HYPERENDEMIC FASCIOLIASIS ASSOCIATED WITH SCHISTOSOMIASIS IN VILLAGES IN THE NILE DELTA OF EGYPT

JOSE-GUILLERMO ESTEBAN, CAROLINA GONZALEZ, FILIPPO CURTALE, CARLA MUÑOZ-ANTOLL, MARIA ADELA VALERO, MARIA DOLORES BARGUES, MABROUK EL SAYED, ALY A. W. EL WAKEEL, YEHIA ABDEL-WAHAB, ANTONIO MONTRESOR, DIRK ENGELS, LORENZO SAVIOLI, AND SANTIAGO MAS-COMA

Departamento de Parasiologia, Facultad de Farmacia, Universidad de Valencia, Valencia, Spain; Istituto Superiore di Sanità, Ministry of Health, Rome, Italy; Strengthening Rural Health Services Project, Ministry of Health and Population, Behera Regional Health Office, Damanhour, Egypt; National Schistosomiasis Control Program, Ministry of Health and Population, Cairo, Egypt; Parasitic Diseases and Vector Control, Communicable Diseases Control, Prevention and Eradication, World Health Organization, Geneva, Switzerland

Abstract. Coprologic surveys were carried out in villages of the Behera Governorate in the Nile Delta region of Egypt to characterize the epidemiologic features of human fascioliasis caused by Fasciola hepatica and F. gigantica in this lowland endemic area by comparison with fascioliasis caused by only F. hepatica in areas hyperendemic for human disease in the Andean highlands of South America. The fascioliasis prevalences detected (range = 5.2–19.0%, mean = 12.8%) are the highest obtained in Egypt. The comparison with previous results suggests that in the Nile Delta, fascioliasis is spreading from an original situation of sporadic human cases in well-known endemic foci for animal disease to an endemic distribution in humans, which may be characterized as a mesoendemic region that includes several hyperendemic areas for human disease. As in Andean countries, a relationship with sex was found, although in Egypt prevalences, but not intensities, appeared to be significantly higher in females. All ages appear to be susceptible to liver fluke infection, with prevalences and intensities being lower before and after school age, a situation that is consistent with that detected in Andean countries, although the peak in the 9–11-year-old age group appears less pronounced in Egypt. The intensities were very high when compared with those found in subjects sporadically infected in areas endemic for animal disease, but relatively low for a hyperendemic situation, although the intensities may not be conclusive because of the transmission seasonality of fascioliasis in the Nile Delta. The marked similarities in the qualitative and quantitative spectrums of protozoans and helminths, multiparasitisms, and associations between liver flukes and other parasitic species suggest physiographic-hydrographic and behavioral-social characteristics similar in all areas hyperendemic for human fascioliasis, which are independent of other factors such as climate, altitude, and cultural or religious features. The significant positive association between liver fluke infection and schistosomiasis mansoni detected in one locality has never been described elsewhere, and must be considered relevant from clinical, pathologic, diagnostic, and therapeutic points of view. Interestingly, the relationships of schistosomiasis prevalences and intensities with sex and age follow patterns similar to those found in fascioliasis.

INTRODUCTION

Fascioliasis is a well-known parasitic disease because of its veterinary importance and the great losses it causes in livestock production. However, human fascioliasis was only considered a secondary disease by public health officials, with only approximately 2,000 cases reported between 1970 and 1990. This picture has changed in recent years; the pathogenicity of fascioliasis in humans has been recognized, the number of cases reported has increased in 51 countries in five continents, and areas endemic for human disease that are not necessarily related to those endemic for animal disease have been described, in which fascioliasis chronically and superimposed repetitive liver fluke infections pose additional pathologic complications. We now know that fascioliasis can no longer be considered merely a secondary zoonotic disease, but is now an important human parasitic disease, with estimated ranging from 2.4 to 17 million people infected. Despite these restrictions, F. hepatica has succeeded in expanding from the original European geographic area to five continents. Fascioliasis caused by F. hepatica is the vector-borne disease with the widest latitudinal, longitudinal, and altitudinal distribution known. In Europe, the Americas, and Oceania only F. hepatica is present, but the distributions of both species overlap in areas in Africa and Asia. Several areas in Central and South America, Europe, Africa, and Asia have recently been shown to be endemic for human disease, ranging from hypoendemic to highly hyperendemic situations. These areas present a wide spectrum of epidemiologic characteristics related to the wide diversity of environments. The areas endemic for human disease whose epidemiologic characteristics are best known are those in South America, where the regions with the highest hyperendemicity appear to be associated with high altitude (2,000–4,100 meters) in Andean countries such as Bolivia and Peru. The northern Bolivian Altiplano, with an altitude of 3,800–4,100 meters, shows the highest prevalences and intensities of human fascioliasis known: up to 72% and 100% by coprologic and immunologic methods, respectively, and more than 5,000 eggs per gram (epg) of feces in given localities. The situation is similar in Peru.

