INTESTINAL HETEROPHYIDIASIS: AN EMERGING FOOD-BORNE PARASITIC ZOONOSIS IN SOUTHERN PHILIPPINES

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Abstract. Heterophyidiasis is an infection of the small bowel by minute intestinal flukes of the genus *Heterophyes* or related members of the family Heterophyidae. To provide a better understanding of this rarely reported condition, this study attempted to determine the infection rate, intensity of infection as well as the clinical spectrum of heterophyid infection. A stool survey was conducted in barangay San Isidro, Monkayo, Compostela Valley. Thirty-six percent of patients with history of bowel disturbance (abdominal discomfort/pain and/or diarrhea) in the past 4 weeks were found to have heterophyidiasis. All age groups were infected, with the youngest patient being 1 year 7 months of age, while the oldest patient was 73 years of age. Prevalence was highest in the 15 to 30 years old group at 55.3%. The most common clinical manifestations of heterophyidiasis were signs and symptoms of acid peptic or peptic ulcer disease. Early diagnosis and treatment are important to ensure prompt resolution of heterophyid infection, hence, decreased morbidity and decreased chances for complications like heart or brain involvement. Proficiency of laboratory staff should be enhanced to ensure accurate diagnosis which will then make appropriate treatment possible.

INTRODUCTION

Heterophyidiasis is an infection of the small bowel by minute intestinal flukes of the genus *Heterophyes* or related members of the family Heterophyidae which are normally parasites of fish-eating birds and mammals. Heterophyidiasis occurs in humans in many parts of the world. It is endemic in Southeast Asia and is found in most countries of the Far East, the Middle East, and in some countries in the Mediterranean littoral, as well as in Brazil, the Ukraine, and Hawaii. In the Philippines, the prevalence of heterophyidiasis has been noted to be low (Belizario and Solon, 1998). Less than 1% of more than 30,000 stools examined in nationwide surveys were found positive for heterophyid ova (Cross and Basaca-Sevilla, 1984) (Fig 1).

Two community surveys were done in 1998 and 1999 in Monkayo, Compostela Valley Province in Southern Mindanao in connection with an outbreak of intestinal capillariasis. Results showed heterophyid infection rates of 16.7% and 15.7%, respectively (Belizario *et al*, 2000), which may indicate a real problem of underreporting of this condition probably due to lack of consideration by clinicians and a lack of recognition in diagnostic laboratories. Further studies of this condition, in particular its clinical spectrum and the efficacy of treatment, will lead to a better understanding of this rarely reported condition which happens not to be uncommon in areas that have been visited.

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Fig 1- Heterophyid adult and egg.

This study therefore attempted to achieve the following: 1) to determine the parasite rate (infection rate) and intensity of heterophyid infection; 2) to describe the clinical spectrum (clinical manifestations) of heterophyid infection; 3) to describe the efficacy of therapy for heterophyid infections; and, 4) to describe the eating habits of affected populations.

MATERIALS AND METHODS

Study site

The barangay of San Isidro is in the municipality of Monkayo, Compostela Valley Province in Region XI (Southern Mindanao). Farming is the most common occupation. Corn is the major crop produced. Based on Rural Health Unit (RHU) records, there are 85 (31.5%) households with water-sealed toilets, 92 (34.1%) with Antipolo-type toilets and 93 (34.4%) with no toilet facilities. According to the Monkayo Rural Sanitary Inspector (RSI), the people of San Isidro get water from two sources: rainwater and the Saug River. Local residents normally collect rainwater and use it for cooking and washing purposes. Since the discovery of the intestinal capillariasis in the area in 1998 (Belizario, 2000), there has been a total of 17 barangays with reported cases of heterophyidiasis in June 2000. Intestinal parasitism was the second leading cause of morbidity in Monkayo in 1998, while anemia was fourth. Hookworm was the most common helminth identified followed by *Ascaris* and *Trichuris* (Monkayo RHU Records, 1998).

Conduct of study

The study was conducted in full accordance with Good Clinical Practice Guidelines including the provisions of World Medical Association Declaration of Helsinki.

