

## Fish Borne Trematodes and Zoonosis: An Overview

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### SUMMARY

Fish is an excellent source of minerals including iron, zinc, iodine, magnesium and potassium in addition to being high in calcium and phosphorus. Fish-borne parasitic zoonosis are diseases transferred to humans from fish by parasites. The significance of this health problem has been recognized globally. Fish-borne zoonosis has also resulted from many groups of parasitic organisms, mainly trematodes (flukes), cestodes (tapeworms) and nematodes (roundworms). Humans usually acquire them through raw or undercooked fish consumption. The most prevalent and hazardous fish-borne parasitic infections are those by trematodes parasites, especially Metagonimiasis and Clonorchiasis. Most life cycles involve more than one host-fish, snails and mammals-which complicates their control. Humans get infected when the larvae in the fish are consumed and grow into adult parasites within the body. Control measures are based on the disruption of the life cycle of the parasites by improved sanitation and safe preparation of fish. Freezing and adequate cooking are excellent ways of preventing these infections. However, difficulties persist as the cultural value placed on eating raw fish is quite high and diagnosis often proves problematic because of their often-non-specific symptoms. Countermeasures against fish-borne parasitic zoonosis need to focus on public health activities, food safety regulations and information campaigns that help the general public reduce the occurrence and consequences of these diseases.

### INTRODUCTION

With the increase in the population, food requirements are also increasing day by day. Food scarcity has reached that level where hunger has become life-threatening. It is killing people more than AIDS, TB and malaria collectively every year. On the other hand, about 925 million people are affected with severe malnutrition in developing countries and about 6.6 million children die due to malnutrition every year. More than 2 billion people are fighting malnutrition of dietary micronutrients also (Tacon & Metian, 2013).

Among all the malnutrition of micro and macronutrients, protein deficiency is one of the great concerns. There are many sources of diet that fulfill protein requirements such as chicken, beef, mutton and beans etc., but the consumption of fish has proven a major source to beat malnutrition in many ways. It is rich in protein, omega-3 fatty acid, water and fat-soluble vitamins [Vit-A, B2 (Riboflavin), D, E and Folic acid, etc.]. It is also a rich source of a wide range of minerals including Calcium, zinc, phosphorus, iron, potassium, and magnesium etc. It not only fulfills the deficiency of nutrients but also prevents obesity, cholesterol problem, heart and many other diseases. American Heart Association recommends eating fish twice a week as a part of a healthy diet. It decreases

the risk of mortality due to heart diseases, strokes, myocardial infarctions, and heart failure along with lowering the risk of depression and cognitive decline. It also lowers the risk of several cancers, including multiple myeloma, lung cancer, brain cancer, and gastrointestinal (GI) cancer (Li et al., 2020).

Since 1961 average fish consumption has increased by 3.1% annually. In 2017, consumption of fish reached about 17% of total animal protein (FAO, 2020). Where fish is a healthy addition of our diet and nutrition, it can also have drastic effects on our health. It can cause infections due to our carelessness and wrong eating habits. There are many zoonotic pathogens that can be transferred to humans due to fish consumption (Han et al., 2016; WHO 2020). These zoonotic pathogens could be bacterial, viral, fungal and parasitic (Fig 1). Among all these, parasitic diseases are of great concern because they have caused many outbreaks in history and are still alarming (Rahman et al., 2020).

### FISH-BORNE PARASITIC ZOONOSIS

Fish-borne parasitic pathogens can be transferred to humans by consuming infected fish and fish products. These parasites include nematodes, trematodes, cestodes and protozoans. They can be parasitic internally, invading systemically or attaching themselves to external surface of

fish. The severity of infection caused by a parasite depends upon many factors, such as the type of parasite, its abundance, host's health, behavior, population size, the dynamics of the food web and the coexistence of other pathogenic agents (Lagrué & Poulin, 2015). The infections and lesions caused by fish parasites can also infect other creatures. *Anisakid*, *Metagonimus*, *Gnathostoma*, *Diphyllobothrium*, *Cryptosporidium*, *Giardia*, *Toxoplasma* etc., are some major parasites infecting both commercial fish and squids (Shamsi, 2019, 2021; Chalmers et al., 2020). They can infect the whole flesh, reduce the shelf life of fish meat, and are responsible for the majority of the economic damage and infection in humans.