In these regions of South America, high altitude markedly influences disease transmission. Temperature has no wide seasonal variation and its mean value is low throughout the year, (approximately 10°C or less). However, there are large variations in temperature within the daily 24-hour period. Rainfall distribution is seasonal, with a long dry season coin-
ciding with the lowest minimum temperatures and a long wet season in which the majority of rainfall occurs. This pattern is markedly different from those in endemic areas in Europe and the Mediterranean region, in which fascioliasis is traditionally biseasonal, appearing in the spring and fall. In South America, evapotranspiration is very high, with temporary bodies of water being of short duration. This explains why lymnaeids are almost always restricted to permanent bodies of water and transmission can occur throughout the year, contrary to what is typical of fascioliasis in European and Mediterranean lowlands, where transmitting lymnaeids are markedly amphibious and develop mainly in temporary bodies of water.18

Egypt is a flat, lowland country in which fascioliasis has been present since ancient times, where its effects can be seen in the cattle represented in Egyptian tombs, as well as in the liver of an Egyptian mummy.19 The June 1998 report of the General Organization of Veterinary Services of the Ministry of Agriculture indicated that the lost in meat and milk in Egypt due to fascioliasis was 30% per year (one billion Egyptian pounds).20 Although animal fascioliasis is present in many governorates,19,20 until 1960 only sporadic human cases of fascioliasis were reported in Egypt, mainly in the Nile Delta region. Since 1980, the number of cases has risen drastically and human infection has been reported in different governorates,20 i.e., in Alexandria, Behera, Cairo, Dakahlia, Kafr El-Sheikh, Qalyoubia, Menoufia, and Sharkia. The World Health Organization has estimated that 830,000 people are infected with liver flukes in the Nile Delta region.21

Although the number of cases in Egypt increases every year, almost all information is based on patients diagnosed in hospitals. Population-based data on the epidemiologic characteristics of fascioliasis infection are scarce, insufficient with regard to prevalence, and provide no information on intensity and concomitant parasitic infections. The interest in such an epidemiologic study lies in the fact that the lowland characteristics of Egypt, where both F. hepatica and F. gigantica are present,22,23 differ markedly from those in the Andean highlands, where only F. hepatica is present.24 In the Nile Delta region, the mean annual temperature is relatively high (20.7°C), with a monthly range from 13°C in January to 27°C in August. The total annual rainfall is only 99 mm, with a monthly range from 0 mm in June–September to 24 mm in January, resulting in a dry period throughout the year. The large delta area has been transformed into an agricultural plain due to a large irrigation system consisting of numerous canals, ranging from main large canals to small secondary channels. The mean annual level of potential evapotranspiration is 144 mm, with a monthly range between 71 mm in January and 216 mm in June.7 Thus, a comparison is needed to see whether human fascioliasis shows epidemiologic features that vary in the areas endemic for human disease according to climatic, physiographic, and human characteristics.

MATERIALS AND METHODS

Study population. This study was conducted in the Behera Governorate, an area where fascioliasis is an important public health problem because infected children have been diagnosed in almost every district and there is a relationship between fascioliasis and anemia.25,26 It is one of the largest governorates in Egypt and covers an area of 10,757 km², with an estimated population of nearly five million. It includes the territory on the west side of the delta, from the Nile River to the desert and from the Mediterranean Sea to the outskirts of Cairo. This governorate is administratively divided into 15 districts with wide differences in population density. The economy of the governorate is based mostly on agriculture, although various industrial activities are present in the Kafr El Dawar district. Fishing is common in the villages near the Mediterranean Sea and Idco Lake. A small portion of the population lives in the desert and consists of Bedouin nomads. The living conditions of the people in Behera appeared to be good. Dwellings are usually built with bricks and cement, are supplied with public water (only a 25% of the people use hand pumps), electricity, and toilets or latrines. Nevertheless, a system for garbage and sewage collection is present in only some areas, and the population in rural houses usually disposes garbage and sewage in canals, rivers, and open fields.27 Fascioliasis has a great impact in animals in the Behera Governorate, with prevalences of 52.8% in cattle, 47.5% in buffaloes, and 29.0% in sheep.28

Four villages were selected to obtain a good representation of the most traditional way of life in the agricultural area, within a transect covering from near the main Alexandria-Damanhour route, where most people live, to the rural, more isolated inland areas (Figure 1). El Aaly and Bolin (Kafr El Dawar district) are two villages of approximately 10,000 inhabitants. They are surrounded by rice and cotton fields. Drainage canals are common, ranging from a large main channel to small irrigation channels. El Kaza (Hosh Esa district) is a smaller village of approximately 7,000 inhabitants that contains several urban population clusters and is surrounded by rice fields and irrigation canals of various sizes. Tiba (Delengate district) is a rural village of approximately 13,000 inhabitants that is also surrounded by rice fields, but is a greater distance from large human populations and large canals.

