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Zoonotic Trematodiasis

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Abstract

Parasitic zoonoses are diseases caused by parasites shared between animal hosts and humans. Most of parasitic zoonoses are considered as neglected because of the absence of campaigns destined to prevention control and treatment of these diseases in most developed and undeveloped nations, ignoring that parasitic zoonoses affect almost half of the world human population and the vast majority of livestock worldwide is at risk of acquiring or sick because of a zoonotic disease. Zoonotic trematodiasis are numerous in almost every nation and responsible for serious and debilitating helminthic diseases in about 75 million people as well as the billions of dollars in production losses to the livestock industry. The perspective of global warming, habitat loss and new host range adaptation indicates that unless a new approach based in genomics, transcriptomics and proteomics assessment of new biomarkers and anthelmintic targets is achieved, the incidence of zoonotic trematodiasis will increase for both human and animal hosts.

Keywords: zoonoses, emerging diseases, trematodes, parasites, disease, diagnostics

1. Introduction

Parasitic zoonoses affect almost half of the world's population and cause billions of dollars in losses to the livestock industry. Under the current trend of climate change, wild habitat loss, intensive agriculture-aquiculture activities combined with human demographic increase, zoonotic parasites represent a constant health threat for people and livestock living in most of the developing nations with a deficient or nonexistent healthcare policies or infrastructure [1].

Among zoonotic infections, most of those caused by parasitic pathogens are considered as neglected by the World Health Organization (WHO), in part because these diseases are endemic in undeveloped nations, which cannot afford to allocate economical resources destined to diagnosis prevention and control of at least the most important zoonoses affecting their inhabitants and livestock [2].

The situation is aggravated by a pharmaceutical industry reluctant to invest in research and development efforts for new pharmaceutical treatments in countries that are not a profitable market place [3], resulting in a lack of efficient treatments for the most important parasitic zoonoses around the globe. Zoonotic diseases are those naturally exchanged between vertebrate animals and humans [4], and several modes of zoonotic diseases were identified according to direction of transmission, number of hosts and types of symptoms, definitions of which are indicated in **Table 1**.

Natural habitat invasion by livestock and people are considered the most important detonator for the emergence of zoonotic outbreaks worldwide (**Figure 1**) [5].

Terminology	Definition
Zoonoses	Diseases naturally transmitted between vertebrate animals and humans
Anthropozoonoses	Diseases in animals that can be transmitted to man
Zooanthroponoses	Diseases affecting humans that can be transmitted to animals
Amphixenoses	Diseases that are exchanged between animals and human occasionally
Euzoonoses	Diseases in which humans are an obligatory host of the pathogen
Cyclozoonoses	Diseases that require two different vertebrate hosts but no invertebrate vector
Pherozoonoses	Pherozoonoses isosymptomatic, similar symptoms are observed in animals and humans Pherozoonoses anisosymptomatic, symptoms are different in animals and humans
Cryptozoonoses	Zoonotic diseases in which symptoms are only evident in humans
Saprozoonoses	Diseases that depend upon inanimate reservoirs and vertebrate hosts
Emerging parasitic zoonoses	Zoonotic diseases caused either by new parasites or by old known species in an area where the disease was previously unknown

Table 1. Modes of zoonotic diseases identified according to direction of transmission, number of hosts and types of symptoms.