Parasites in fish are abundant in muscles, coiled in the body cavity, in gonads or gonadal membrane, pyloric caeca and along the intestine. It can be easily detected by cutting the fish flesh and muscles into strips and then by microscopical examination (Svanevik et al., 2014). Larvae can be examined morphologically and with molecular methods to differentiate among different species.

Body discoloration, open sores, reddening of the skin, bleeding, spots on skin, swollen areas, abnormal lumps, or popeyes are some early warning signs of fish with sickness or

parasite infections can be some early signs of infection in fish. Some other signs are weakness, sluggishness, lack of activity, abnormal fish distribution, such as crowding at the surface, inlet, or pond borders, abnormal activity, such as flashing, twisting, whirling, convulsions, loss of buoyancy, loss of appetite or unwillingness to eat are all early symptoms of infection. With proper observation of fish and water testing we can timely stop the spread of infection and treat the fish (Helfrich, 2009).

### FISH-BORNE ZOONOTIC TREMATODE INFECTIONS

Trematodes are a major group of parasites of fish and considered as most pathogenic. It is estimated that more than 18 million infection cases were reported due to the fish-borne parasitic trematodes by the start of new millennium. Fish-borne zoonotic trematodes belong to four families, Opisthorchiidae, Nanophyetidae, Echinostomatidae and Heterophyidae (Hung et al., 2013). About 59 species of zoonotic trematodes are recorded belonging to four families. There are 12 species in the family Opisthorchiidae, also known as liver flukes. One species belongs to Nanophyetidae, 10 species in Echinostomatidae and 36 species belong to

