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REVIEW ARTICLE

Potential of Anisakiasis in Foodborne Zoonosis

Liliana Aguilar-Marcelino[1], Carlos Ramón Bautista-Garfias[1], Tean Zaheer[2], Amber Maqsood*[3], Shameeran Salman Ismael Bamarni[4], Bland Husamuldeen Abdullah[5], Ashraf Zaman Faruk[6], Muhammad Salman[2], Tayyaba Akhtar[7], Wajiha[8], Fernando Edgar Marinez Silva[9] and Riaz Hussain*[10]

[1]National Center for Disciplinary Research in Animal Health and Safety (INIFAP), Km 11 Federal Road Cuernavaca-Cuautla, Jiutepec 62550, MR, Mexico
[2]Department of Parasitology, Faculty of Veterinary Science, University of Agriculture, Faisalabad, Pakistan
[3]Department of Zoology, Faculty of Sciences, University of Agriculture, Faisalabad, Pakistan
[4]Department of Medical Laboratories Sciences, College of Health Sciences, University of Duhok, Iraq, Iraq
[5]Department of Medical Microbiology, College of Health Sciences, University of Duhok, Iraq
[6]Department of Livestock Services, Ministry of Fisheries and Livestock, Bangladesh
[7]KBCMA College of Veterinary and Animal Sciences, Narowal, Sub-Campus UVAS-Lahore, Pakistan
[8]Department of Zoology, Faculty of Biological Sciences, Quaid I Azam University, Islamabad, Pakistan
[9]Instituto Nacional de Investigaciones Forestales, Agricolas y Pecuarias (INIFAP), Mexico
[10]Department of Pathology, The Islamia University of Bahawalpur, Pakistan
*Corresponding author: ambermaqsood667@gmail.com (AM); driazhussain@yahoo.com (RH)

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ABSTRACT

Seafood is an essential part of nutrient acquisition and is considered a staple food in areas located nearby water bodies. The potential pathogens associated with seafood consumption are often neglected to make foodborne zoonosis more likely to occur. Anisakiasis resulting from infected nematodes *Anisakis* has worldwide distribution including developing continents like Asia (China, Japan, Korea and Bangladesh) and some developed areas like the Netherlands and the United States. Despite a global burden of morbidities and fatalities, Anisakiasis remains a neglected zoonotic disease. The intensity and distribution of disease rise owing to the consumption of different kinds of raw or improperly cooked seafood like sushi etc. There is no proper treatment for Anisakiasis owing to the delays in reaching out for medical opinions. Keeping in view the gaps in Anisakiasis research and surveillance, we should improve the treatment with medicine, surgery, and essential oil and curtail the transmission of diseases from parasites to humans. There are gaps in the existing information on the epidemiological significance of the so far known species of *Anisakis*, both in their natural and accidental host-like human population worldwide. This review signifies the importance of awareness, knowledge of Anisakiasis among humans and animals from a global viewpoint. A holistic approach by thorough assessment of the rapidly spreading disease Anisakiasis in natural and accidental hosts as well as in marine ecosystems is required to prevent morbidities and mortalities in humans.

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INTRODUCTION

Anisakiasis is a food-borne disease that is caused by the consumption of fish and the etiological agent for this notorious zoonotic disease is a parasite named "Anisakis" (El-Dib *et al.,* 2015; Smaldone *et al.*, 2020). *Anisakis* nematodes are present worldwide affecting a wide range of marine animals and humans (Andreoletti *et al.*, 2010). Fish having Anisakiasis infection are still being reported to have increased in EU Countries according to databases of the European Union rapid alert system for food and feed (RASFF) (Calderia *et al.*, 2021). It may be directly or indirectly and naturally or accidentally ingested by humans and animals (Hochberg and Hamer, 2010; Shamsi *et al.*, 2019). This nematode transmission is not only by food consumption, but it also occurs by infected larvae transmitted to the human or animal body. In humans, larvae inhabit the stomach and intestinal wall of host organisms and are transmitted by raw food, inadequately cooked seafood (Sohn and Murrell, 2011) and contaminated preserved seafood, pickled, salted, marinated, broiled, baked, or smoky fish which do not destroy the *Anisakis* (Wolfe *et al.*, 2007). *Anisakis simplex* causes allergic reactions (Audicana *et al.*, 2022) like itching, rash, and anaphylaxis (Daschner *et al.*, 2012) in the human body. The infections can be both cutaneous and systemic (Ivanovic *et al.*, 2017) occurring with different frequencies associated with diarrhea, nausea, constipation, abdominal pain, vomiting, fever, respiratory symptoms, etc. (Fazii *et al.*, 2006).

Anisakis larvae being the infective stage, cycle from one host to another. These nematodes increase in numbers when they live in large size and old-aged organisms (Smith and Wotten, 1978). *Anisakis spp.* complete their life stages in the stomachs of humans and animals where a lot of mucus is present. Unembryonated eggs of *Anisakis* may be released in fecal matter through the definitive host (Danson *et al.*, 2003). When these unembryonated eggs are transmitted to water, they are converted into embryonated eggs and generate 3rd stage free-swimming larvae of *Anisakis* (Nieuwenhuizen and Lopata, 2013). Crustaceans consume these larvae which grow in the hemocoel. Fish and cephalopod's paratenic larvae consume these infected crustaceans (Anderson, 2000) and after this, the larvae move in the digestive system. Humans do not have any crucial role in the parasite developmental cycles other than being affected as an incidental host. Due to some serious symptoms of disease, the human infection remains untreated because there is no specific medicine for any larval stage that's why the parasite itself becomes hard to prevent.