Stool collection and laboratory methods. The coprologic survey was conducted in June 2000 and involved 678 subjects.
(226 males and 452 females) 1–80 years of age (mean ± SD = 22.1 ± 16.4 years). The population of each village surveyed was informed at meetings with public health officials of the relevance and impact of intestinal and hepatic parasitic infections on the development of control programs at the national, regional, district, and village levels. The surveys were made on randomly selected persons on a given day among all participating subjects.

A clean, plastic, wide-mouth, numbered container with a snap-on lid was given to every person. All subjects were then asked to try to fill the container with their own feces and to return it immediately. One stool sample per subject was collected and personal data (name, sex, and age) were recorded on delivery of the container. Fecal specimens were transported to the Parasitology Laboratory of the Behera Regional Health Office in Damahour within 1–3 hours of collection. In this laboratory, a Kato-Katz slide was made from each stool sample following the recommendations of the World Health Organization using a template delivering approximately 41.7 mg of feces.28 These slides were examined within one hour of preparation to avoid overclarification of some helminth eggs. If sufficient material from each stool sample was present, one aliquot was preserved in 10% formalin solution (1:3).

Parasitologic studies were carried out at the Departamento de Parasitología (Valencia, Spain). Samples fixed in 10% formalin were processed by a formol-ether concentration technique29 and one aliquot of sediment obtained with this technique was stained using a modified Ziehl-Neelsen technique.30 Two slides per specimen were examined by one of the authors (CG) and then by the first author. Microscopic slides and materials from the human parasite collection of the Parasitology Department of the University of Valencia were used for quality control when needed.

The sediments of the concentration technique and the Kato-Katz slides were used to obtain prevalence data. Based on the techniques used, the prevalence obtained for the pinworm Enterobius vermicularis may not be considered definitive because anal swabs would be the adequate technique for the detection of the eggs of this nematode species. The Kato-Katz slides were analyzed for egg counts. Intensity of infection, measured as epg as an indicator of F. hepatica, F. gigantica, and Schistosoma mansoni burden in infected subjects, is reported as range, arithmetic mean, geometric mean, and classes of intensity. No attempt was made to differentiate between F. hepatica and F. gigantica. Because of the difficulty of differentiating the two species at the egg level, both will be referred to as Fasciola spp.

Institutional ethical review procedure. The surveys were carried out after informed consent was obtained from the local authorities in the villages. The project was reviewed and approved by the Ministry of Health and Population of Cairo and was performed in collaboration with the Behera Regional Health Office of the Ministry of Health and Population in Damahour. The ethical aspects of the study were reviewed and approved by Communicable Diseases Control, Prevention and Eradication of the World Health Organization (Geneva, Switzerland), the Integrated Control of Diseases, Regional Office of the World Health Organization for the Eastern Mediterranean (Cairo, Egypt), and the Directorate General for Development Cooperation, Italian Embassy (Cairo, Egypt).

Diagnostic results were sent to the Egyptian authorities responsible for child health. Health workers of Ministry of Health and Population were subsequently charged for appropriate anthelmintic and antiprotozoal treatments within the framework of the bilateral cooperation project between the Ministry of Health and Population and the Italian Cooperation.27

Statistical analysis. Statistical analyses were done using SPSS version 6.1 (SPSS Institute, Chicago, IL) for Windows. For the evaluation of categorical variables, the chi-square test or Fisher’s exact test was used. The Mann-Whitney U test and the Kruskal-Wallis H test were used for non-normally distributed data. Associations between liver fluke infection and other parasite species were investigated by 2 × 2 contingency tables, from which the chi-square value was calculated. A P value < 0.05 was considered statistically significant.

RESULTS

This coprologic study identified 12–13 protozoan and 7–9 helminth species. Prevalences in each village surveyed and in the total study are shown in Table 1. Blastocystis hominis (49.6%), Entamoeba coli (40.7%), and Giardia intestinalis (23.3%) were the most prevalent protozoans, while Fasciola and S. mansoni were the most common helminthes, with an overall mean prevalence of 12.8% and 12.3%, respectively. It is worth mentioning that a large majority (minimum = 73.3%) of the subjects studied showed infection with at least one parasite species. The lowest prevalences were detected in El Aaly, and the low prevalence of Fasciola in this village (χ² = 0.98, P = 0.0001) was statistically significant (Table 2).