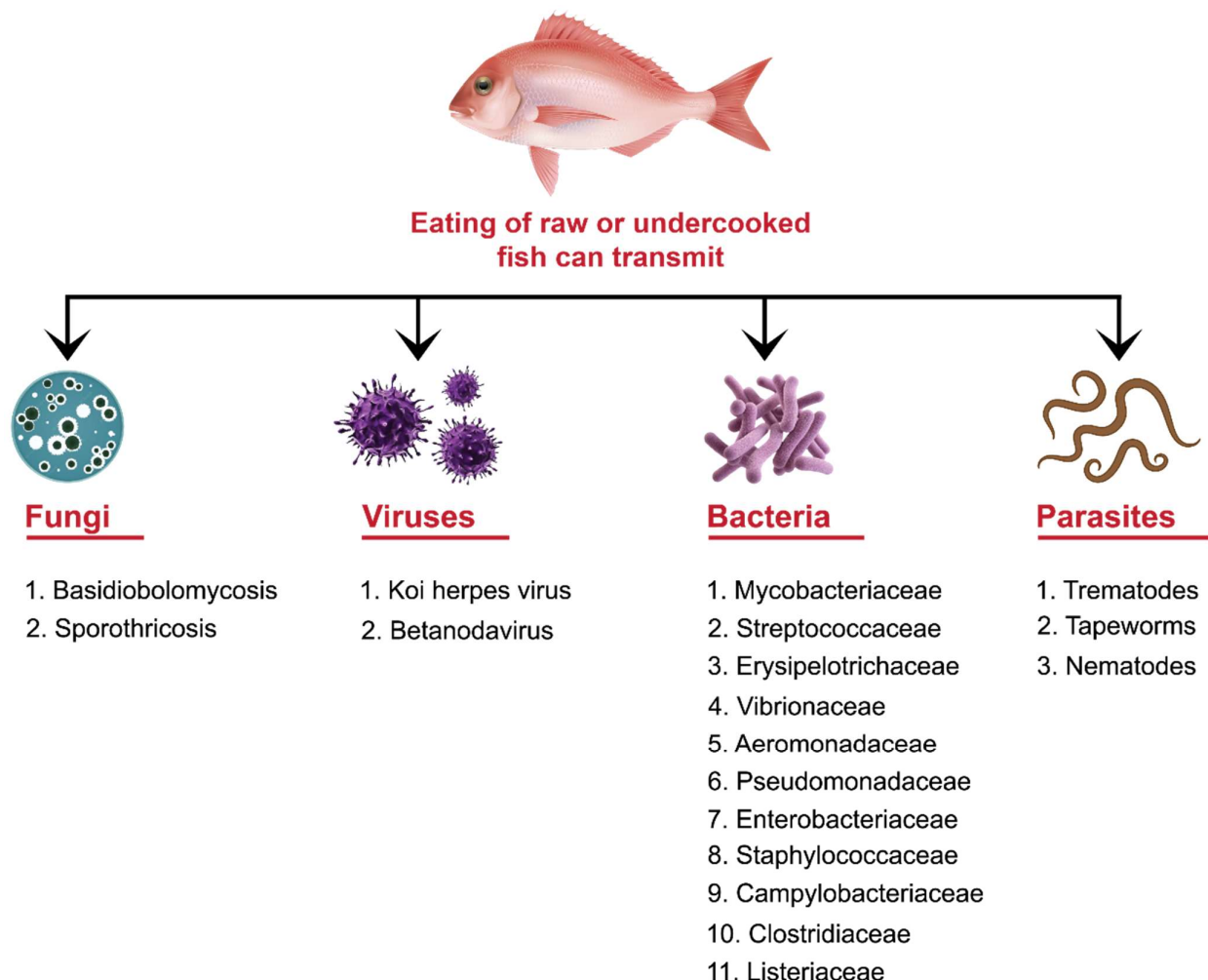


Fig 1. Fish-borne zoonotic pathogens that can cause disease in humans

Heterophyidae, also called Intestinal flukes (Keiser & Utzinger, 2009). Liver flukes can infect the liver and cause serious health issues such as, Cholangitis, pancreatitis, choledocholithiasis and cholangiocarcinoma. Some species of intestinal flukes can also pose fatal issues in the brain, spinal cord and heart (Hung et al., 2015). Some fish-borne zoonotic trematode infections in history, their distribution and prevalence is depicted in Table 1.

### Life cycle of fish trematode

The life cycle starts when mammals and humans eat an infected fish. The fish tissues are broken down and metacercariae are released into the small intestine, then these metacercariae are excysted and travel to the other organs and become adults there. After complete maturation, adult trematodes are released in feces and reach the water systems where they are eaten by a snail and then by an intermediate host fish and the cycle continues (Hung et al., 2013). Fig 2 demonstrates the life cycle of a trematode infecting the fish species.

## SOME IMPORTANT FISH-BORNE PARASITIC TREMATODES

### Metagonimiasis

Many intestinal flukes, lung flukes and liver flukes can infect the fish or seafood and then transmit to humans. They cause serious problems and may also lead to death (Mahanta, 2022). The genus *Metagonimus*, a group of intestinal flukes infecting the GI system of fish "Metagonimiasis" and infects the GI tract. There are five pathogenic and zoonotic species of *Metagonimus* (*M.*) *yokogawai*, *M. takahashii*, *M. minutes*, *M. katuradai* and *M. miyatai*. The most pathogenic among these is *M. yokogawai*. It is reported in East Asia, Asian regions of Russia, Japan, Taiwan and Korea. It is most prevalent in Japan, Taiwan and Korea because of eating raw or undercooked fish habits (Mahanta, 2022).

**Symptoms:** It is mostly asymptomatic, but a high parasite load can lead to clinical signs and symptoms. The parasite resides in the human small intestine and causes enteritis. It shows many other symptoms including abdominal pain, diarrhea, weakness, weight loss, discomfort and anorexia. On the other hand, it can also cause diabetes mellitus and brain hemorrhage in rare cases. In immunosuppressed people, it can also infect the brain, spinal cord and myocardium (Cong & Elsheikha, 2021).

**Diagnosis and Treatment:** The infection can be diagnosed by isolating metacercaria from fecal samples. Parasites can be detected by microscopy, fecal smear, concentration technique and PCR. It can be prevented by eating finely cooked fish and continuous monitoring of your domestic cats and dogs because they are reservoirs of many parasitic trematodes. After the diagnosis of infection, it can be treated by giving one oral dose of 20mg/kg of praziquantel. In case of heavy infection, it can be given for up to 3 days.

### Clonorchiasis

Clonorchiasis is an infection of the liver and bile duct caused due to a liver fluke species *Clonorchis* (*C.*) *sinensis*. Humans and animals are the reservoirs of this parasite. The eggs of adult liver fluke parasites reside in the liver of many mammals including humans and transferred to the gut. The majority of parasites that cause liver and biliary disorders reside in the parenchyma of the liver, gallbladder and bile ducts. Consuming raw or undercooked infected fish is the major cause of clonorchiasis in humans (Sripa et al., 2010). It is a very infective parasite and is prevalent in South Korea, Japan, China, Taiwan, Eastern part of Russia and Northern Vietnam (Rim, 2005). It has become a predominant infectious disease in Korea. According to a survey in 2004, there were about 1.78 million cases reported due to the infection of helminthiasis. Out of these about 1.17 million cases were only of clonorchiasis and estimated 15 million people were infected with this disease in 2004 worldwide (Qian et al., 2012). This infection is increasing due to the increasing habit of eating raw fish.