Cross sectional survey

Active case detection (ACD) was conducted through a cross sectional survey in the early part of May 2000 in the barangay of San Isidro. An interview and a stool survey were conducted on residents with a history of bowel disturbance (abdominal discomfort/ pain and/or diarrhea) in the past 4 weeks prior to the survey. Chief complaints along with associated signs and symptoms were taken note of, and stool specimens from the same patients were examined using Kato-Katz method (WHO, 1995) and the formalin ether concentration technique (FECT) (WHO, 1994). Initial reading was done by trained field microscopists who are normally assigned to government health facilities in the area, and quality control was provided by a microscopist from the College of Public Health, University of the Philippines Manila (UP-CPH). Cross checking was done with a UP-CPH microscopist who was available while microscopy was conducted in the field. This microscopist re-read 20% of slides brought in to the UP-CPH Diagnostic Parasitology Laboratory.

Heterophyid eggs were counted as in counting *Ascaris*, *Trichuris* and Hookworm eggs using Kato Katz method (WHO 1994, 1995) where the number of heterophyid eggs in the stool specimen measured by a standardized template was multiplied by 24 to obtain the number of eggs per gram (EPG). With the use of results of stool examination and egg counting, a frequency distribution of egg counts was prepared using a proposed scheme for classification of intensity of heterophyid infection devised by the researchers (Table 1).

All study participants who were found to be positive for one or more intestinal parasites were provided with the appropriate drugs from the Regional Field Office XI and the Monkayo Rural Health Unit. Praziquantel 75 mg/kg in three doses given in one day was given to patients who had heterophyidiasis (WHO, 1995), while albendazole 400 mg chewable tablet was given to patients who had common intestinal helminthiasis like ascariasis, trichuriasis, enterobiasis and hookworm infection (WHO, 1996). Metronidazole was given to patients who were infected with pathogenic intestinal protozoans. Praziquantel-albendazole combination was given to patients who had mixed heterophyid and common intestinal helminth infections.

Table 1
Proposed classification of intensity of heterophyid infection (Belizario *et al*, 2000)

	Classification of intensity		
	Light	Moderate	Heavy
Heterophyid	1-100 epg	101-1,000 epg	>1,000 epg

epg eggs per gram

Follow up of heterophyid infected patients

Stool specimens of infected and consenting participants were collected one to three days after treatment to collect parasites expelled and to identify the heterophyid species in the area. Stool specimens submitted were comminuted with water, after which the mixture was made to pass through two layers of screen. The filtrate was then examined for possible adult worms expelled after treatment.

Seven to fourteen days after treatment, stool specimens were collected from patients who were diagnosed to have heterophyids. Specimens were processed using the Kato Katz method. Initial reading was done by the Monkayo RHU microscopist, and the processed specimens were forwarded to the UP-CPH Diagnostic Parasitology Laboratory for quality control purposes. Response to treatment of each patient was categorized as one of the following: 1) Clinical cure - absence of eggs on repeat stool examination; 2) Clinical improvement - lower intensity of infection on repeat examination; 3) Clinical failure - same or higher intensity of infection on repeat stool examination; 4) Indeterminate - no repeat stool examination or lost to follow up.

Interviews on food preparation, food preferences and eating habits

Key informant interviews and group interviews were conducted to help describe practices of food preferences, food preparation, and eating habits that possibly expose local residents to heterophyid infections.

Collection and identification of possible intermediate hosts and parasite stages

Known and possible intermediate hosts were also collected from the field and were forwarded to the Institute of Marine Biology of the University of the Philippines Los Baños for species identification and examination for larval stages of heterophyid flukes. In the laboratory, the fish were identified to the lowest possible taxon following Conlu (1986). Before examination, the total length of each fish was measured in centimeters. The external parts such as the fins and scales, gills, gut (intestines and cecum), and abdominal muscles of fish were carefully examined for parasites under a dissecting microscope. Parasites were identified to the lowest possible taxon and their stage in the life cycle determined. Abundance was recorded as number of parasites counted in 8 mm^2 under a dissecting microscope.

RESULTS

Cross sectional survey

A total of 242 study participants consulted and submitted stool specimens. All age groups were represented with the majority of study participants coming from age groups 45 years old and below. Of the study participants, 137 (56.6%) individuals were found to be positive for at least one parasitic infection using Kato Katz method. There were more infected males than females (57.7% and 42.3%, respectively). One hundred seventeen (48.3%) people were found to be infected with at least one organism (parasite or commensal) using FECT. There were also more infected males than females (58.1% and 41.9%). One hundred and eighty-one (74.8%) people were found to be infected with at least one organism (parasite or commensal) using either Kato Katz method or FECT. As in using either diagnostic procedure alone, there were more infected males than females (57.5% and 42.5%).