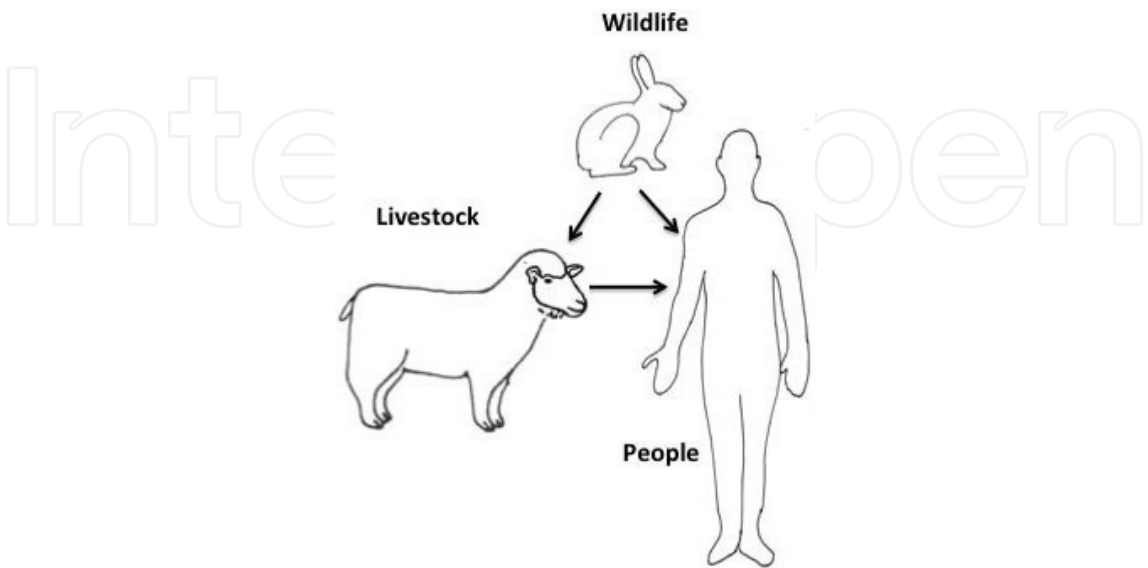


Figure 1. Zoonotic parasite flow among wildlife, livestock, and humans. A condition such as wild habitat invasion by livestock and humans is a major factor in the emergence of a parasitic zoonosis.

Some of the most important zoonoses are those caused by well-known pathogens, imported from endemic areas to new ones where the diseases that cause those parasites have not being previously documented. This phenomenon, called “infectious emerging diseases” by the WHO, is defined as newly recognized or newly evolved or that has occurred previously but shows an increase in incidence or expansion in geographical, host, or vector range [6].

Neglected emerging diseases cause around 75% of human infectious diseases worldwide [7, 8]. Parasitic zoonosis, include protozoans and helminths, such as nematodes, cestodes, and trematodes, some of which, exhibit very complex life cycles that require invertebrate vectors that may look as innocuous as a garden snail but instead could be extremely dangerous vectors of very serious and debilitating parasitic diseases. **Table 2** depicts some of the most important parasitic zoonoses, its transmission vehicle and distribution.

Phylum	Genus	Disease	Species	Vector/transmission vehicle	Distribution	Hosts
Protozoa	<i>Trypanosoma</i> spp.	American trypanosomiasis	<i>T. cruzi</i>	Triatomid bugs	All American countries except Canada	Ruminants Canines Cats Marsupials Humans
		African trypanosomiasis	<i>T. brucei</i>	Glossina flies	African countries	Ruminants Canines Cats Humans
	<i>Leishmania</i> spp.	Middle East leishmaniasis	<i>L. donovani</i>	Plebotomid flies	Middle and Far East countries	Ruminants Canines Cats Humans
		American leishmaniasis	<i>L. mexicana</i> <i>L. brasiliensis</i> <i>L. tropica</i>	Plebotomid flies	Meso American tropical and subtropical countries	Ruminants Canines Cats Humans
	<i>Cryptosporidium</i> spp.	Cryptosporidiosis	<i>C. parvum</i>	Food and waterborne	Worldwide	Aquatic fowl Humans
	<i>Toxoplasma</i> spp.	Toxoplasmosis	<i>T. gondii</i>	Cat feces raw meat	Worldwide	Ruminants Canines Cats, birds, reptiles, humans
Nematoda	<i>Ancylostoma</i> spp.	Hookworm disease	<i>A. duodenale</i>	Skin penetration	Worldwide	Canines Humans
	<i>Ascaris</i> spp.	Roundworm disease	<i>A. suum</i>	Foodborne Pig feces	Worldwide	Pigs Humans
	<i>Toxocara</i> spp.	Toxocariasis	<i>T. canis</i>	Foodborne Dog feces	Worldwide	Dogs Cats Humans
	<i>Strongyloides</i> spp.	Strongyloidiasis	<i>S. stercoralis</i>	Skin penetration	Worldwide	Dogs Humans
	<i>Dirofilaria</i> spp.	Heart Filariasis	<i>D. immitis</i>	Mansonia, Anopheles and Aedes mosquitoes	Worldwide	Dogs Humans
	<i>Brugia</i> spp.	Lymphatic filariasis	<i>B. malayi</i>	Mansonia, Anopheles and Aedes mosquitoes	Southeast Asia	