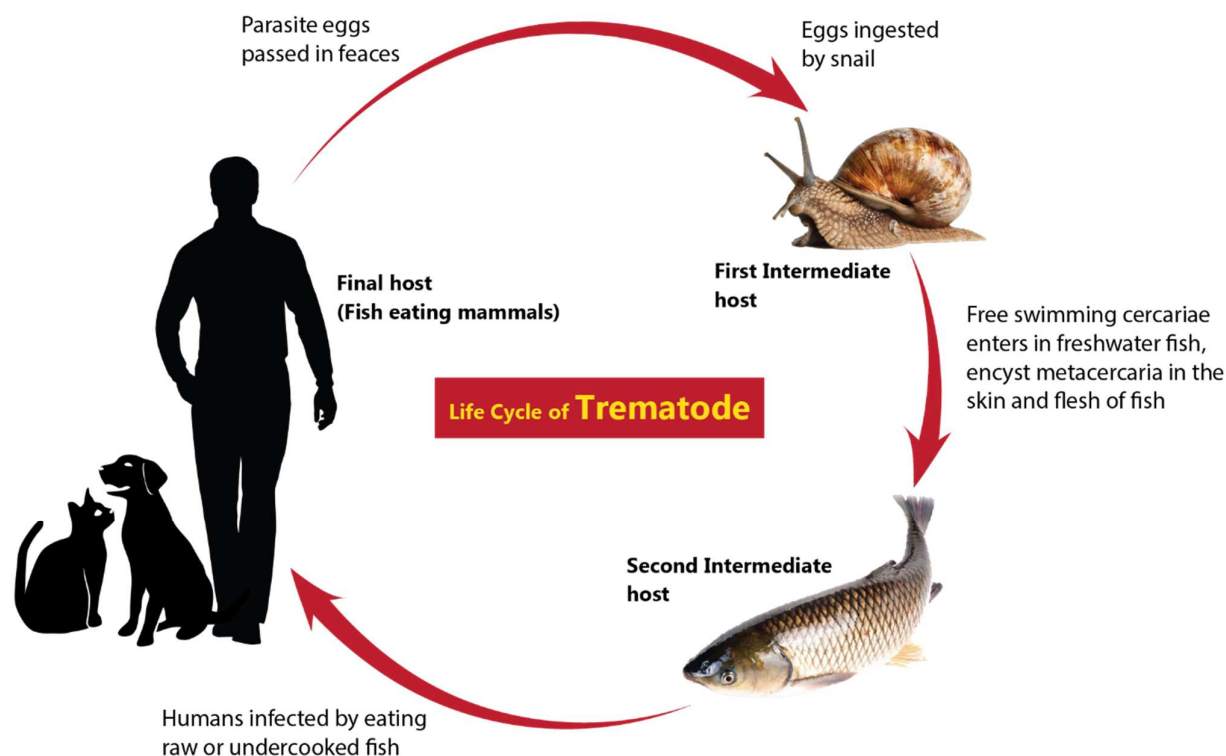
**Symptoms:** The signs and symptoms of disease are usually dependent on parasite burden inside the host. In case of low parasitic burden, infection is usually asymptomatic. But in case of high parasite load, the patient shows unspecific symptoms, including headache, nausea, asthenia, dizziness, indigestion, abdominal pain, and diarrhea. A relatively high parasitic burden may also lead to jaundice, liver tenderness and hepatomegaly. In chronic cases, parasites can infect liver and bile duct leading to development of cholangitis, cholecystitis and cholelithiasis. It can also retard the development of children (Na et al., 2020).

**Diagnosis and treatment:** There were many drugs used in history to treat this infection but resistance to these drugs has also been reported. These drugs had limited efficacy. Recently, Praziquantel is still found effective and being used to treat clonorchiasis. A dose of 25mg/kg of praziquantel is given three times a day to an individual for 1 to 2 days. It is highly efficacious in reducing the eggs of the parasite and preventing its reoccurrence (Qian et al., 2016; Na et al., 2020). Some other efficient methods to manage clonorchiasis also include feces treatment, snail control, and health education.