The distribution of fascioliasis prevalences according to sex and age groups is shown in Table 2. Prevalences between males and females were significantly different (8.8% versus 14.8%; χ² = 4.8, P = 0.0284). Age groups were established according to the following criterion: infants (1–5 years old); school children (6–11 years old); adolescents (12–18 years old); and adults (> 18 years old). The lowest prevalences were detected in the infants group, but no statistically significant differences between the prevalence rates by age groups were detected. All ages appeared to be susceptible to infection (positive cases from 2 to 70 years old).

The overall intensities of fascioliasis by village, according to sex and age groups, are shown in Tables 3 and 4. Absolute egg counts in the infected subjects ranged from 24 to 432 epg, with arithmetic and geometric means of 72 and 51 epg, respectively. No statistical differences were found in intensities between villages, or according to sex and age groups within villages, although the highest overall egg counts were detected in the infants and school children. The results on fascioliasis intensity levels according to villages surveyed and sex and age groups indicated that the highest percentage (85%) of subjects infected were shedding not more than 100 epg. A nine-year-old girl from El Kaza excreting 432 epg was the subject with the highest intensity.

Numerous multiparasitism cases associated with Fasciola infection were detected. Up to nine species were found in a 25-year-old woman from Bolin: E. coli, E. histolytica/E. dis-
par. Endolimax nana, G. intestinalis, Chilomastix mesnili, B. hominis, Fasciola spp., S. mansoni, and Hymenolepis nana.

A detailed analysis of Fasciola coinfected with other parasites showed significant positive associations with E. coli ($\chi^2 = 6.5, P = 0.0107$) and C. mesnili ($\chi^2 = 6.9, P = 0.0087$) in the global study, as well with S. mansoni ($\chi^2 = 11.1, P = 0.0008$) in the village of Tiba.

The prevalence of S. mansoni was significantly higher ($\chi^2 = 48.4, P = 0.0001$) in El Kaza (31.4%) than in the other villages (Table 1). Prevalences of S. mansoni between sexes (males = 11.1%, females = 12.6%) were not significantly different, while the highest prevalences of the 6–11- and 12–18-year-old age groups (14.0% and 18.8%, respectively) were statistically different from the infant (1–5) and schoolchild (6–11) age groups (14.0% and 18.8%, respectively). Despite the fact that no significant differences were detected, all the ages were susceptible to S. mansoni infection (positive cases from 2 to 60 years old).

Schistosomiasis intensities according to villages, sex and age groups are shown in Table 5. Absolute egg counts in the individuals infected ranged from 24 to 1656 epg, with arithmetic and geometric means of 174 and 64 epg, respectively. Despite the fact that no significant differences were detected, the highest values of range, arithmetic, and geometric means were obtained in El Kaza in females and in the infants group (1–5 years old).

To quantify the proportion of subjects with heavy intensity infections with S. mansoni, results are also expressed in classes of intensity (Table 5) following the recommendation of the World Health Organization. Among the positive subjects, 69.3% can be classified as light intensity (< 100 epg).

### Table 1

<table>
<thead>
<tr>
<th>District</th>
<th>El Aaly</th>
<th>Kafr El Dawar</th>
<th>Bolin</th>
<th>Hosh Esa</th>
<th>Delengat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Village</td>
<td>El Aaly</td>
<td>Kafr El Dawar</td>
<td>Bolin</td>
<td>Hosh Esa</td>
<td>Delengat</td>
</tr>
<tr>
<td>Total</td>
<td>568</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. tested (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 2

Techniques applied to the stool samples collected and prevalence of fascioliasis in the villages studied by sex and age group

<table>
<thead>
<tr>
<th>Villages surveyed</th>
<th>Stool samples</th>
<th>Total prevalence</th>
<th>Male</th>
<th>Female</th>
<th>Age group (years)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>El Aaly</td>
<td>286</td>
<td>240</td>
<td>15</td>
<td>5.2 (2.6)</td>
<td>1–5</td>
</tr>
<tr>
<td>Bolin</td>
<td>115</td>
<td>106</td>
<td>21</td>
<td>18.3 (7.1)</td>
<td>6–11</td>
</tr>
<tr>
<td>El Kaza</td>
<td>105</td>
<td>84</td>
<td>20</td>
<td>19.0 (7.5)</td>
<td>12–18</td>
</tr>
<tr>
<td>Tiba</td>
<td>172</td>
<td>138</td>
<td>31</td>
<td>18.0 (5.7)</td>
<td>&gt;18</td>
</tr>
<tr>
<td>Total</td>
<td>678</td>
<td>568</td>
<td>87</td>
<td>12.8 (2.5)</td>
<td></td>
</tr>
</tbody>
</table>