The *Anisakis* cases (Suzuki *et al.*, 2010) continue to increase in Asian countries including China, Japan, Korea, and Bangladesh, and many areas of technologically advanced countries like the United States and the Netherlands. *Anisakis* shows severe infection (Cong and Elsheikha, 2021) in high numbers of animal hosts. Anisakiasis disease damages the stomach, body wall, and intestine of human and animal hosts because these larvae (Endiputra *et al.,* 2019) can survive at low temperatures and undercooked or raw seafood. Anisakiasis could be caused by the transport of seafood, hoteling, marinating, vinegar dipped, smoky or frozen seafood, infected skin, and some seasonal changes encouraging the emergence or re-emergence of the parasite larvae. *Anisakis* can affect those people who intake seafood in large quantities. Anisakiasis is an endemic infection being recognized at least 20-25 years old parasitic disease illness which has been neglected for a long time. This is ignored due to limited information, and lack of awareness about the parasite and its life cycle and way of transmission that's why people of endemic areas still consume inadequately cooked and raw seafood. Larvae of *Anisakis* can be medically treated by Albendazole (it cannot be used in a 6 months old baby and used at least in 1-year-old baby). In pregnant women (Cong and Elsheikha, 2021), it may cause some teratogenic effects, and the exact effect of medicine on lactating females is completely unknown.

The host and parasite relationship: Parasite species require more than one host animal for the completion of their life cycle (Stryinski, 2022). Because these parasites cannot survive without any host as well as the presence of parasites harms their host animal. Here we discuss Anisakis *spp.* which causes disease by attaching to the wall of stomach, intestine and esophagus (Cong and Elsheikha, 2021). *Anisakis* is mostly seen in Japan (Yorimitsu, 2013), China (Qin, 2013), Europe, South America, the Netherlands, Taiwan (Li, 2015), Spain, and Korea (Sohn *et al.*, 2015) and it has a wide global prevalence. In all these countries, the cases of *Anisakis prevailed*, and the first case was reported in the Netherlands (Van *et al.*, 1960). A summary of the global prevalence of *Anisakis* species has been given in Table 1. The prevalence of the fish zoonotic disease varies seasonally but should be regularly monitored for evaluation in the fish population. *Anisakis* was reported to have approximately 7700-8320 cases per year in the Spanish region (Bao *et al.*, 2017) and WHO estimated approximately 56 million cases reported as fish parasites due to consumption of infected seafood (WHO, 2012). The safety aspects such as the potential transmission of zoonotic diseases play a vital role in human health (Debeneditti *et al.*, 2019). *Anisakis* is endemic in Asia and Western Europe, where most of the cases are reported from Japan and the remaining cases have been reported mainly in Germany, France, Netherlands and Spain.

Anisakis larvae need a host for survival and evenly complete their life cycle stages. These larvae move from one host to another and increase their numbers in apparently healthy as well as in older animals (Smith and Wotten, 1978; Jabbar *et al*., 2013). The larvae complete their life cycle in host's stomach or intestine or body wall and the female adult lays eggs in the stomach. Then host animals expel (Danson *et al.*, 2003) these eggs out in their excreta. When the eggs come in contact with water (Endiputra*et al.,* 2019) then they are converted into developmental larval stages like L1 to L3 (non-infected free-swimming larvae). Another possible pathway for transmission could be that the eggs are eaten by intermediate hosts (EFSA-BIOHAZ, 2010; Levsen and Karl, 2014) crustaceans (copepods, decapods, isopods, amphipods, euphausiidae) and some mollusks as hosts. At this stage, larvae are swallowed by crustaceans and then larvae start growing in crustaceans' hemocoel (Anderson *et al*., 2000). These L3 larvae are eaten by fish and transfer to the next host from the stomach to the intestine or muscular tissues and invade walls through penetration in the intestinal mucosa. *Anisakis* larvae cause destructive effects on animal hosts (World health organization, 2011). Some factors drive the major risk of disease transmission of parasites in the host. These competent hosts are widespread across geographical areas and different ecosystems (Kapel *et al*., 2006).

Symptoms: Anisakiasis is a global ailment with having an increasingly high spread of disease and has been reported in Japan (Yorimitsu, 2013), Germany (EFSA-BIOHAZ, 2010), Korea (Sohn *et al*., 2015), Italy (Mattiucci *et al*., 2013), China (Qin, 2013), Taiwan (Li, 2015), Spain and Netherland. The symptom arises for the first time which shows the presence of *Anisakis* larvae diagnosed in the Netherlands 1955–59 (Van *et al*., 1960).

Table 1: Summary of the global prevalence of Anisakiasis

Parasite species	Country of report	Method of identification	Clinical findings/ Site of sample collection	Zoonotic importance	Reference
Anisakis L3 *A.pegreffii*, *A. typica* and *A. simplex* (*sensustricto*) × *A. pegreffii*	China	PCR gene/protein (ITS1-5.8S-ITS2)	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 (ITS1-5.8S-ITS2)	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	Esophagogastro-Duodenoscopy (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
Anisakis larvae	Caucasia	Abdominal computed Tomography (CT)	Intestinal mucosa	Yes	Ishii *et al*., 1989
A. typica	China	Colonoscopy	Stomach	Yes	Soewarlan*et al*., 2015
Anisakis larvae	Japan	Morphological identification	Body cavity and liver	May be	Li *et al*., 2017
A. pegreffii Hybrid genotype (A. pegreffii+ A. simplex)	Taiwan	Morphological and PCR- RFLP	Fish fillets	Yes	Sonko *et al*., 2019
A. simplex	Italy	Colonoscopy	Caecum	Yes	Choi *et at*., 2009
A. typica	Italy	Microscopic	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 Esmaeili*et al*., 2021
A. pegreffii	China	Morphological identification	Chronic and inflammatory cells	May be	Vergis*et al*., 2021
A. typica	Brazil	PCR-RFLP	Muscles	Yes	Palm *et al*., 2008

The most common symptoms shown (Fig. 1) are the presence of severe abdominal pain, nausea, vomiting, diarrhea, intestinal pain, allergic reactions like itching, reaction with rash, blood or mucous in stool, mild fever, angioedema, bronchospasm, respiratory issues, and eventually anaphylactic shocks (Pulido *et al*., 2000). All these symptoms are shown after the consumption of infected fish containing larval stages.