## SOME OTHER IMPORTANT PARASITES OF FISH

### Anisakiasis

Anisakiasis is caused by an intestinal nematode parasite of genus *Anisakis*. It has nine species out of which two species are highly pathogenic. These are *Anisakis* (*A.*) *simplex*, *A. pegreffii*. Anisakiasis cases are reported in Asia, Germany, France, Spain, Netherlands and Japan. Before 2010, The European Food Safety Authority (EFSA) reported about 20,000 anisakiasis cases, out of which more than 90% were from Japan (Bao et al., 2017). Humans can get this infection by ingesting third stage infective larvae in raw or lightly cooked fish meat. Increasing trends of eating raw or marinated fish dishes such as smoked and salted herring, sushi, sashimi, lomi lomi and ceviche contributed to the spread of anisakiasis.



**Fig 2.** A general life cycle of a trematode showing its life stages in Snail (First intermediate host), fish (Second intermediate host) and humans (Final host)

infection on a great level. Anisakiasis have different types depending on the site of infection in humans, such as gastric anisakiasis, gastro-allergic anisakiasis, extra-gastrointestinal anisakiasis and intestinal anisakiasis (Mattiucci et al., 2013).

**Symptoms:** Anisakiasis causes abdominal pain, sudden epigastric pain, vomiting, nausea, urticaria, low-grade fever, diarrhea and allergic reactions. Due to its vague symptoms, it is mostly misdiagnosed with appendicitis, gastric tumor, ileitis, diverticulitis, pancreatic cancer and tuberculous peritonitis.

**Diagnosis and treatment:** Diagnosis of anisakiasis is based on observing symptoms. Diagnosis can be done by upper endoscopy and capsule endoscopy. In severe misdiagnosis, it can be confirmed by exploratory laparotomy. After diagnosis, proper treatment can be done to cure anisakiasis. There are many treatments available including, Physical removal of larvae with the help of endoscopy, conservative therapy, albendazole administration and surgical interventions.

### Gnathostomiasis

Gnathostomiasis is an emerging infectious parasitic zoonosis caused by *Gnathostoma*; a nematode parasite of fish. In *Gnathostoma* genus, there are twelve species, out of which five species are considered important about public health and can cause serious infections in humans. These species are *Gnathostoma* (*G.*) *spinigerum*, *G. doloresi*, *G. hispidum*, *G.*

*malaysiae*, *G. binucleatum* (Waikagul & Chamacho, 2007). The prevalence of this infection in humans is more than Anisakiasis. Many cases are reported in Central America, South America, Japan, Vietnam, Mexico and Thailand. The first case of this infection was reported in the year 1889 and to date, more than 5000 cases of gnathostomiasis have been reported globally. It is most prevalent in Japan, Mexico, Thailand and Colombia. People traveling through endemic areas are also reported to have infection symptoms and it is also increasing in non-endemic areas day by day (Liu et al., 2020). The number of cases reported is increasing due to changes in eating habits and the increasing trend of eating raw fish, undercooked fish and by eating delicacies such as sushi, ceviche etc.

**Symptoms:** *Gnathostoma* species larvae are very motile and that's why it shows a wide range of symptoms. If it reaches the pulmonary region, it causes pleuric chest pain, pneumothorax, cough, collapse and pleural effusion. When infection occurs in GI system, it causes sharp pain in abdomen, iliac pain, fever, appendicitis and intestinal obstruction. When these larvae reach the Genito-urinary tract it causes vaginal bleeding, balanitis, hematospermia or cervicitis. If the larvae reach the eyes, it can cause uveitis, intraocular hemorrhage, iritis, glaucoma and retinal scarring. When this parasite larva reaches the auricular system, it can cause hearing loss. It can also infect the auditory canal, soft plate, tympanic membrane, tongue tip or cheeks. There are also several cases reported when larvae

reach the central nervous system (CNS). After reaching CNS,

**Table 1.** Fish-borne zoonotic trematode infections in history, their distribution and prevalence (Hung et al., 2013; 2015).