* According to infants (1–5), schoolchildren (6–11), adolescents (12–18), and adults (>18) criteria.
† FEC = formal ether concentration; KK = Kato Katz.
‡ Number of F. hepatica infected subjects.
§ Percentage CI = 95% confidence interval.
¶ Number of Fasciola hepatica infected subjects/number tested (percentage with respect to the number tested).
# $P < 0.05$.
infection, and 19.4% and 11.3% showed moderate (100–400 epg) and heavy (>400 epg) intensity infections, respectively. The highest percentages of heavy infections were detected in the village of El Kaza (28.6%) in females (6.5%) and in the youngest age group (4.9%).

**Table 3**

Intensities of fascioliasis by sex in the villages surveyed

<table>
<thead>
<tr>
<th>Village</th>
<th>Range</th>
<th>AM/GM</th>
<th>&lt;100</th>
<th>100–400</th>
<th>&gt;400</th>
</tr>
</thead>
<tbody>
<tr>
<td>El Aaly (n† = 257) (n‡ = 14)</td>
<td>24–168</td>
<td>104/96</td>
<td>14.3</td>
<td>7.1</td>
<td>–</td>
</tr>
<tr>
<td>Male</td>
<td>24–96</td>
<td>39/34</td>
<td>78.6</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Female</td>
<td>24–168</td>
<td>53/43</td>
<td>92.9</td>
<td>7.1</td>
<td>–</td>
</tr>
<tr>
<td>Total</td>
<td>Bolin (n† = 67) (n‡ = 16)</td>
<td>24–144</td>
<td>62/49</td>
<td>25.0</td>
<td>6.3</td>
</tr>
<tr>
<td>Male</td>
<td>24–360</td>
<td>81/55</td>
<td>26.5</td>
<td>6.3</td>
<td>–</td>
</tr>
<tr>
<td>Female</td>
<td>24–360</td>
<td>75/53</td>
<td>87.5</td>
<td>12.6</td>
<td>–</td>
</tr>
<tr>
<td>El Kaza (n† = 97) (n‡ = 15)</td>
<td>24–336</td>
<td>180/90</td>
<td>6.7</td>
<td>6.7</td>
<td>–</td>
</tr>
<tr>
<td>Male</td>
<td>24–432</td>
<td>98/58</td>
<td>60.0</td>
<td>20.0</td>
<td>6.7</td>
</tr>
<tr>
<td>Female</td>
<td>24–432</td>
<td>109/62</td>
<td>66.5</td>
<td>26.7</td>
<td>6.7</td>
</tr>
<tr>
<td>Total</td>
<td>Tiba (n† = 151) (n‡ = 23)</td>
<td>24–432</td>
<td>109/62</td>
<td>66.5</td>
<td>26.7</td>
</tr>
<tr>
<td>Male</td>
<td>24–72</td>
<td>41/38</td>
<td>30.4</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Female</td>
<td>24–432</td>
<td>71/51</td>
<td>64.7</td>
<td>8.8</td>
<td>1.5</td>
</tr>
<tr>
<td>Total</td>
<td>24–432</td>
<td>72/51</td>
<td>85.3</td>
<td>13.2</td>
<td>1.5</td>
</tr>
</tbody>
</table>

* epg = eggs per gram of feces; AM = arithmetic mean; GM = geometric mean; <100–400 = distribution of the intensity ranges in epg in the subjects infected, expressed as a percentage with respect to the total number of Fasciola-infected subjects in each village surveyed.
† Number of subjects examined by Kato-Katz.
‡ Number of subjects infected.
§ Number of subjects infected.