Marine mammals release eggs of Anisakis along with their feces into the water which ultimately hatch to release free-swimming Larvae into the water. These larvae are then ingested by crustaceans which are eaten by bigger preying marine animals (paratenic hosts). L3 larvae migrate into the body tissues of these marine animals. These marine animals are further hunted and eaten by the Marine mammals (definitive hosts) completing the life cycle of the parasite (Fig. 2). If humans consume uncooked or raw meat of the paratenic or definitive hosts, the condition turns out to be zoonotic (Anisakiasis).

Risk factors: *Anisakis* exposure has already been linked to a higher risk of diseases, and a recent study of *Anisakis* infection has been shown to pose a greater risk of stomach or colon cancer (Garcia-Perez *et al.,* 2015). There are some risk factors (Fig. 3) based on fish characteristics (Meladineo *et al*., 2014) for Anisakiasis like fish weight, fishing area, habits and habitat of fish, fish gonad weight, seasonal changes and their effects on fish infected larvae, eating of infected skin cells, eating of Carpaccio and sushi (Abattouy *et al.*, 2011) raw seafood and consumption of lower weighted fish. In the area of higher seafood consumption, increasing risk factors of Anisakiasis disease (Mladineo *et al.*, 2014) may be attributed to the procedure and type of storage/cooking approaches of seafood, for instance, even in the salted, caned, smoky, frozen, marinated fish (Karl *et al*., 1995), the *Anisakis spp.* are not killed at low temperature and through inadequate cooking practices (Reino *et al.*, 2015). The infection may be caused by removal of any infectious skin or wound, dead bodies like some killed animals and aborted remains, packing, fishing, export from one place to another, shipping, hoteling, temperature/seasonal changes e.g., moisture, humidity, drought, raining etc. Some of the important approaches to prevent food-borne Anisakiasis in different fish species have been summarized in Table 2.

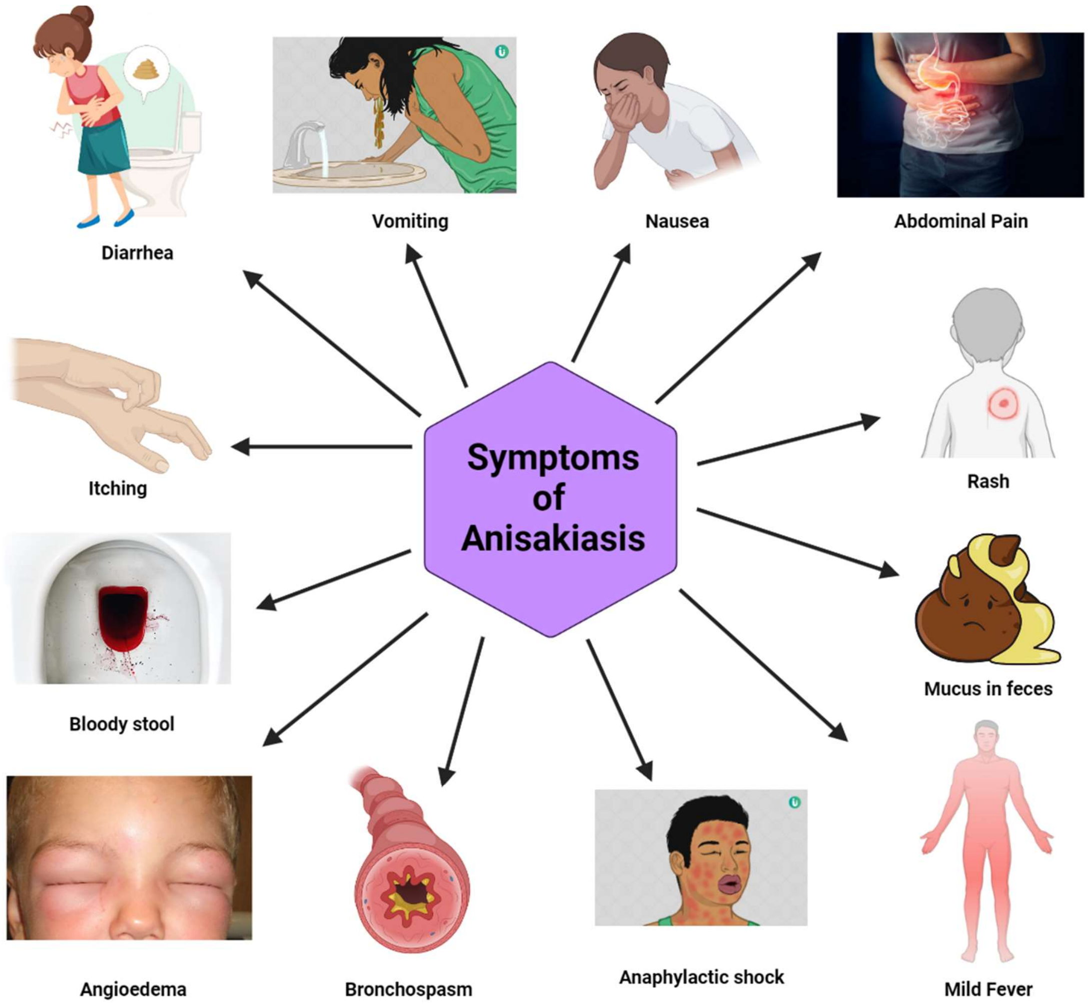

Fig. 1: Symptoms of Anisakiasis after consumption of seafood.