| Name of the trematode            | Distribution and prevalence                                                                                                                                                                                                      |
|----------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Family: Echinostomatidae</b>  |                                                                                                                                                                                                                                  |
| <i>Echinostasmus fujianesis</i>  | It was reported in 1992 in 5 cities of China<br>Its prevalence was 3.2% in humans and 29.2% in dogs                                                                                                                              |
| <i>Echinostasmus japonicus</i>   | It was reported in 1926 in China, Japan, Korea and Vietnam<br>Its prevalence was 4.9% in humans                                                                                                                                  |
| <i>Echinostasmus jiufoensis</i>  | It was reported in 1988 in China                                                                                                                                                                                                 |
| <i>Echinostasmus liliputanus</i> | It was reported in 1896 and then in 1910 in China, Egypt, Palestine and Syria<br>Its prevalence was 13.4% in humans, 50% in dogs and 45% in cats                                                                                 |
| <i>Echinostasmus perfoliatus</i> | It was reported in 1908 and then in 1911 in China, Taiwan, Denmark, Hungary, Russia, Japan, Italy and Vietnam<br>Its prevalence was 1.8% in humans                                                                               |
| <i>Echinostoma angustitestis</i> | It was reported in 1992 in China in 2 people                                                                                                                                                                                     |
| <i>Echinostoma hortense</i>      | It was reported in 1926 in China, Korea and Japan<br>Its prevalence was 22.4%                                                                                                                                                    |
| <b>Family: Heterophyidae</b>     |                                                                                                                                                                                                                                  |
| <i>Appophthalmus donicus</i>     | It was reported in 1931 in the United States, Canada and East Europe<br>Human infection was found in the US but its prevalence was unknown                                                                                       |
| <i>Centrocestus caninus</i>      | It was reported in 1912 in Thailand and Taiwan<br>2 cases were reported in Thailand. Human infection cases were also reported in Taiwan                                                                                          |
| <i>Centrocestus cuspidatus</i>   | It was reported in 1896 in humans in Taiwan and Egypt<br>Prevalence was unknown                                                                                                                                                  |
| <i>Haplorchis microchis</i>      | It was reported in 1932 in Japan in humans<br>Prevalence was unknown                                                                                                                                                             |
| <i>Heterophyes katuradai</i>     | It was reported in 1916 in Japan, China, Korea and the Philippines<br>Its prevalence was about 10-70% in people living in Coastal areas of Korea                                                                                 |
| <b>Family: Nanophyetidae</b>     |                                                                                                                                                                                                                                  |
| <i>Nanophyetus salmincola</i>    | It was reported in 1927 in the US and Russia<br>Its prevalence was 5% and in some areas 10% which reached up to 60%                                                                                                              |
| <b>Family: Opisthorchiidae</b>   |                                                                                                                                                                                                                                  |
| <i>Chlonorchis sinensis</i>      | It was reported in 1875 in China, Japan, Taiwan, Korea and North Vietnam<br>It was very prevalent and posed very drastic impacts. It infected about 7-10 million people and 290 million people were at risk of getting infection |
| <b>Metorchis orientalis</b>      | It was reported in 1919 in Japan and China<br>Its prevalence was 4.2%                                                                                                                                                            |
| <b>Opisthorchis felineus</b>     | It was reported in 1884 in France, Greece, Italy, Poland, Russia and Germany<br>It was very prevalent and infected about 1.6 million people worldwide                                                                            |
| <b>Opisthorchis viverrini</b>    | It was reported in 1886 in Laos, Thailand and Cambodia                                                                                                                                                                           |

it can cause radiculomyelitis, eosinophilic meningitis, radiculo-myeloencephalitis and hemorrhage. CNS manifestation can cause a high mortality rate of about 8-25% (Herman, 2009).

**Diagnosis and Treatment:** Gnathostomiasis can be diagnosed with a number of serological tests (most widely used is immunoblot in Europe), ELISA, and magnetic resource imaging. After diagnosis, it can be treated with surgical excision of the larvae. A few years ago, surgical excision was the only method to treat this infection but continuous research has proved that Albendazole and Ivermectin are promising treatments to treat gnathostomiasis with an efficacy rate >90%. In case of high parasite load, a second course of drug administration is needed (Herman, 2009).

### Diphyllobothriasis

Diphyllobothriasis is a zoonotic infectious disease caused by adult tapeworm *Diphyllobothrium* spp. There are many species associated with human infection, as *Diphyllobothrium* (*D.*) *latum*, *D. ditremum*, *D. dendriticum*, *D. dalliae*, *D. ursi*, *D. alascense*, *D. vogeli*, *D. pacificum*, *D. nihonkaiense* and *D. klebanovskii* (Dick et al., 2001; Cong & Elsheikha, 2021). It is very prevalent in North temperate region, North America, Arctic region, Europe, France, Russia, Japan, Korea, Switzerland and Italy. The infection rate due to *D. latum* is higher than any other species of *Diphyllobothrium*. However, the infection rate due to *D. nihonkaiense* is higher in Japan than any other species. *Diphyllobothrium* is reported to infect about 20 million people worldwide up till now.