Table 2 shows the infection rate with intestinal helminth infections using Kato Katz method and FECT. With Kato Katz method, heterophyidiasis was found to be most common with 31.0% infected. The next most common helminth infections were hookworm infections, ascariasis, trichuriasis and enterobiasis (27.3%, 11.2%, 9.1% and 1.2% respectively). With

Table 2
Infection rate with intestinal helminth infections using Kato-Katz method and FECT (n=242).

Parasite seen	Kato-Katz		FECT	
	No.	%	No.	%
Ascaris	27	11.2	13	5.4
Trichuris	22	9.1	8	3.3
Hookworm	66	27.3	106	43.8
Enterobius	3	1.2	3	1.2
Heterophyid	75	31.0	33	13.6

FECT, heterophyidiasis was found in only 13.6% of study participants, while hookworm infection was seen in 43.8%. Less common helminth infections were ascariasis, trichuriasis and enterobiasis (5.4%, 3.3% and 1.2%, respectively).

Using FECT alone, *Endolimax nana* and *Entamoeba coli* infections were most common in 15.7% and 11.2% of study participants, respectively. Other less common intestinal protozoans seen were *Blastocystis*, *Giardia*, *Entamoeba histolytica*, and *Iodamoeba* (9.1%, 7.4%, 4.5% and 1.7%, respectively). Note that *Endolimax*, *E. coli* and *Iodamoeba* are non-pathogenic amoebae (Table 3).

With the use of either Kato Katz method or FECT alone (31.0% vs. 13.6%), a total of 87 patients were shown to have heterophyidiasis. This gives an overall infection rate of 36.0%. Intestinal fluke infection was seen in all age groups with the youngest patient being 1 year 7 months of age, while the oldest patient was 73 years of age (mean age = 27.15; SD = 17.11). Prevalence was highest in the 15 to 30 years old group at 55.3%. Infection rates were generally higher in age groups 5 years old and over, although the infection rate in children less than 5 years of age may not be considered insignificant. Males 60 years old and younger had higher infection rates compared with their female counterparts (Table 4).

Table 3
Infection rate with intestinal protozoan infections using FECT (n=242)

Parasite seen	No. of patients	%
Entamoeba histolytica	11	4.5
*Entamoeba coli**	27	11.2
*Endolimax nana**	38	15.7
Blastocystis hominis	22	9.1
Giardia lamblia	18	7.4
*Iodamoeba butschlii**	4	1.7

*non-pathogenic

The proposed scheme for classification of intensity according to the distribution of egg counts among all infected patients was utilized. Overall, patients with moderate to heavy intensities of infection made up the majority with a combined percentage of 70.7%. This pattern of distribution was seen in age groups 15 years old and over. In age groups less than 15 years of age, most infected patients had light intensities of infection. The range of counts of heterophyid eggs among infected patients was from 24 to 26,256. The arithmetic mean egg count was 988.4 (SD = 3146.7), while the geometric mean egg count was 256.0 (median = 192; mode = 48). Mean egg counts fell within the range of moderate intensities of infection.

Of the patients who were found to have heterophyid infection in San Isidro, 83 patients were interviewed. A review of their histories showed that 38 (45.8%) patients complained of peptic ulcer-like symptoms. Upper abdominal discomfort/pain was reported by 35 (42.2%) patients, while a gurgling abdomen was noted by 20 (24.1%) patients. Other common complaints were nausea, diarrhea and weight loss. Fourteen (16.9%) patients were asymptomatic.

Follow up of heterophyid infected patients

Six patients treated with praziquantel submitted stools for adult collection and identification. Because of the technical difficulties with collecting the minute organisms, the project team was not successful in collecting heterophyid adults for species determination.

Table 4
Age and sex specific heterophyid infection rates using Kato Katz method and FECT (n=242).