Phylum	Genus	Disease	Species	Vector/transmission vehicle	Distribution	Hosts
						Dogs, cats Monkeys and humans
Platyhelminths Cestoda	<i>Hymenolepis</i> spp.	Dwarf tapeworm disease	<i>H. nana</i>	Foodborne	Worldwide	Rodents Humans
	<i>Dipylidium</i> spp.	Flea tapeworm disease	<i>D. caninum</i>	Accidental flea ingestion	Worldwide	Cats Dogs Humans
	<i>Diphyllobothrium</i> spp.	Fish tapeworm disease	<i>D. latum</i>	Raw fish	Worldwide	Fish Ichthyophagus mammals Humans
	<i>Taenia</i> spp.	Pig tapeworm disease	<i>T. solium</i>	Raw pork	Worldwide	Pigs Humans
		Cow tapeworm disease	<i>T. saginata</i>	Raw beef	Worldwide	Bovines Humans
Platyhelminths Trematoda	<i>Fasciola</i> spp.	Liver fluke	<i>F. hepatica</i> <i>F. gigantica</i>	Snail. Fresh vegetables	Worldwide	Ruminants Pigs Rodents Humans
	<i>Fasciolopsis</i> spp.	Giant intestinal fluke	<i>F. buski</i>	Snail. Fresh vegetables	Southeast Asia	Pigs Humans
	<i>Clonorchis</i> spp.	Chinese liver fluke	<i>C. sinensis</i>	Snail. Fish	Southeast Asia	Pigs Cats Canines Ruminants Humans
	<i>Schistosoma</i> spp.	Cercarial dermatitis	Nonhuman <i>Schistosoma</i> spp.	Waterborne	Worldwide	Birds Most mammals Humans
Arthropoda	<i>Paragonimus</i> spp.	Lung fluke	<i>P. westermani</i> <i>P. mexicanus</i>	Snail, crustaceans	Southeast Asia Central America	Cats Canines Rodents Humans
	<i>Sarcoptes</i> spp.	Scabies	<i>S. scabiei</i>	Direct contact	Worldwide	Dogs Humans
	<i>Trombicula</i> spp.	Trombiculosis	<i>T. alfreddugesi</i>	Direct contact	North America	Mammals Birds Humans
	<i>Ixodes</i> spp.	Deer tick	<i>I. scapularis</i>	Direct contact	North America	Mammals Humans

Table 2. Important global parasitic zoonoses.

2. Zoonotic trematodes life cycle and transmission

Zoonotic parasites are transmitted to livestock and people using well-known routes, these may include blood sucking invertebrate vectors such as the sand flies role in transmitting river blindness, foodborne like in the case of zoonotic trematodiasis or direct contact with wildlife

and/or domestic animals such as in the case of scabies [9]. Human zoonotic helminthiasis are of particular importance because of their insidious nature, showing a tendency to increase for a number of factors, most notably global population growth and global warming trends [7].

Part of the emergence of zoonotic parasites is due to the climate change expectative [10–12], and climate change may disrupt vertebrate and invertebrate hosts or their habitat, increasing contact with human population and livestock or favoring conditions of vector proliferation [13]. When livestock and aquaculture is considered as additional factors, the risk to human health increases dramatically due to the inability of most undeveloped nations to put in place efficient methods of vertebrate-invertebrate hosts control, resulting in high prevalence of zoonotic helminthiasis among farmers and fisheries workers [14].