**Symptoms:** Diphyllobothriasis infects the small intestine of its final host. It causes abdominal pain, discomfort, diarrhea, weight loss, abdominal distension, indigestion, dyspepsia, vomiting, fever, anorexia, and fatigue depending upon species (Arizono et al., 2009).

**Diagnosis and Treatment:** Infection can be diagnosed with different methods, including colonoscopy, microscopy, ultrasonic examination, capsule endoscopy, removal of the parasite, serological and hematological analysis and PCR. After the diagnosis, an infection can be treated with the complete removal of worm with the help of endoscopy. In this method, a basket retrieval instrument is used to grasp and pull the complete worm through the anus. It can also be treated with drugs. If the patient is infected with *D. latum*, Bithionol and Niclosamide are the possible drugs to be administered. In the case of other species infection, Praziquantel at the dose rate of 15-25mg/kg is administered.

### PREVENTION AND CONTROL IN FISH BORNE PARASITIC ZOONOSIS

The prevention and control of fish borne parasitic zoonosis is very crucial. Chemical control of pathogen through antiparasitic drugs is widely used method. However, the emergence of antiparasitic resistance is major limitation in control of pathogens (Williams et al., 2020). On the other hand, the issue of chemical residues, lack of withdrawal period, cost of drugs and low efficacy are major hurdles. Hence, some of the preventive measures can be practiced as discussed below (Fig 3).

### Educating people

The awareness about the fish borne parasites and associated risk factors can be key to control this threat at mass scale. The launch of community awareness programs by experts, scientists and public health officials should be carried out extensively. The trend of eating raw fish, undercooked fish and raw fish delicacies should be prevented. The recommendations about the cooking temperature for fish should be followed as 62 °C is optimum temperature. Aware people with the correct way to deep freeze the fish to inactivate the parasite cycle. For this purpose, fish handlers should be instructed to freeze fish at -20 °C for at least 24 hours (Cong & Elsheikha, 2021). Quality control measures and routine monitoring of imported fish and fish products should also be followed strictly.

### Personal protection

Fish handlers should wear protective gloves and disposable dresses while handling and processing the fish. Keep your skin and wounds away from the fish mucous. Wash hands after

direct contact with fish. Immediately see your physician if any symptoms of infection are observed (Ziarati et al., 2022).

### Cleaning the fish rearing ponds

Cleaning and proper sterilization of the pond are necessary to avoid the development of infective pathogens and larvae. The construction of concrete banks and removal of vegetation along the fish rearing ponds may be helpful to limit the intermediate host and break the life cycle of parasite. Sterilization and proper drying of a pond before refilling can reduce the chance of retaining the intermediate host (Ziarati et al., 2022).

### Removal of snails

Snail serves as primary intermediate host for most of the trematode parasites. Proper cleaning of ponds should be done. The use of molluscicides can also be practiced for effective removal of snails from the surroundings. In this way, the