	Male		Female		Total	
Age group	No. of patients with stool samples	No. of infected patients	No. of patients with stool samples	No. of infected patients	No. of patients with stool samples	No. of infected patients
		(%)		(%)		(%)
< 5	13	3 (23.1)	23	3 (13.0)	36	6 (16.7)
5-14	36	11 (30.6)	26	6 (23.1)	62	17 (27.4)
15-30	25	16 (64.0)	22	10 (45.4)	47	26 (55.3)
31-45	34	17 (50.0)	29	11 (37.9)	63	28 (44.4)
46-60	8	2 (25.0)	9	2 (22.2)	17	4 (23.5)
> 60	6	2 (33.3)	11	4 (36.4)	17	6 (35.3)
Total	122	51 (41.8)	120	36 (30.0)	242	87 (36.0)

Of the 75 patients found to have heterophyidiasis, 67 (89.3%) individuals were given treatment with praziquantel. Only 35 (52.2%) patients submitted specimens for follow-up stool examination using Kato Katz method. Of these, 11 patients were found to have at least one helminth infection which gave a cumulative prevalence of 31.4%. Only one patient (2.9%) was still found to have heterophyid eggs. Cure rate among those with heterophyidiasis was 97.1% (34 out of 35 patients who were infected, treated and were seen on follow-up). Clinical cure was seen in 34 (45.3%) patients and clinical improvement was in one (1.3%) patient. None of the patients exhibited clinical failure. Clinical outcome indeterminate was seen in 40 (53.3%) patients. Egg reduction rates for arithmetic and geometric means were 99.3% and 98.4%, respectively.

Food preparation, food preferences and eating habits

Interview of key informants and group interviews revealed that the Saug River is a major source of food for the local residents. Local people are fond of eating freshwater fishes, shrimps, crabs and frogs. Freshwater fishes are normally seasoned with salt and vinegar as a local preparation called *kilaw*. Among the variety of fishes eaten as *kilawin* are *tilapia*, *paitan* and *buriring*. *Sabaw* is a way of cooking fishes, like *tilapia*, *karpa* and *haluan*, by boiling for several minutes. *Sugba* is grilling the fish over charcoal. Grilled fishes consist of *tilapia*, *paitan*, *karpa* and *pantat*, the first two being a favorite *pulutan* of alcoholic beverage drinkers. Another form of cooking is *gata* or cooking with coconut milk. This is more commonly done on freshwater shrimps, crabs and frogs. *Pantat* is the type of fish which is cooked in *gata*.

Possible intermediate hosts and parasite stages

A total of 6 species of fish and 3 other aquatic animals were identified from all samples collected. The identification of all fish samples was validated except for two. The identification of the fish *Ophiocara aporos* and *Poecilla* sp is tentative and will require further validation in the future. All samples examined were positive for parasite, which occurred in various stages of their life cycle, and at various parts of the hosts. Metacercariae were found in scales of *Ophiocephalus striatus* (*dalag*) and *Hypophthalmichthys molitrix* (*paitan*). Larval forms of the nematode *Capillaria* were present in gills of *Oreochromis* sp (*tilapia*). Metacercariae of a digenetic fluke were also observed in freshwater crabs (*talangka*) from the area. The abundance of the metacercaria was estimated at about 50 individuals/8 mm^2. Microsporidia parasites appearing as xenoma were observed in muscles of *Ophiocara aporos* (*uko*). The number of this parasite exceeded 100/8 mm^2. Unidentified metacercariae were also present in muscles of the *Hypophthalmichthys molitrix* (*paitan*). In the fish *Ophiocephalus striatus* (*dalag*), three types of parasites were observed in the intestines. These were a pseudophyllid tapeworm, a digenetic fluke and a nematode, *Acanthocephala*. Parasites also occurred in the intestines of the frog *Rana crancivora* and a gastropod snail. Adult and larval forms and eggs of the nematode *Icosiella* were present in the intestines of the frog while sporocysts and cercariae of a fluke were observed in the intestines of the snails. The sporocysts and cercaria in snails were estimated to exceed 100/8 mm^2.

DISCUSSION

The heterophyid infection rate in San Isidro was unexpectedly high comparing to the results of previous surveys from the late 1960s to the early 1980s (Belizario *et al*, 2000). It is even much higher than infection rates in surveys in 1998 and 1999 (WHO, 1998). This means that intestinal fluke infection may be an emerging parasitic infection that should be considered in an area with poor environmental sanitation and high consumption of freshwater fishes.

All age groups were affected by intestinal fluke infection. The possibility of exposure through the usual food consumed by the whole family is likely. Higher infection rates and intensities of heterophyid infection among males and among age groups 15 to 45 years old may suggest higher transmission in these groups of people in the community. Higher transmission may mean higher consumption of infected intermediate hosts. Higher infection rates and intensities of infection may actually result in greater morbidity with greater chances of developing complications which deserve further investigation.