Zoonotic trematodiasis depends on several species of gastropod mollusks to complete their life cycle. Part of the successful conquest of new habitats depends on the adaptation of the different parasitic trematodes to new intermediate hosts around the world (**Figure 2**) [15]. This is the case of *Fasciola* spp. parasitic trematodes, which spread from Europe to the rest of the world by adapting to *Radix* sp., *Bithynia* sp., and new species of *Lymnaea* sp. slimes in the American countries [16].

Intermediate host adaptation is an important factor in the emergence of a neglected disease where endemicity is low or nonexistent. Food-borne trematode zoonoses (FBTZ) start their life cycle as miracidium, a 100-micrometer ciliated developmental stage result of trematodes embryonated eggs, highly mobile in aquatic conditions, upon finding a compatible snail, the miracidium penetrates the tegument of the intermediate host shedding its cilia [17] turning into germinal masses of cells called sporocysts.

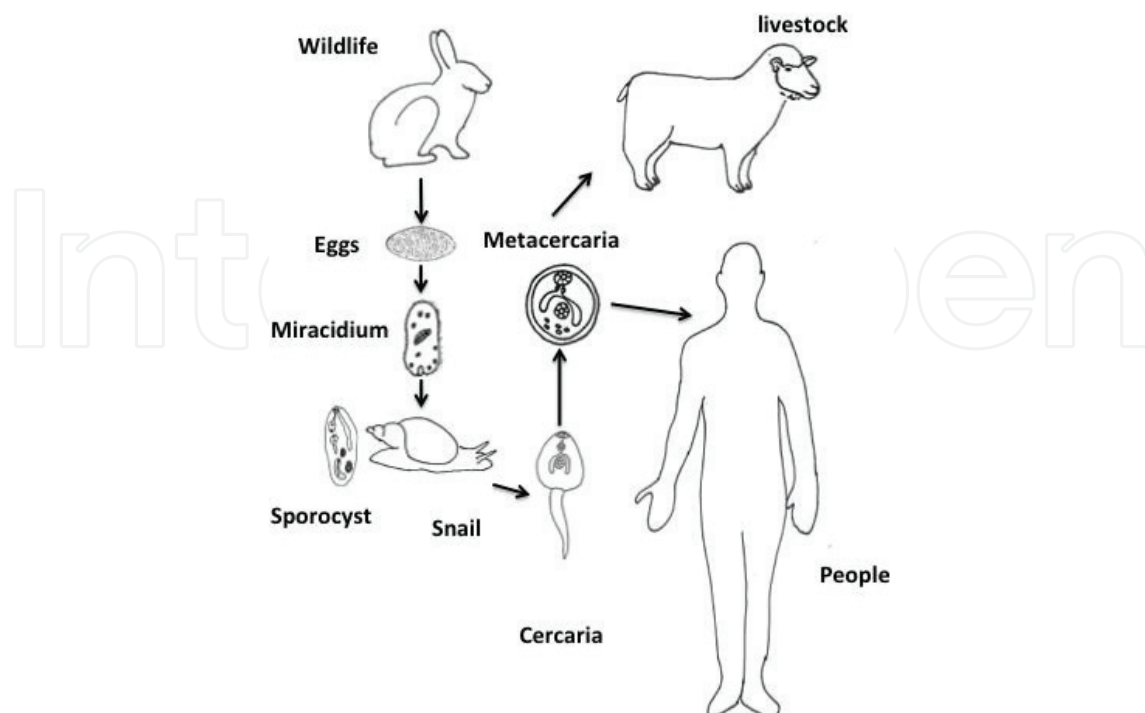


Figure 2. Life cycle of zoonotic trematodes.