Table 2: Summary of approaches to prevent food-borne Anisakiasis in different fish species

Fish	Treatment	Parameters	References
Herring	Salting	5% NaCl, > 17 weeks	Karl *et al*., 2018
		8 to 9% NaCl, 6 weeks	Lorenzo *et al.,* 2000
	Marinating	28 days in brine, 6.3% NaCl, 3.7% acetic acid	Karl *et al*., 2018
	Irradiation	6 to 10 kGy	Soewarlan *et al*., 2015
Stocky salmon	Freezing	–35°C for 15 h, then –18°C for 24 h	Wharton and Aalders, 2002
King salmon	High pressure	414 MPa for 30 to 60 s	Mladineo *et al.,* 2012
		276 MPa for 90 to 180 s	
		207 MPa for 180 s	
Anchovies	Marinating	10% acetic acid, 12% NaCl for ≥ 5 days	Lorenzo *et al.,* 2000
		2.4% acetic acid, 6% NaCl for 35 days	
		10% acetic acid, 12% NaCl for 5 days	

Diagnosis: The first case was reported (Van *et al*., 1960) in coastal areas of Japan, Korea due to feeding habits of undercooked food and raw seafood. *Anisakis* larvae cause infections (Mattiucci *et al*., 2018) and allergic sensitivity. Due to these feeding habits, thousands of clinical cases were reported in western countries like North America (Stallone *et al*., 1996) including Canada. Soewarlan *et al.* (2015) reported a case of *Anisakis* larvae in a 50 years old person which had shown symptoms like vomiting, a hard gastric pain one hour after eating salmon.

Computed Tomography scan (CT): CT scan has been used for quick examination as well as in emergency cases of internal injury (Eslami *et al*., 2011) and any other trauma. CT scans can also be utilized for diagnosis, medicinal plans and treatments including both the surgical and radiation methods for almost all parts of the body. With some recent techniques development (Kasai *et al*., 2021), computed tomography diagnosis of bowel obstructions has been expanded but not allowed accurate diagnosis in the cases of incomplete obstructions. In a study (Yasunaga *et al*., 2010), scanning performed thinner sections and multi-planar image reformation suggested during the test together by intravenous injection. A thickening of the distal small bowel walls (Yasunaga *et al*., 2010), hyper-enhanced mucosa, mural stratification,

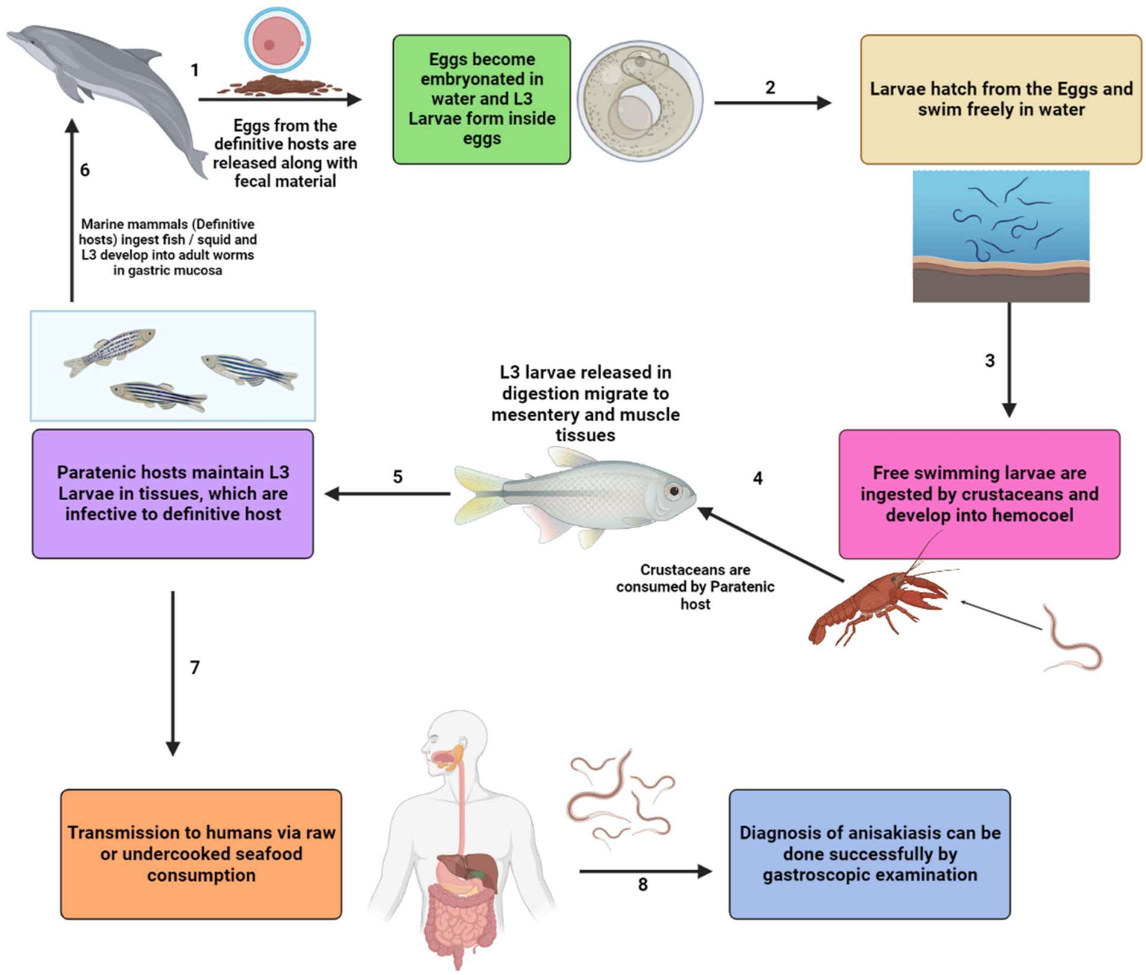

Fig. 2: Life cycle of *Anisakis simplex* in fish and way of transmission in human and animals.

fluid accumulation within dilated small-bowel loops, and hyperemia of intestinal veins were all seen by CT scanning. This case predominantly reported on males rather than females due to feeding habits e.g., sushi (Van *et al*., 1960). It has been noted that a large percentage of cases exhibits wall thickening and noticed that submucosal edema of the affected segments, creating the appearance of a target, this can be particularly dramatic in the stomach (Caramello *et al*., 2003), where thickening is linked to gastric folds attached with the wall.