Also, a number of intestinal parasitoses abound in the areas studied. All of these are certainly preventable and curable. Soil-transmitted helminthiases like roundworm, whipworm and hookworm infections will continue where a significant number of individuals continue to be infected and untreated, where there is indiscriminate defecation and low levels of sanitation, where the problem of availability of clean water supply exists and where no effective program for control is in place. Although infection rates were not alarmingly high except for hookworm infection, soil-transmitted helminthiases surely pose threats to health, life and productivity especially in the younger population where infection rates are surely much higher. A cost effective and feasible control program focused on possibly targeted mass or even universal treatment,

health education and improvements in the environment is highly recommended.

The presence of intestinal amebae in the general population, though generally underreported possibly due to difficulties in laboratory diagnosis, indicates a poor level of environmental sanitation in the areas surveyed. With a lack of sanitary toilet facilities and indiscriminate defecation, contamination of water supplies is a likely consequence. Again, environmental hygiene coupled with provision of safe water supply may help solve the problem of intestinal protozoan infections. The importance of and the need for accurate laboratory diagnosis of these intestinal protozoans should be made possible in the local health unit level to enable early case detection and, if needed, early treatment.

The use of Kato Katz method demonstrated a higher efficiency (31.0% *vs* 13.6%) in diagnosis of heterophyid infection compared with FECT. Laboratory diagnosis gives a definitive assessment of intestinal fluke infection, but not too many laboratories in the Philippines may be able to recognize the diagnostic stage, that is the heterophyid ova. Proficiency of laboratory staff therefore needs to be prioritized to ensure accurate diagnosis that will then make possible appropriate treatment. Early diagnosis and treatment are important to ensure prompt resolution of infection and decreased morbidity, thereby preventing complications like heart or brain involvement.

One striking observation on the clinical manifestations of heterophyidiasis is the finding that this parasitic disease may usually manifest with signs and symptoms of acid peptic disease (APD) or peptic ulcer disease (PUD), a common diagnosis of especially out-patients. Epigastric or upper abdominal discomfort/pain, abdominal fullness/flatulence, nausea, vomiting, anorexia are consistent with APD/PUD. It is important therefore for clinicians to consider intestinal fluke infection and the need for a stool examination when dealing with a patient presenting with APD-like manifestation with a history of possible exposure.

Praziquantel at a dose of 25 mg/kg for three doses in one day appears to be an excellent treatment for heterophyid infections as supported by excellent cure and egg reduction rates as were observed during follow up of infected individuals. Good patient compliance helps to ensure good treatment outcome and should be an important goal when instructing patients for treatment since the number of milligrams and the number of tablets to be taken in a day may sound as too much for the usual patient.

As for the possible intermediate hosts, the high incidence of these parasites in freshwater fish species is alarming if we consider that fish is a major source of nutrition in the area. This may have a large implication to the health conditions of the locals, and it is necessary that this problem be well understood to develop strategies to ease this problem. Recommendations regarding the possible intermediate hosts include the need to inform locals to prepare fish properly. Gills, scales and guts should be removed and the flesh cooked properly to kill whatever parasites are in the animal. *Rana crancivora* is an edible field frog. This animal must be de-gutted properly as majority of parasites was observed in its gut. There may be a need to survey all fish food in the area for the presence of parasites. Consequently, it is also important to do ecological studies such as trophic dynamics to determine components of the food chain in the environment. The food chain is certainly where humans become infected by these parasites. Intensive education campaign is indicated to inform them of the various risks and how to reduce these risks. Once parasites are identified, there is a need to study their life history patterns. Information generated by this type of study is important to understand how these parasites are dispersed, what are their host animals, how they are transmitted to humans, and how infection can be prevented. Based on this information, various control strategies (*eg* biological controls) should be proposed and implemented to limit the spread of food borne parasitoses among the locals.

The results of this study illustrate the importance of recognition of the possible problem of heterophyidiasis and accurate laboratory diagnosis, collection of basic epidemiologic data and recognition of possible intermediate hosts that will be crucial for control and prevention of this health problem at the community and local health system levels. Good laboratory diagnosis of heterophyidiasis during the intestinal capillariasis outbreak in the study area, the sharing of this technical expertise to the local microscopist, and the development of the capability in the local health unit to diagnose and treat this parasitic infection are essentials for continued surveillance and eventual control of this intestinal parasitosis.

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