These sporocysts multiply into several masses of germinal cell each of them originating a redia [18], and these are intermediate germinal stages that develop into cercariae, a highly mobile developmental stage that finally exits the intermediate host by perforation of the snail's tegument and then migrates into an aquatic environment, the cercariae, depending on the parasitic trematode species, can penetrate the skin of a second intermediate host and encyst in the muscles of it [19]. Cercariae may also penetrate the skin of the definitive host [6] or lose its tail and become a cyst, an environment-resistant developmental stage on surrounding vegetation or in drinking water. Cercariae and metacercariae are the infestant stage of zoonotic trematodes, and upon ingestion or penetration, they grow into a juvenile worm [20]. Alternative infestation modes have been reported [6] in places where raw meat consumption is common, accidental ingestion of juvenile/adult flukes can occur, a phenomenon known as paratenic trematodiasis [7].

Once established in their target organs, parasitic trematodes may induce a chronic trematodiasis producing a serious illness that may last decades [21]. Livestock may carry zoonotic trematodiasis during their entire life span within endemic areas, and several definitive hosts have been reported such as American and Asian camelids, rodents, deer, hare, and pigs [22].

3. Socioeconomic impact and distribution

Trematode zoonoses are neglected diseases mostly due to the lack of funds required for diagnosis prevention and control of zoonotic parasites [5]. Trematode zoonosis include the liver, intestinal and lung flukes [20] and are endemic worldwide; although they can be found in developed nations, the most important socioeconomic impact occurs in undeveloped nations where around 750 million people are at risk of acquiring trematodiasis [23], most cases related to clonorchiasis, paragonimiasis, fascioliasis, and opisthorchiasis [23].

SouthEast Asian countries are the most affected with clonorchiasis estimated as 35 million people [24] followed by paragonimiasis and opisthorchiasis with 20 and 10 million affected humans, respectively [25]. *Fasciola* sp. trematodiasis affects some 17 million people globally and a large amount of livestock constituting both a world health problem and livestock production issue [22]. Intestinal flukes mostly due to *Fasciolopsis burki* are estimated to affect some 50 million inhabitants [26]. Human trematodiasis occurs via water or food products contaminated by the intermediate host that may be fish, mollusks, or vegetables [16]. Part of the social and economic importance of FBTZ is the fact that several animal species are also affected, which makes these kinds of diseases a veterinary issue as well as a human health problem [6].

Fasciola hepatica is the causative agent of fascioliasis, a debilitating parasitic disease that destroys the hepatic parenchyma and blocks the bile ducts of equines, bovines, swine, sheep, goats, rabbits, and humans [27]. Fascioliasis is considered a neglected zoonotic parasitic disease, because it is ignored by most countries where fascioliasis is endemic, in spite of 91 million more human beings at risk of acquiring fascioliasis in endemic areas, where 2.4 million new human cases are reported each year [28, 29].

Latin America, human fascioliasis is dangerously neglected by the official health system and as in many other neglected diseases, there is no collection of the most basic epidemiological figures on the subject and only sporadic clinical reports are found on the medical literature

[30]. High rates of ovine and bovine fascioliasis prevalence are reported in Latin American countries slaughterhouses, and the livestock industry worldwide reports annual losses of 4 billion dollars associated with poor conversion of livestock feed into meat, wool and milk, low weight gain, and reduced fertility [29, 31].

The veterinary impact of zoonotic parasitic food-borne trematodiasis is mainly economical due to loss of animal products of the affected livestock [13]. Cercarial dermatitis is an aberrant form of zoonotic trematodiasis caused by several avian parasitic trematodes or *Schistosoma* spp., and it may occur anywhere around the planet and on a seasonal basis with most cases reported during the summer time [32]. It happens when the invertebrate intermediate hosts or snails releases cercariae in water ponds coinciding with human activities such as recreational swimming or fishing [33], aquiculture and agricultural such as rice planting activities are also important occupational risk factors [34]. In these environments, where there are abundance of cercariae, they tend to penetrate any warm blooded vertebrate including people, and thousands of cases are reported each year in North America, Europe, and Asia [33].