**Table 4**

Intensities of fascioliasis by age group (years) in the villages surveyed

<table>
<thead>
<tr>
<th>Village</th>
<th>Range</th>
<th>AM/GM</th>
<th>&lt;100</th>
<th>100–400</th>
<th>&gt;400</th>
</tr>
</thead>
<tbody>
<tr>
<td>El Aaly (n† = 257) (n‡ = 14)</td>
<td>1–5</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>6–11</td>
<td>24–168</td>
<td>67/51</td>
<td>28.6</td>
<td>7.1</td>
<td>–</td>
</tr>
<tr>
<td>12–18</td>
<td>24–96</td>
<td>48/38</td>
<td>21.4</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>&gt;18</td>
<td>24–72</td>
<td>44/39</td>
<td>42.9</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Total</td>
<td>Bolin (n† = 67) (n‡ = 16)</td>
<td>24–144</td>
<td>88/79</td>
<td>12.5</td>
<td>6.3</td>
</tr>
<tr>
<td>1–5</td>
<td>24–144</td>
<td>42/34</td>
<td>30.4</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>6–11</td>
<td>24–360</td>
<td>86/58</td>
<td>28.6</td>
<td>6.3</td>
<td>–</td>
</tr>
<tr>
<td>12–18</td>
<td>24–120</td>
<td>72/54</td>
<td>60.9</td>
<td>8.7</td>
<td>–</td>
</tr>
<tr>
<td>El Kaza (n† = 97) (n‡ = 15)</td>
<td>24–360</td>
<td>57/53</td>
<td>91.3</td>
<td>8.7</td>
<td>–</td>
</tr>
<tr>
<td>1–5</td>
<td>24–360</td>
<td>57/53</td>
<td>91.3</td>
<td>8.7</td>
<td>–</td>
</tr>
<tr>
<td>6–11</td>
<td>24–336</td>
<td>109/62</td>
<td>66.5</td>
<td>26.7</td>
<td>6.7</td>
</tr>
<tr>
<td>Tiba (n† = 151) (n‡ = 23)</td>
<td>24–432</td>
<td>109/62</td>
<td>66.5</td>
<td>26.7</td>
<td>6.7</td>
</tr>
<tr>
<td>1–5</td>
<td>24–96</td>
<td>56/48</td>
<td>13.0</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>6–11</td>
<td>24–120</td>
<td>67/59</td>
<td>17.4</td>
<td>4.3</td>
<td>–</td>
</tr>
<tr>
<td>12–18</td>
<td>24–360</td>
<td>63/41</td>
<td>20.6</td>
<td>2.9</td>
<td>–</td>
</tr>
<tr>
<td>&gt;18</td>
<td>24–192</td>
<td>56/47</td>
<td>39.7</td>
<td>2.9</td>
<td>–</td>
</tr>
<tr>
<td>Total</td>
<td>24–432</td>
<td>72/51</td>
<td>85.3</td>
<td>13.2</td>
<td>1.5</td>
</tr>
</tbody>
</table>

* epg = eggs per gram of feces; AM = arithmetic mean; GM = geometric mean; <100–400 = distribution of the intensity ranges in epg in the subjects infected, expressed as a percentage with respect to the total number of Schistosoma-infected persons.
† Number of subjects examined by Kato-Katz.
‡ Number of subjects infected.
§ Number of subjects infected.
∥ Number of males infected.
¶ Number of females infected.

**DISCUSSION**

The fascioliasis prevalences detected in this study (Table 1) are pronouncedly higher than those previously obtained in community surveys carried out in Egypt: 5.6% in Abis, Alexandria Governorate;32 5.1% and 10.9% by coprologic and serologic methods, respectively, in Sharkia Governorate;33 5.0–7.7% according to seasons, with a mean of 6.0% in Kafr El-Sheikh Governorate, including local maximums of 10.0% in two villages in given seasons;34 and 0.4% and 7.5% in Dakahlia Governorate.26,35 Previous studies performed on school children in 1996–2000 in other localities in the Behera Governorate also showed lower prevalences, ranging from 3.5% to 9.5% in districts with children infected with liver flukes and with positive cases found in almost every district, with a mean of 3.0%.25,26 Based on these prevalences and to the case reports in the last two decades,20 the pattern of liver fluke infections appears to be changing in the Nile Delta. The infection is spreading from the original situation of sporadic human cases in well-known foci endemic for animal disease to the present distribution in humans, which may be classified as a mesoendemic region that includes several areas hyperendemic for human disease, such as the Behera Governorate, based on the classification of epidemiologic situations of human fascioliasis.8 Such a situation is consistent with the general impression that human fascioliasis is an emerging public health problem in the Nile Delta region,20,26 a fact which has been related to the introduction of *F. hepatica* in livestock imported from Europe during the 20th century.19

The prevalence of liver fluke infection in females appeared to be significantly higher than in males (Table 2). This result contrasts with the fascioliasis epidemiologic characteristics in high-altitude areas of endemic human disease in Andean countries, where prevalences do not differ between the sexes.15,17 The sex role in Egypt may be related to cultural, hygienic, and behavioral factors, with females being associated more with the washing of clothes and kitchen utensils in...
large canals where transmitting lymnaeids are present, with
agricultural tasks in irrigated plantations such as rice fields, as
well as with meal preparation in houses and management of
freshwater plants that potentially carry attached metacercariae. In Egypt, many species of vegetables and weeds are
eaten raw in salads, including non-aquatic plants that need
frequent irrigation and are cultivated along the banks of wa-
ter channels, among which *Erica sativa* (El gargeer), *Lactuca
sativa* (El khas), *Allium porrum* (El korrat), *Petroselinum sa-
tivum* (bakdoones) and *Portulaca oleracea* (El regl a) have
been found to contain attached liver fluke metacercariae.36,37
Girls may have more contact with transmission foci, based on
data showing that girls are absent from schools more often
than boys.27