Polymerase Chain Reactions (PCR): PCR is a technique used in the laboratory to make millions of copies of a particular section of DNA (Wang *et al*., 2022). In fact, there are currently specific and quick DNA assay tests available to be performed on fragments of larval nematodes and bioptic tissues removed by endoscopy, as well as on parasites embedded in paraffin (Yuan *et al*., 2006). These tests include reverse transcription-polymerase chain reaction primers-probe systems. In addition, the Immunoblotting assay of the patient's serum has been suggested for use in conjunction with anamnesis examination of the patient and application of the molecular technique for apt diagnosis of anisakiasis. Later studies revealed that morphological identification alone was insufficient for nematode taxonomy, as evidenced by a number of examinations. *Anisakis* nematodes recovered from human, fish and frozen samples as well as soil nematodes could be identified using this identification method (Saunders, 2004). Finding and choosing a pertinent DNA region (genetic marker) is essential, the small (18S rRNA) and large subunits (28S rRNA) of ribosomal RNA were also used for *Anisakis* using ribosomal DNA sequencing like ITS1, ITS2, and others. To enhance the number of genetic markers, PCR can be used in conjugation with other techniques. Real-time PCR is regarded as a sensitive and accurate tool (Pontes *et al*., 2005) for suspected cases (Palm *et al*., 2008) of diagnosing *Anisakis* infection (Arias-Godinez *et al*., 2019).

Ultrasound imaging: Ultrasound produces an image of the internal structure of the body using sound waves. It not only helps in the diagnosis of most anomalies through physiological organ visualization but also helps to guide biopsy procedures (Ripollés *et al*., 2020). Ultrasound is a relatively safe diagnosis and is non-invasive. Anisakiasis should be diagnosed by a radiologist using ultrasound findings of wall thickening, particularly segmental edema owing to hyper peristalsis and dilation of small bowel loops close to the afflicted segment and hyperemia could be visualized with the help of color doppler ultrasound (Masaki *et al*., 2020). In clinical studies, ribbon-like objects that are moving freely inside the intestinal tract

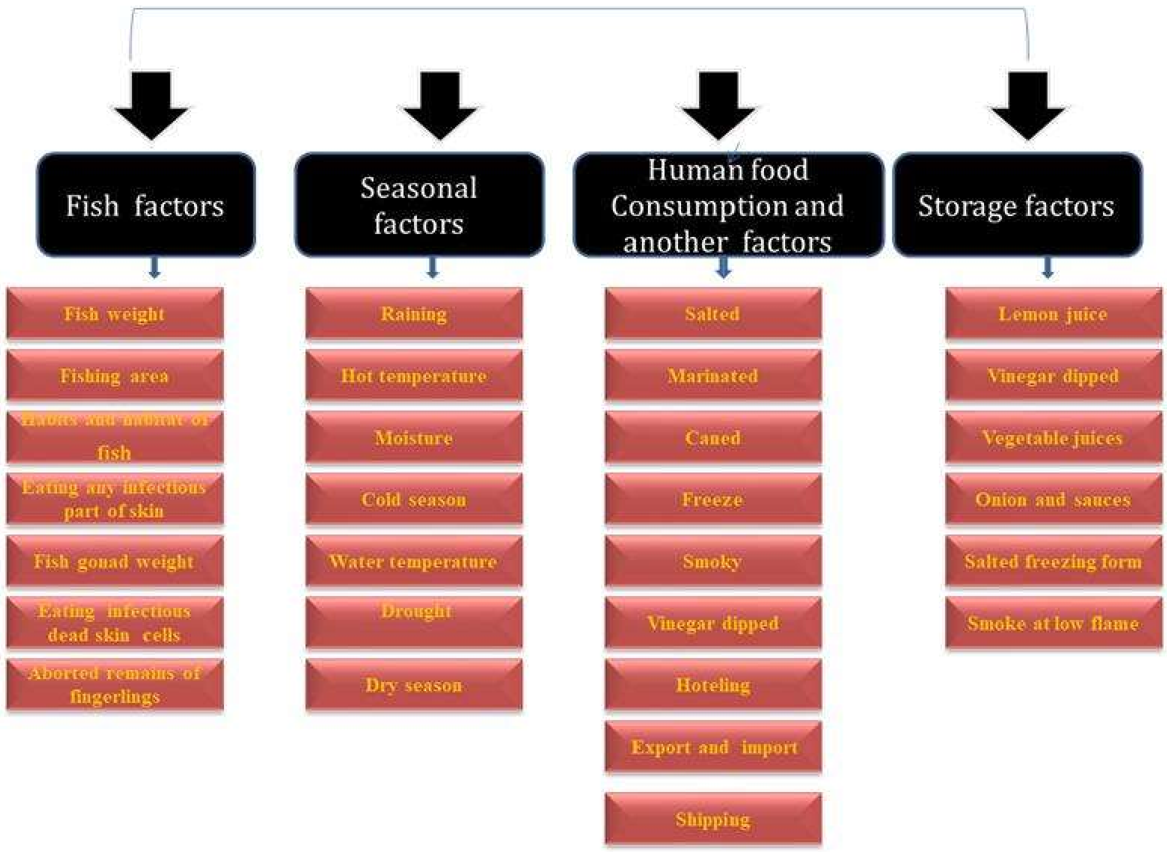

Fig. 3: Flow sheet diagram showing some factors having risk for Anisakiasis.

and may be seen during abdominal ultrasonography, indicative of *Anisakis*. Since the *Anisakis* nematode utilizes scolex to parasitize the intestinal mucosa not only in the terminal ileum and ileocecal valve but also in the jejunum, gastroduodenoscopy and colonoscopy may fail to reach the predilection site having scolex (Cong and Elsheikha, 2021). This makes it challenging to decide whether additional anthelmintics therapy is required to get rid of the residual nematode portion that includes the scolex. If additional therapy is required, capsule endoscopy which can find the scolex of nematodes in the jejunum may be utilized. Following capsule endoscopy, the patient would require further anthelmintic therapy (Rodríguez *et al*., 2017) to fully recover from diphyllobothriasis and eliminate the entire nematode, including scolex (Cong and Elsheikha, 2021).