4. Emerging zoonotic diseases

Zoonotic trematodiasis are also emerging diseases due to the inevitable spread of the intermediate host to new habitats and global warming and increasing activities of aquiculture, representing a threat to new populated areas where zoonotic trematodiasis was not previously documented [15] (Table 3).

Most of zoonotic trematodiasis affected areas are located in tropical and subtropical areas where tropical neglected diseases are endemic in coincidence with the world poorest nations where health care is nonexistent and funding for prevention and control of tropical neglected diseases such as parasitic zoonosis is negligible [14]. Respiratory infections, diarrheal diseases, and HIV cases in global health impact only surpass currently zoonotic trematodiasis over the world population [31].

Disease	Intermediate hosts genus	Distribution
Echinostomiasis	<i>Planorbis</i> sp. <i>Lymnaea</i> sp. <i>Redix</i> sp. <i>Gyraulus</i> sp. <i>Hippeutis</i> sp.	Worldwide
Schistosomiasis	<i>Bulinus</i> sp. <i>Oncomelania</i> sp. <i>Biomphalaria</i> sp. <i>Neotricula</i> sp.	Worldwide
Fascioliasis	<i>Lymnaea</i> sp.	Worldwide
Fasciolopsiasis	<i>Segmentina</i> sp. <i>Hippeutis</i> sp.	
Clororchiasis	<i>Alocinma</i> sp. <i>Bulinus</i> sp. <i>Melanoides</i> sp. <i>Parafossarulus</i> sp. Intermediate host: Fish	Worldwide
Dicrocoeliasis	<i>Cionella</i> sp. <i>Bradybaena</i> sp. snails and <i>Formica</i> sp. ants	Worldwide

Table 3. Distribution of invertebrate hosts of different zoonotic trematodes around the world.

Given the high proportion of people at risk of acquiring zoonotic trematodiasis, and the perspective of global warming driving the current situation toward the worst-case scenario, neglected parasitic zoonoses should be addressed as a world health priority by international health organisms [32–35]. Although there have been advances in approaching neglected parasitic zoonoses in recent years, with new treatments and increasing research founding, zoonotic trematodiasis when compared to other zoonoses, remains ignored, in part because of intense competition for the attention and funding of the health organisms and health offices of different developing countries, that are already investing in the control of other high priority neglected diseases [36]. This is also the case for the WHO which has postponed important programs destined to prevention, control and treatment against zoonotic trematodiasis for lack of funding support [37].

Pressure on wild ecosystems adds an important factor for the increase of risk factors of acquiring zoonotic trematodiasis by both animals and human populations. This, mainly due to the destination of new areas for intensive agriculture and livestock production which enable favorable conditions for the proliferation of the intermediate host, and several animal definitive host perpetuating conditions of endemicity in an habitat otherwise unfavorable for parasitic trematodes [37]. Conditions are even worse when aquiculture activities are adopted, increasing transmission hot spots where intermediate host, livestock, and human population converge in a more frequent basis [31]. A description of the zoonotic trematodes invertebrate hosts ubiquity is described in **Table 3**.

5. Anthelmintic resistance

Lung and intestinal trematodiasis are treated with praziquantel, and although some suspicious have emerged regarding the appearance of trematode resistance against this anthelmintic, no solid scientific evidence has been produced so far [35, 38]. On the other hand, fascioliasis is mostly treated with triclabendazole, a halogenated derivative of thiol-benzimidazole [39, 40]. Trematodes metabolize triclabendazole by their xenobiotic metabolizing enzymatic complex (XME). Fascioliasis treatment with triclabendazole has resulted in ever-growing fasciolicide resistance and/or tolerance in several countries around the world [41].

XME complex include enzymes such as Cytochrome P450, alcohol and aldehyde dehydrogenase glutathione S transferases and carboxylesterases [27], which protect trematodes against the toxic action of natural xenobiotics and now are the main defense against synthetic anthelmintic compounds [42]. There is the necessity to use the XME complex as anthelmintic resistance marker and particularly their DNA sequence within their respective genes in order to design fasciolicide resistance diagnostics by DNA technology [28].