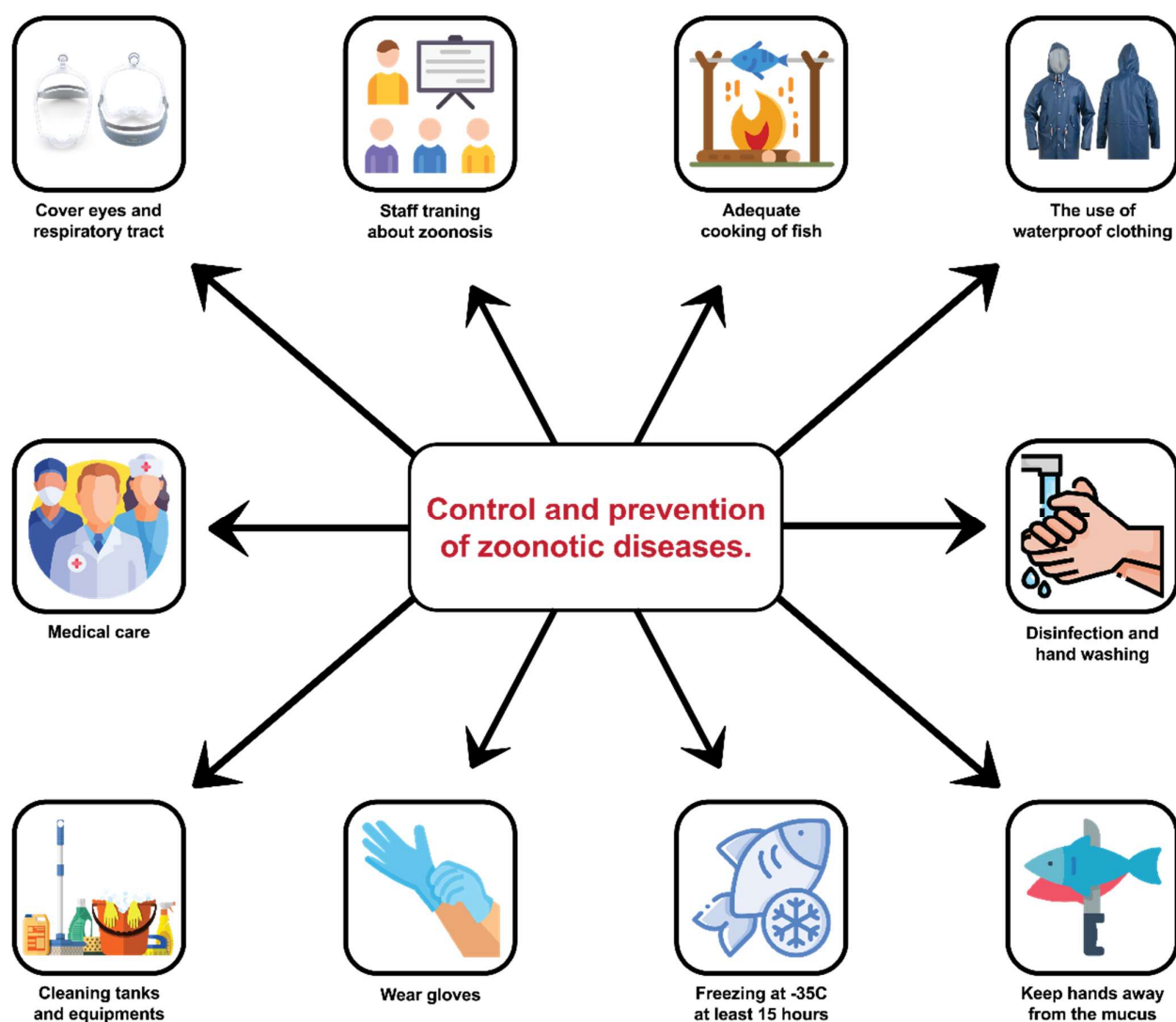


Fig 3. Control and preventive measures to control the spread of zoonotic diseases

parasite transmission cycle can be disrupted, and parasite

transmission can be prevented from reaching the fish (Cong & Elsheikha, 2021).

### Reduce the water pollution

Farmers should apply different strategies to reduce water pollution. In an intensive culture system, high density of fish provides less distance among fishes, increasing the chance of getting infection but on the other hand closed water system is under continuous observation and maintenance thus decreasing the chance of intermediate host and also reduces the chance of spread of infection. In a closed system, the use of frozen or artificial diet can reduce the chance of parasites to a great level (Barber, 2007). For an open water system, people should avoid excreting feces near the open water system because it can transmit embryonated eggs to the water and then it is ingested by snails and parasite cycle starts (Ziarati et al., 2022).

### Use of chemicals

There are many anthelmintic chemicals available commercially to treat parasitic infections in fish and ponds. With proper observation, detecting the presence of intermediate host and fish behavioral changes can timely predict the issue and with proper diagnosis, parasitic infection can be prevented from spreading and treated (Qian et al., 2016; Na et al., 2020).

### CONCLUSION

Fish is considered a healthy diet option in middle- and low-income countries. However, fish-derived zoonotic parasites especially nematodes, trematodes and tapeworms can be transmitted to humans due to the consumption of infected raw or undercooked fish. Fish-borne zoonotic parasites infect millions of people worldwide and even in many regions they have become fatal and taking the lives of thousands of people. However, with proper prevention and control measures, this zoonotic infection rate can be reduced. It is essential to discourage people from eating raw fish and aware them of cooking fish properly to avoid the chance of infection. If still infection occurs the anthelmintic treatment could be a possible way to cure the fish-borne zoonotic infection.

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