Upper endoscopy: Upper endoscopy is also called esophagogastroduodenoscopy (EGD). It is a long, thin, and flexible tube with a smart camera at the distal end. The technique provides us with high quality images used for examination of the throat, esophagus, stomach, rectum and colon. Newer modification to this is the use of wireless endoscopy pill camera, that pill is swallowed by the patient, due to its size aiding the visualization at different positions of the digestive tract (Kapral *et al*., 2009). During this time that capsule containing an endoscope captures 50 to 60 thousand tract images. An endoscope also offers an opportunity to collect tissue samples (biopsy) to test for diseases and conditions that may be causing anemia, bleeding, inflammation or diarrhea (Vaughan *et al*., 2015). It can also detect some cancers of the upper digestive system. A study suggested that treatment of enteric Anisakiasis could be done with endoscopic extraction of *Anisakis* larvae using double-balloon enteroscopy (Berasategui *et al*., 2011).

Colonoscopy: Colonoscopy is a non-surgical technique having a flexible tube fixed smart camera at the distal end, inserted through the rectum which is used frequently for examination of cancer and gastrointestinal bleeding, lining of the large intestine, colon (Pons *et al*., 2015) and rectum. Colonoscopy, widely regarded as the most accurate way to find colorectal cancer, provides us with a close view. Precancerous polyp removal during a colonoscopy can entirely prevent colorectal cancer as all colorectal cancer starts with these polyps (Nieuwenhuizen and Lopata, 2013). In a study, the clinical case appeared in 58 years old woman being hospitalized at an emergency in Italy with right-side abdominal pain after consumption of raw marinated seafood it was diagnosed by colonoscopy at the caecum area and showed live larvae almost of 2.5cm (Soewarlan *et al.*, 2015).

Serological testing: Serological testing is a simple, reliable, accurate, and easy way of diagnosis (Daschner *et al*., 2012) of intestinal and gastric Anisakiasis larvae and adult stages (Fiorenza *et al*., 2020). In this method, blood samples of patients are procured (Caldeira *et al*., 2021) for testing serum in the laboratory. The clinical history may

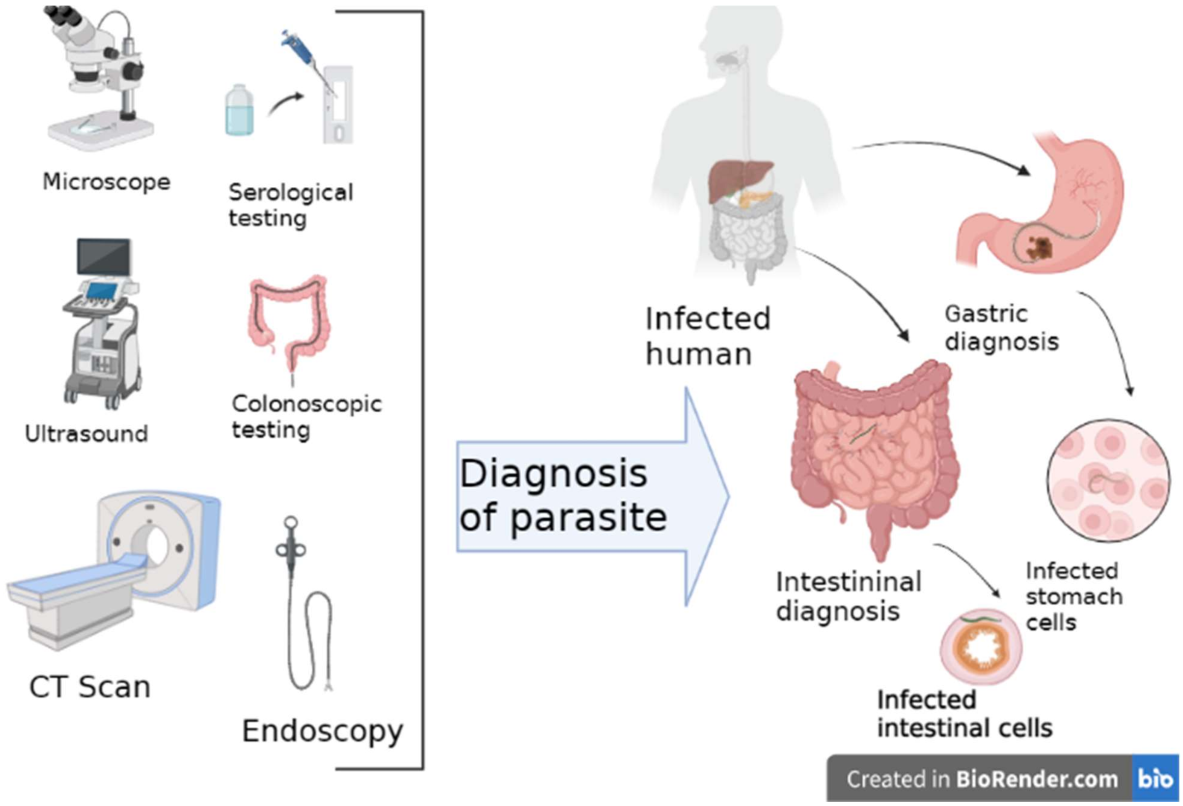

Fig. 4: Diagnostic techniques used for diagnosis of parasite *Anisakis.*

be less clear in chronic patients like chronic urticaria, contact dermatitis, asthma, and rhino conjunctivitis. A better diagnostic test (Moneo *et al*., 2017) would be used for allergens of *Anisakis* which does not appear in cross-react specie, but these allergens are associated with the cooking reactions, and this approach aided with some dietary prescriptions (Choi *et al*., 2009).

Microscope-assisted diagnosis: The visualization by microscope is frequently used to support the results of other tests (Serrano *et al*., 2000) or to provide details for the diagnosis of *Anisakis spp*. Larvae were identified by microscopic inspection of segments as having helminths sections in the muscle layer that were surrounded by acute inflammatory cells (granulocytes and eosinophils) and diffuse interstitial edema (Caramello *et al*., 2003). Seven days prior to admission, a history of consuming fish that was insufficiently cooked was noted. Another clinical case was reported in Italy (35 year old man) after 2 to 3 days of consumption of raw seafood with some symptoms of abdominal pain, nausea, fever, and some intestinal issues, and it was diagnosed microscopically (Couture *et al*., 2003). Microscopy helps in better visualization of nematode morphology and is considered a common and easy-to-use approach among all others.