Prevalence results according to age groups suggest that all
ages (from 2 to 70 years old in the present study) are suscep-
tible to liver fluke infection (Table 2). However, it must be
remembered that liver fluke adults are able to survive up to
13.5 years in humans,1 which means that infected subjects
have not necessarily infected recently. The results ob-
tained show that school age children represent the primary
target for liver fluke infection, with prevalences being lower
before and after school age. This findings is consistent with
that observed in Andean countries,15 although the peak in the
9–11-year-old age group found in those South American re-
gions appears less pronounced in Egypt.

The fascioliasis intensities detected in Behera, although
very high when compared with those found in subjects
sporadically infected in areas endemic for animal disease,
e.g., Europe, appear to be relatively low if one considers that
prevalences indicate a hyperendemic situation. The majority
of epg counts were less than 100 epg (Tables 3 and 4), and the
maximum egg output (432 epg) was detected in a nine-year-
old girl from El Kaza. The maximum egg counts, the arith-
metic mean epg, and the geometric mean epg were much
lower than those observed in hyperendemic areas of human
disease in Bolivia and Peru.15,17 Thus, the intensity results
obtained in the present study may not be considered conclu-
sive because of the transmission seasonality of fascioliasis in
the Nile Delta,19 which are similar to those in other Mediter-
ranean endemic agricultural areas.38 Experimental studies on
Mediterranean liver flukes showed consistent egg shedding
peaks in the spring and fall, and this chronobiological pattern
appears to favor parasite transmission because of the seasonal-
y of the Mediterranean lymnaeid populations.39 In Egypt,
the maximum snail infection is observed in June and July,
while the number of acute human infections peaks in Au-
gust,40 with summer being the highest transmission season in
which both animals and humans show the highest preva-
lences.34 This indicates that the infected subjects detected in
the present surveys in June were mainly previous infections
from the fall or spring of the previous year, or even earlier.
Surveys performed throughout the year that included the
months of August and September would most probably show
markedly higher epg counts. Unfortunately, there are no data
on human intensities from other Nile Delta governorates.
However, children such as those in Behera with higher egg
counts (e.g., 936 and 2,016 epg) have already been diagnosed
in other districts.25,26

Statistically significant differences in intensities were not
detected between the different villages as a function of sex
and age. The absence of intensity differences between males
and females contrasts with what is known in Andean high-
lands, where females shed significantly more eggs than males.15,17 However, the intensity studies in different age
groups in Behera show results similar to those observed in
Bolivian and Peruvian highlands, where the higher egg counts
are found in infants and school children.15,17 The higher prob-
abilities of repetitive infection in these age groups may be
related to both behavioral patterns, such as chewing plants or
playing in transmission foci, and an immature immunologic
state that is partially related to nutritional deficiencies.10

The high number of other parasitic species infecting hu-
mans in the fascioliasis-endemic villages studied in Behera
(Table 1), and the numerous cases of multiparasitism de-
tected (up to nine different species, among which five consid-
ered pathogenic parasites) reflect the poor hygiene-sanitation
status of the human populations in question. The lower preva-
lences of both protozoans and helminths in El Aaly may be
related to its proximity to a large town (Kaf El Dawar) com-
pared with the other three villages, which are more rural.
Interestingly, the large spectrum of protozoan diseases and
helminthiases detected, several of recognized pathogenicity,
is consistent with a parasitic framework similar to that known
in the Bolivian and Peruvian hyperendemic areas for human
fascioliasis.13,17,41–43 The absence or very low prevalence of
Cryptosporidium (only one case in a 30-year-old man from El
Kaza) is surprising, especially if one considers the importance
of livestock in the villages surveyed, with many animal species
living close to human dwellings. This contrasts with the high
cryptosporidiosis prevalences in the northern Bolivian Altipl-
ano,41 although results similar to those in Behera were also
detected in the Puno endemic area.17 Similar results concern-
ing balantidiasis may be related to the absence of pigs in the
Behera and Puno areas17 and the high number of porcines in
the Bolivian Altiplano.42 The sporadic finding of *Cyclospora
cayetanensis* in a 12-year-old girl in El Aaly is worth noting
because this parasite was absent in the Bolivian and Peruvian
areas with human fascioliasis, even though it is a well-known
parasite in Peru.