Previous comparative transcriptomics in the liver fluke showed that the oxidative metabolic pathway and glutathione-dependent enzymes, which include the XEM complex, exhibited gene overexpression in triclabendazole-resistant *F. hepatica* when cytochrome P450 and glutathione S transferase transcription were assessed [59]. These results suggest that the XME complex is responsible for the transformation of fasciolicides to less toxic bioproducts during the liver fluke's triclabendazole-resistance process [27]. Comparative genomics on *F. hepatica*

highlights important changes on the β -tubulin expression, which suggest that the triclabendazole target molecule is playing a role on the liver fluke's anthelmintic resistance [28].

6. Diagnostics and treatment

Most diagnostic procedures of zoonotic trematodiasis start with suspicious symptoms and blood indicators such as eosinophilia [23], and further studies should request for search of eggs in feces, sputum, or urine alone with complementary diagnostics such as hepatobiliary enzyme levels in blood and use of imaging devices like ultrasound or high-resolution nuclear magnetic resonance spectroscopy [43].

The World Health Organization (WHO) has issued several recommendations to countries affected with zoonotic trematodiasis, regarding laboratory procedures of coprology, immunological and molecular diagnostics, as well as treatment prevention and control of zoonotic trematodiasis; WHO also indicates that clinical signs such as hepatomegaly and eosinophilia are clear indicators of trematodiasis [44]. Confirmation, however, relies mostly on the identification of trematodes eggs in feces, urine, or sputum samples [5]. The problem with this diagnostics approach is due to variations of the life cycles of different parasitic trematodes, and most acute clinical signs occur when trematodes are unable to produce eggs, which adds to low sensitivity or reproducibility of the laboratory procedures currently applied [45, 46]. Acute fascioliasis produces liver damage revealed by hepatic enzymes screening in blood and liver imaging; however, juvenile trematodes are not revealed by neither procedure and only 50% of adult flukes are identified [47].

A number of immunological procedures based on hemagglutination, immunofluorescence, and indirect enzyme-linked immunosorbent assay test have been reported as useful both during acute and chronic stages of most trematodiasis [48]. In spite of the success of immunological procedures, most of them rely on the identification of circulating antibodies and are therefore indirect procedures [49]; additionally, blood-circulating antibodies may show high titers long after the elimination of the parasites [53]. For direct confirmation of the causative agent on any zoonotic trematodiasis, some epidemiological studies are carried out by ELISA serological surveys in search for specific blood excretory or secretory antigens [55]. Certain variations of immunodiagnosics search for secretory antigens in fecal samples coupled to an ELISA assay [50], and several other immunological procedures for trematodiasis diagnostics have been developed with mixed results, but in general, trematodiasis may be efficiently diagnosed by immunological procedures with sensitivity of between 89% and 100% [51].

The advancement on the DNA-based technology diagnostic procedures has permitted the applications of PCR diagnostics on feces, urine, and sputum samples in search for trematode specific DNA sequences, PCR depends on parasitic development stages to be present for nucleic acids to be obtained from them, for example: parasitic eggs in fecal or urine samples; a minor disadvantage is that DNA extraction procedures for biological samples, have to be modified in order to obtain a proper amount of nucleic acids for the PCR diagnostics, additionally PCR requires an appropriate set of primers and specialised reagents and equipment which are reviewed

Zoonotic trematodiasis	Parasite	Transmission vehicle	Population at risk (millions)	Estimated cases (millions)	Symptoms	Diagnosis	Treatment
Liver flukes	<i>Fasciola</i> spp.	Vegetables	91	17	Fever, diarrhea, loss of appetite, dyspepsia, epigastric pain, nausea, pancreatitis	Eggs detection in feces, Immunodiagnosis, PCR	Triclabendazole
	<i>Clonorchis</i> spp.	Raw fish	601	11			Praziquantel
	<i>Opisthorchis</i> spp.	Raw fish	80	35			
Lung fluke	<i>Paragonimus</i> spp.	Crabs, crayfish	292	21	Cough, fever, bloody sputum, chest pain, headache		Praziquantel
Intestinal fluke	<i>Fasciolopsis buski</i>	Vegetables	50	Unknown	Diarrhea, constipation, headache, flatulence, loss of appetite, abdominal pain, nausea	Eggs detection in feces, PCR	Praziquantel