Treatment of anisakiasis: The surgical treatment for *Anisakis* infection is removing all the larvae found in the digestive tract during the endoscopic inspection, either by gastroscopy or colonoscopy depending on the affected zone (Audicana and Kennedy, 2008). Albendazole is the most commonly used medication; others include thiabendazole, flubendazole, and ivermectin, though none of these are totally effective (Shimamura *et al*., 2016). There is no single approved anthelmintic known to control all stages of *Anisakis*. But in these situations, no pharmacological treatment is necessary because endoscopy enables the prompt removal of the larvae, which improves the patient's condition within a few hours. By removing the worm using an endoscope, stomach Anisakiasis can frequently be diagnosed and treated (Hochberg and Hamer, 2010). Intestinal mucosa Anisakiasis is more challenging to diagnose, but it can typically be handled without removing the worm because it will eventually die (Yasunaga *et al*., 2010). When intestinal blockage appears, appendicitis or peritonitis (Pacios *et al*., 2005) may occur, and surgery may be necessary to treat intestinal or extra-intestinal illnesses. For instance with presumptive (very suggestive history and serology) diagnosis, treatment of Anisakiasis with Albendazole (400 mg orally twice daily for 6 to 21 days) has been observed to be effective (Hochberg and Hamer, 2010). The World Health Organization (WHO) permits the use of Albendazole but it is not FDA-approved for this indication. Oral albendazole is available for human use in the United States. Despite the lack of information on albendazole usage during pregnancy, the evidence that is now available does not support any differences in congenital defects between children born to mothers who unintentionally received albendazole during mass preventive efforts and those who did not use (Endiputra *et al.,* 2019). It is important to weigh the danger of treatment as well as the risk of illness development in pregnant women who are known to have an infection. Some studies showed thenegative impact of drugs on fetuses (teratogene) of humans and animals used during pregnancy. It has also been reported that albendazole is not safe for kids at the age of six months or one-year-old (Stryinski, 2022).

Other therapeutic options: Some studies advise a conservative approach using fluid therapy and antibiotics when the larva is found in regions of the bowel that are otherwise difficult to access (Audicana and Kennedy, 2008; Shrestha *et al*., 2014). However, occasionally a laparotomy and excision of the impacted intestinal piece are necessary '*Anisakis*' allergy needs to be addressed right away, and the patient is advised to avoid consuming inadequately cooked seafood (Petithory, 2007). An injectable dose of adrenaline must be given to allergic individuals suspected of experiencing anaphylactic shock in order to prepare for the possibility, and if it does, they must be immediately referred to a hospital (Audicana and Kennedy, 2008).

Double balloon enteroscopy: Enteric Anisakiasis can be treated by collecting *Anisakis* larvae using endoscopic extraction employing double-balloon enteroscopy via the anal route (Amano *et al*., 2013). Double balloon enteroscopy is not frequently done and warrants a high level of competence. Although using steroids and an anti-allergic medication like stronger Neo-Mino phage C is effective, it is only one of the conventional therapies and is not a radical cure (Ramos *et al*., 2005; Yamamoto *et al*., 2012). In order to determine the best method of prophylaxis, Kasuya and coworkers (Kasuya *et al*., 1998) investigated the killing effects of foods like *Perilla frutescens*, viridis Makino, *Zingiber officinale*, *Wasabia japonica*, *Ilium sativa*, and ethanol. They found that these foods were effective in curtailing the motility of the worms *in vitro* (Yasunaga *et al*., 2010). Regarded as effective as a prophylactic, these proposed things would need to be ingested in excessive amounts.

Gastrografin: It is secure, practicable, and efficient to remove enteric *Anisakis* larvae using gastrografin administration therapy. In some documented cases (Yasunaga *et al*., 2010), using gastrografin over the wound has helped people with gastric Anisakiasis; the effect on enteric Anisakiasis is less evident (Amano *et al*., 2013). The use of gastrografin treatment, however, has been shown to be effective in the management of *Taenia saginata* and other gastrointestinal tapeworm infections (Yamamoto *et al*., 2012). Gastrografin is a diatrizoate, a three-iodine molecule that is water-soluble and present in a 76% solution. It contains 66% meglumine salt solution and 10% sodium salt solution. It is a hypertonic solution with a specific gravity between 1.416 and 1.420, a pH range between 6.0 and 7.7, an iodine concentration of 370 mg/mL, and an osmotic pressure of 1900 mmol/L (Yamamoto *et al*., 2012). High osmotic pressure in gastrografin frequently results in diarrhea in those with upper gastrointestinal symptoms. It seems that the extraction of *Anisakis* larvae is brought by this purgative impact (Shibata *et al*., 2014). Thus, the administration of gastrografin is the most practical and helpful therapy out of the known treatment choices (Sasaki *et al*., 2003).

Prevention from Anisakiasis: For prevention from Anisakiasis in humans, vaccines that have the ability to control the infectious disease could be utilized (Mattiucci *et al.*, 2018). Albendazol is used for prevention from Anisakiasis in both children and old aged people. It is used orally 400 mg twice daily for 6 to 21 days in old person and 2 years old children. According to European Commission (EC), fish freezing at -20°C for 24 hours is used for commercial purpose (European Commission, 2004). Fresh meat should be adequately cleaned (World health organization, 2011) and for dry seafood, some acetic acid may be used to prevent the chances of nematode survival. For aquaculture or intensive seafood farming, the use of chlorine solutions, NaCl solution and some sugar solutions (Smaldone *et al.*, 2017) for the prevention of disease (Mattiucci *et al.*, 2018) and infection in fish/seafood could be done (Sanchez *et al*., 2005). Frozen preservation may adversely impact the fish protein and the texture of seafood muscle that's why other ways for the proper preservation of fish are recommended in conjunction with the visual inspection of the fish for *Anisakis* (European Commission, 2011). There is a great challenge for food preservation technology in developing methods to preserve the fish that keeps their composition closest to that of nature. There are some methods of preventing foodborne Anisakiasis such as.