With regard to helminths, the absence of *Taenia* spp. in our
survey in Egypt is consistent with their absence or very low
presence in the Bolivian and Peruvian localities endemic for
fascioliasis endemic, and the prevalence ranges of trichuriasis
and ascariasis, which are relatively low for zones of poor hy-
giene-sanitation status within developing countries,43 are
similar. Thus, the only important difference is the presence of
*S. mansoni* in Behera. Schistosomiasis caused by this species
is present in South America and potential intermediate plan-
orbids snails are present in Bolivia,44 although they are unable
to reach high altitudes because of the ecologic needs of the
transmitting planorbid.

The significant associations of *F. hepatica* with protozoan
species sharing a direct life cycle pattern are consistent with
the significant association between *F. hepatica* and *G. intesti-
nalis* in the areas of Bolivia and Peru hyperendemic for hu-
mans fascioliasis.13,17 In Behera, the association between *F.
hepatica* and *G. intestinalis* was not found to be significant,
although the relatively high prevalences of giardiasis detected
in the villages surveyed are worth noting because infection
with *G. intestinalis* is the only protozoa significantly associ-
ated with anemia, as is the case with fascioliasis.25 These find-
ings in the Behera Governorate must also be emphasized
because they suggest a similar mode of transmission.
The marked similarities in the qualitative and quantitative spectrums of protozoan and helminthic species in the multi-parasitisms observed and in the associations between liver flukes and other parasitic species suggest physiographic-hydrographic and behavioral-social characteristics that are similar in all areas hyperendemic for human fascioliasis. These are independent of other aspects as climate, altitude, and cultural or religious features.

The positive association between liver fluke infection and schistosomiasis detected in the locality of Tiba is also worth mentioning. This association has never been previously described, although many cases presenting with this concomitant infection have been diagnosed in several Egyptian governorates.\textsuperscript{20} It may be explained by the association of both diseases to fresh water snails inhabiting the same type of water bodies. Thus, the main snail species transmitting fascioliasis in Egypt appears to be \textit{Lymnaea caulleri}.\textsuperscript{19,34} an east African molluscan form related to the widespread African \textit{Lymnaea natalensis}, and it shows a preference for relatively large, deep, permanent, and moderately polluted water bodies with relatively dense surface vegetation cover.\textsuperscript{45,46} In these bodies of water, it usually coexists with \textit{ Biomphalaria alexandrina} and \textit{ Bulinus truncatus}, the planorbid snail species transmitting \textit{S. mansoni} in the Nile Delta region, as was observed in the surroundings of Tiba and El Kaza, the latter location in which fascioliasis and schistosomiasis prevalences were the highest.

Interestingly, the relationships between schistosomiasis prevalences and intensities and sex and age follow patterns similar to those found in fascioliasis. The association between fascioliasis and schistosomiasis must be considered relevant from clinical, pathologic, diagnostic, and therapeutic points of view. \textit{Schistosoma mansoni} causes a hepatic form of schistosomiasis that is related mainly to the deposition of eggs in the intrahepatic portal circulation and subsequent encapsulation granulomas in the liver, followed by marked portal fibrosis (Symmers’ fibrosis) in the host. In Egypt, inflammatory polyps of the colon are frequently seen in patients infected with \textit{S. mansoni}.\textsuperscript{47} Both schistosomal colonic polyposis and Symmers’ fibrosis are most frequent in heavily infected patients.\textsuperscript{48} Hepatosplenic schistosomiasis is associated with prolonged viremia after hepatitis B infection; hepatic failure in patients with Symmers’ fibrosis frequently accompanies chronic active hepatitis B.\textsuperscript{49} In addition, the relationship detected between parenteral antischistosomal therapy and hepatitis C virus in Egypt must be taken into consideration.\textsuperscript{50} In Behera, \textit{S. mansoni} infection was found to be a risk factor for anemia in children.\textsuperscript{55}

With regard to diagnostics, problems may be found with immunologic testing because of the possibility of cross-reactions between fascioliasis and schistosomiasis,\textsuperscript{4,51} as has already been observed in Egypt.\textsuperscript{20,52,53} as well as with hepatitis C virus infection.\textsuperscript{54} From a therapeutic point of view, one problem is that there are no currently available drugs that are effective against both trematodiasis, and fascioliasis is the only trematodiasis that does not respond to praziquantel.\textsuperscript{4} Consequently, the most appropriate treatments for humans coinfect with \textit{F. hepatica} and \textit{S. mansoni} is triclabendazole (Egaten\textsuperscript{TM}, Novartis Pharma AG, Basle, Switzerland), is the current drug of choice for treatment of fascioliasis\textsuperscript{55} and praziquantel, respectively.


tion, Editing and Printing Center, Extension of the Medical Research Institute of Alexandria University.