Table 4. Zoonotic trematodiasis, public health impact, symptoms, diagnostics, and treatment.

elsewhere [18], however, in spite of these disadvantages, the sensitivity and specificity of this diagnostic test, once performed properly, have no equal when compared to other tests.

7. Genomics of zoonotic trematodiasis

The need for new treatments for zoonotic trematodiasis requires a comprehensive genomics, transcriptomics and proteomics assessment of all parasitic trematodes [60]. Several draft genome efforts are reported for *S. mansoni* [54] and *S. haematobium* [55], similar efforts detailing transcriptomics and proteomics data sets for *S. japonicum* are available [52, 56, 57]. A number of expressed sequence tags have been described for Fish-borne zoonotic trematodes such as *O. viverrini* [58], and the sequence of genes coding for hundreds of important invasive factors are described for *F. hepatica* [28, 59].

As a result of comparative transcriptomics assessment, novel treatments using miRNA interference of invasive factor have shown encouraging results for schistosomiasis and fascioliasis [60, 61, 66]. Previous reports on partial genome outline of *F. hepatica* describe an unusual genome of 10 chromosome pairs and 1.3 Gbp in size, and this duplicates and triplicates the genome size of phylogenetically related parasitic trematodes such as *Clonorchis sinensis* [547 Mbp] and *Schistosoma* spp. [398 Mbp] [28]. This excess of genomic information is considered a sample of the parasite’s genetic plasticity that allows it to adapt rapidly to a changing environment, which may include the occupation of new ecological niches during the global warming process, adaptation to a wide range of hosts, and tolerance or resistance to fasciolicide treatment of the livestock.

All these possibilities may increase the future risk on public health [17]. Recently, an online database with a functional genomics query engine has been described [Trematode.net], the site hosts complete and draft genomes data of 16 trematodes species and offers unlimited

Trematode	Genome size millions of base pairs	Open reading frames	GenBank available EST	GenBank available nucleotide sequences	Current status/ references
<i>Fasciola hepatica</i>	1275	15,740	1677	59,631	Completed/[29]
<i>Fasciola gigantica</i>	Uk	Uk	8397	1159	In process/[60]
<i>Fasciolopsis buski</i>	Uk	Uk		18	In process/[60]
<i>Haplorchis taichui</i>	Uk	Uk			In process/[60]
<i>Opisthorchis felineus</i>	Uk	Uk			In process/[60]
<i>Paragonimus kellicotti</i>	Uk	Uk			In process/[60]
<i>Paragonimus miyazaki</i>	Uk	Uk			
<i>Paragonimus westermani</i>	Uk	Uk	505	319	
<i>Clonorchis sinensis</i>	516	16,000	113,414	3401	In process/[68]
<i>Opisthorchis viverrini</i>	634.5	16,379	4194	101,007	Completed/[65]
<i>Schistosoma japonicum</i>	397	13,469	103,881	55,028	Completed/[63, 67]
<i>Schistosoma mansoni</i>	363	14,229	113,714	3401	Completed/[61, 64]
<i>Schistosoma haematobium</i>	385	11,140		4433	Completed/[62]

Uk = Unknown.

Table 5. Zoonotic trematode genome projects efforts completed and in progress. A number of genomic research institution have being working on sequencing the genomes of the most important etiological agents of zoonotic trematodiasis, the table exhibits the status of some of these projects as well as the number of estimated genes already available on line for each parasite.

downloading and online genome-transcriptome analysis tools [62]. **Table 5** depicts some information on the genomic research on zoonotic trematodes.

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