiting, and nausea which appear 2 to 6 hours after the larval ingestion (Table 1). These symptoms persist as long as the larva remains alive. In 72% of cases, this is the most prevalent kind of Anisakiasis (Furuya et al., 2018).

Intestinal Anisakiasis: Anisakiasis can also occur in the intestine and symptoms occur after 2 to 3 days and often include intense abdominal pain sometimes followed by diarrhea, vomiting, and nausea. In some cases, a chronic form may develop, leading to abscesses or granuloma formation, which can mimic conditions such as intestinal obstruction and appendicitis along with edema and fibrinous exudate (Sánchez et al., 2009).

Table 1: Summary of the global prevalence of Anisakiasis (Aguilar-Marcelino et al., 2022)

Parasite species	Country of report	Method of identification	Clinical findings/ Site of sample collection	Zoonotic importance	Reference
A. pegreffii, A. typica and *A. simplex*	China	PCR gene/protein (ITS1-5.8SITS2)	Intestinal Cecum	Yes	Chen et al., 2018
A. pegreffii	Japan	PCR gene/protein	Musculature	Yes	Tamura et al., 2013
A. myriaster	Japan	PCR gene/protein (ITS1-5.8SITS2)	Body cavity and visceral organs	Yes	Qin, 2013
A. simplex, A. pegreffi	Mediterranean Sea or Atlantic Ocean	Chloropeptic digestion	Deboned oil anchovy, sardine fillets	May be	Smaldone et al., 2020
A. typica	Japan	Morphological examination	Skin and miniscule structures	Yes	Zhu et al., 1998
A. simplex	Taiwan	PCR amplification	Muscles	Yes	Chen and Shih, 2015
A. simplex	Thailand	MtDNA cox2	Muscles	Yes	Eamsobhana et al., 2018
A. typica	Italy	Genetic marker	Muscles	Yes	Eamsobhana et al., 2018
A. typica	Japan	Scanning electron micrograph	Protruded mucrons	Yes	Ishii et al., 1989
Anisakis spp.	Italy	EsophagogastroDuodenoscopy (EGD)	Gastric Cecum	Yes	Kapral et al., 2009
Anisakis larvae	Taiwan	Microscope-assisted	Muscles tissues	Yes	Llarena et al., 2013
A. typica	Italy	Abdominal computed Tomography (CT)	Intestinal wall	Yes	Couture et al., 2003
A. typica	China	Colonoscopy	Stomach	Yes	Soewarlanet al., 2015
Anisakis larvae	Japan	Morphological identification	Body cavity and liver	May be	Li et al., 2017
A. simplex	Italy	Colonoscopy	Caecum	Yes	Choi et at., 2009
A. typica	Italy	Microscope-assisted	Intestinal lumen	Yes	Couture et al., 2003
A. typica	Spain	Morphological identification	Respiratory tract	Yes	Pulido et al., 2000
A. simplex	Thailand	Morphological identification	Small intestine	Yes	Nuchjangreed et al., 2006
A. pegreffii	Thailand	Immunoblotting	Gastric and intestinal	May be	Nieuwenhuizen, 2016
A. simplex	Japan	Skin prick testing	Digestive enzyme pepsin	Yes	Shah Esmaeiliet al., 2021
A. pegreffii	China	Morphological identification	Chronic and inflammatory cells	May be	Vergiset al., 2021
A. typica	Brazil	PCR-RFLP	Muscles	Yes	Palm et al., 2008

Gastro-allergic Anisakiasis: This occurs when the live *Anisakis* larva present in the stomach, triggers a severe allergic reaction while trying to penetrate the submucosal layer of the stomach wall (Daschner et al., 2011). Gastro-allergic Anisakiasis is an acute IgE-mediated reaction that causes anaphylaxis, angioedema, and urticaria. The allergic responses typically begin 2-3 hours to 2-3 days after consuming infected fish (Mattiucci et al., 2013).

Alleragic Anisakiasis: Allergic Anisakiasis occurs when allergens from parasite's larvae (whether alive or dead) trigger an allergic reaction in the host. Symptoms can range from urticaria and angioedemas to anaphylaxis (Audícana et al., 2002). These reactions typically manifest within the first hour after eating the infected fish. While it remains unclear if dead larvae (resulting from cooking or freezing) can initially sensitize individuals, evidence suggests that sensitization occurs through contact with live larvae. However, once sensitized, individuals may also react allergically to dead larvae (Daschner et al., 2012).

Occupational Anisakiasis: Evidence suggests that occupational allergies including conjunctivitis, asthma, and dermatitis can be caused by *Anisakis simplex* in fishmongers, fishermen, and workers in the fish processing industry (Nieuwenhuizen et al., 2006).