Non-Thermal Atmospheric Plasma (NTAP): By providing a gas with high energy, brought about by the use of lasers, shock waves, electric arcs, electrical and magnetic fields, the plasma has the ability to create artificial conditions favorable for meat preservation. Plasma generates an ambient pressure and the temperature depends on the conditions in which plasma is produced, leading to the formation of atmospheric plasma which may be thermal or non-thermal (NTAP)(Authority, 2017; EFSA, 2019).Evidently, a wide range of factors could be attributed that can possibly impact meat quality while preservation, notably voltage, frequency, treatment time, working gas composition (WGC), post-treatment effects, and sample area exposed to the plasma system etc. (Olatunde and Benjakul, 2018; Kulawik and Kumar, 2019).

Pulsed light: Pulsed Light technology is a non-thermal technology, where decontamination of foods (Wenming *et al*., 2022) such as fruit juices, meat products, vegetables, and fruits are achieved by using high-intensity light pulses for a short duration of time (Soro *et al*., 2022). The basic principle of Pulsed Light technology is the application of short pulses possessing high-intensity electric fields (in the order of 10-80 kV/cm) within the duration of micro to milliseconds. The processing time is calculated by multiplying the number of pulses with effective pulse duration (Luksiene *et al.*, 2013).

Ultrasound waves: In the food market, ultrasound is one of the top non-thermal techniques that are proven to be extremely efficient (World health organization, 2011) for processes like freezing, cutting, drying, blending, foaming, and extraction. It has also been suggested as an alternative for heat treatments to inhibit microbial growth more recently. In the food industries, low energy, high frequency (16-100 kHz) ultrasonic waves are utilized. Any system used for US production has three main components: 1) a current generator that gives the transducer with energy at a specific frequency 2) a transducer or converter that transfers mechanical stress (pressure waves) through one probe using electrical energy 3) a probe that increases the continuous or irregular vibration created by ultrasonic location (Ripolles *et al*., 2020). A study showed that by following FDA guidelines, living larvae could be eliminated (Adams *et al.*, 2005).

Cold plasma: Cold plasma (CP) is a non-thermal, contemporary food preservation technique intended for inactivating pathogenic bacteria in meats, poultry, fruits, and vegetables. Nematodes might be problematic, particularly if they are consumed raw or with little processing such as in sushi, sashimi, or cold smoked foods (Shamsi *et al.,* 2019; Kulawik and Dordevi, 2022). With some exceptions of recent studies, authors found a 0.8-2 log inactivation of CP (Craighead *et al*., 2020), and there are hardly any reports on the impact of CP on food parasites (Bermudez-Aguirre, 2020). After 0.5-3 minutes of plasma jet CP treatment, oocysts were found on coriander leaves. Nevertheless, this one study found that CP can affect parasite viability, though it may have a less significant impact than high hydrostatic pressure. Since the efficiency of CP depends upon the CP setting utilized, some more studies are required to effectively assess the potential for employing CP to reduce the parasite burden in contaminated food.

High hydrostatic pressure: Some parasites, such as *Anisakis simplex*, appears to be in-active by high hydrostatic pressure (HHP),it frequently requires treatment lengths of at least 5 minutes and pressures of at least 300 MPa to achieve complete inactivation (Franssen *et al*., 2019). Seafood has frequently been mentioned as potential transmission source for this parasite due to the consumption of sporulated oocysts, despite the fact that it does not infect cold-blooded creatures heating (Nayeri *et al*., 2021; Kulawik *et al*., 2022). An established technique for eliminating nematodes in food is heating up to 60°C (Mirza *et al*., 2018). The results from research show that varying levels of pressure and amounts of time for exposure required are different for target pathogens. While some studies claimed that treatment with 300-400 MPa for one minute was sufficient to render oocysts non-infective (Mirza *et al*., 2018). One more study revealed that the treatment with 600MPa for 10-20 minutes was necessary to in activate the parasite in raw and dry cured hams (Gracia *et al*., 2020).

Pulsed electric fields: Pulsed electric field (PEF) processing can inactivate microorganisms. It is a non-thermal food preservation technique. Unlike thermal pasteurization, PEF does not affect vitamins, proteins, and other valuable nutritional and functional components (Tagrida and Benjakul, 2022). The process is based on pulsed electrical currents delivered to a product placed between a set of electrodes; the distance between electrodes is termed as the treatment gap of the PEF chamber. The applied high voltage results in an electric field that causes microbial inactivation (Kanugo*et al*., 2022).

Since HHP, CP, and PEF are frequently used as alternatives to heat treatment, their application may be dangerous if parasitic organisms are present (Rostamabadi *et al*., 2022). Although there is not yet enough information to draw a firm conclusion, it appears that such techniques cannot be used to completely eliminate the risk of parasites in treated food products (Lehel *et al*., 2021; Kulawik and Dordević, 2022). It would be more acceptable to combine those techniques with other well-known treatments targeted at getting rid of parasites, including freezing, in the case of fresh items meant for raw consumption. Given that recent research discovered that freezing alone did not always assure the inactivation of parasites, such a combination, however, might be advantageous (Podolska *et al*., 2019). Seafood can be stored by freezing method at different temperatures. In some studies fish is stored by freezing method e.g.at-4°F (-20°C) freezed meat should be used within 7 days, at -31°F (-35°C) freezed solid seafood and this food should be used within 15 hours. Some food products stored at 20°C,not less than 24 hours, may also be practiced for preventing meat nematodes as proposed by WHO (World health organization, 2011).

Conclusion: The epidemiological impact of *Anisakis* larvae circulating in humans as food-borne disease has been studied in different countries worldwide. The areas of high priority in research regarding *Anisakis* would be its apt diagnosis and prevention of the infection, especially in high-endemic areas. There is an urgency to address the misdiagnosed cases and related diagnostic problems for providing a more affordable estimate for the health of the population at higher risk of contracting *Anisakis* allergies and food-borne infections.

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