Diagnosis

The diagnosis of Anisakiasis typically relies on the assessment of the patient's symptoms as well as medical history, especially their dietary habits (Bucci et al., 2013). The disease is more commonly suspected in patients with a recent history of consuming raw or undercooked fish (Shimamura et al., 2016). Accurate diagnosis is essential, as it plays a crucial role in determining the clinical management of patients (Repiso et al., 2003). In cases of gastric Anisakiasis, a normal physical check-up may reveal mild tenderness in an epigastric region that might be misdiagnosed as a peptic ulcer. Thus, major diagnostic tests such as upper gastrointestinal endoscopy are advised to diagnose gastric Anisakiasis (Sasaki et al., 2003). Upper GI endoscopy can locate a slender ~15 mm worm, lodged in enlarged and inflamed gastric mucosa (Kondo, 2018). Intestinal Anisakiasis conditions are rare, its diagnosis is difficult since it causes non-specific symptoms and could be easily mistaken for acute celiopathy, intestinal blockage, peritonitis, or appendicitis. Diagnosis also becomes complex due to the small intestine's location, which makes it usually unreachable through endoscopic procedures. In some circumstances, exploratory laparotomy may be required to confirm the diagnoses (Takei & Powell, 2007). Other methods like double-balloon enteroscopy or capsule endoscopy are also being used, although these procedures are invasive and can cause certain complications. CT scans can diagnose tenderness and edema of the small intestine (Table 1) (Matsuo et al., 2006), while ultrasound can reveal high levels of local ascites and edema (Shrestha et al., 2014). Laboratory tests for Anisakiasis may show mild to severe leukocytosis and increased C-reactive protein levels (an inflammatory marker) in the blood, though peripheral eosinophilia is uncommon (Carmo et al., 2017). Anisakiasis can also be diagnosed using serological assays to identify anti-Anisakis-specific IgA, IgG, or IgE antibodies, with sensitivities varying from 70% to 80%. However, their effectiveness may be hindered by antigenic cross-reactivity with other similar nematodes and the results may take several days. While serological tests are not effective for invasive Anisakiasis, they are the most effective for diagnosing *Anisakis* allergy (Cong & Elsheikha, 2021).

Treatment

The *Anisakis* larva attached to the gastric wall is typically removed through endoscopy, which often resolves the condition without requiring additional pharmacological intervention (Noh et al., 2003). Conservative treatment generally leads to an improvement in clinical conditions, with acute inflammation resolving within 2-3 weeks. In cases of intestinal *Anisakiasis*, administering an isotonic glucose solution is the preferred approach. Surgical treatment becomes necessary in serious cases linked to intestinal strangulation and segmental stenosis (Matsuo et al., 2006). Patients may also require surgery when their intestinal symptoms are mistakenly diagnosed as intestinal obstructions or acute abdominal issues. Currently, Albendazole and ivermectin have been proven to be effective treatments for Anisakiasis (Moore et al., 2002).

Prevention and Control Measures

Preventing Anisakiasis involves avoiding the ingestion of raw or minimally cooked fish and seafood, as these can carry live *Anisakis* larvae (EFSA-BIOHAZ, 2010). Cooking fish at >60°C for one minute or freezing it at -20°C for ≥24 hours or − 35 °C for > 15 hours effectively kills parasites, though allergic reactions may still occur due to thermostable allergens (European Commission, 2011). Implementing personal and regulatory activities, as well as food-safety procedures, such as inspecting imported and local fish and their products, will aid in control efforts (Gómez-Morales et al., 2018). Public health measures include early evisceration of fish, visual inspections for parasites, and the use of advanced detection methods like UV transillumination or pepsin digestion (Celano et al., 2013). Risk elimination must be achieved through public education and therefore proper fish preparation, cooking, and freezing should be taught to the consumers (Caballero et al., 2004; Vidaček et al., 2011).

Conclusion

In conclusion, Anisakiasis primarily impacts human health and food safety, which calls for the need for health controls of Anisakiasis risks from animal health authorities, public health sectors, and the fishing industry to better understand matters concerning seafood-borne parasitic diseases and the potential solutions. Reliable diagnostic approaches, properly organized fish handling and preparation information, and enhanced food safety measures are vital requirements for controlling risks associated with *Anisakis* infections and allergies. Giving a higher priority to improved diagnostics to fix misdiagnosis issues and to enhance the parasite detection and removal protocols will make research further ahead. Broad-spectrum approaches, and higher sensitization are crucial to ensure that there are minimum negative effects on public health from Anisakiasis all over the world as well as getting better seafood products across the globe.

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