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Evaluation of the seroprevalence and the demographic and clinical findings of fascioliasis patients in the Dicle River Basin in Turkey: a nine-year experience at a university hospital

M. ÇIÇEK[1], K. YALÇIN[2], A. BILDEN[1], F. ÇAKIR[1], N. AKPOLAT[3]

[1]Department of Parasitology, Faculty of Medicine, Ahi Evran University, Kırşehir, Türkiye
[2]Department of Gastroenterology, Faculty of Medicine, Dicle University Hospital, Diyarbakir, Türkiye
[3]Department of Microbiology, Faculty of Medicine, Dicle University, Diyarbakir, Türkiye

Abstract. – OBJECTIVE: ***Fasciola hepatica*** **and** ***Fasciola gigantica*** **are liver trematodes that cause fascioliasis in humans and animals. In Turkey, the medical importance of fascioliasis has been increasing in humans, and it continues to cause great economic loss in the field of animal husbandry. Therefore, it is important to diagnose fascioliasis quickly and reliably. The aim of this study is to show that the ELISA test is a reliable and specific method for diagnosing fascioliasis both in the early stage and in the acute stage.**

PATIENTS AND METHODS: In this study, 640 individuals aged 7-75 years who showed one or more symptoms of fascioliasis, such as abdominal pain, fever, weight loss, weakness, fatigue, headache, sweating, nausea, vomiting, allergic urticaria, liver mass, hypereosinophilia, or liver enzyme elevation, were recruited from the Dicle University Research and Application Hospital in southeastern Turkey. Serum and fecal samples were taken from them to investigate if the ***Fasciola hepatica*** **IgG antibody was present in the serum and if eggs were present in the feces. To detect the IgG antibodies, an enzyme-linked immunosorbent assay (ELISA) kit was used. The stool samples were analyzed for three consecutive days in mini Parasep fecal parasite concentrator tubes using the native-lugol and sedimentation methods. Abdominal ultrasonography and computed tomography were performed in all the patients.**

RESULTS: Among the subjects of this study, 90 (14%) were positive for fascioliasis, of whom 85 (94.4%) were adults and 5 (5.5%), children; 73 (81.1%) were women and 17 (18.8%), men; 57 (63.3%) lived in the rural areas and 33 (36.6%), in the city center; 90 (14%) were positive for ***Fasciola hepatica*** **IgG antibodies; (20%) had helminth eggs in their stools; and 85 (94.4%) had a history of eating watercress.**

CONCLUSIONS: According to the epidemiological classification for fascioliasis by Mas-Coma, the Dicle Basin, which is the setting of this study, is indeed a hyperendemic region. Thus, ELISA is a reliable and specific method of diagnosing fascioliasis, both in the early phase and in the acute phase, when the eggs are no longer seen in the stool.

Key Words:
Fascioliasis, Seroprevalence, Human, Dicle River Basin.

Introduction

Fasciola hepatica and *Fasciola gigantica* are liver trematodes that settle into the liver bile ducts and cause infection[1]. The final hosts of these parasites are usually ruminant animals, such as cattle and sheep, and humans, and their intermediate hosts are mollusks of the genus *Lymnaea*. Humans are infected when they consume contaminated raw aquatic plants and drink water contaminated with metacercariae[2-5].

Fascioliasis is a disease that has high pathogenicity. Its three most important symptoms are pain, fever, and liver enlargement. Other symptoms are pulmonary findings, chest pain, cough, headache, sweating, anorexia, weakness, weight loss, nausea, vomiting, change in bowel habit, and allergy-related urticaria[6-8].

The classical method of diagnosing fascioliasis is observing the eggs in the stool. However, it has been reported that the sensitivity of this method may be low due to the absence of par-

Corresponding Author: Muttalip Çiçek, MD; e-mail: muttalipcicek@hotmail.com; muttalipcicek@ahievran.edu.tr

asite eggs in acute and ectopic cases, and the intermittent ovulation of the parasite during the chronic period. Studies[9-13] have shown that serological and radiological methods [ultrasonography (USG), MR, and computed tomography (CT)] can be used as the main methods of diagnosing fascioliasis even during the acute period, when the eggs are not observed in the stool.

Researchers have emphasized that fascioliasis should be considered in individuals who have eosinophilia, fever of unknown cause, atypical abdominal pain, biliary colic or cholangitis, a family history of fascioliasis, or a history of eating poorly washed greens[8,14,15].

In Turkey, the medical importance of fascioliasis has been increasing in humans, and it continues to cause great economic loss in the field of animal husbandry.

This study investigated the prevalence of fascioliasis in Turkey, in the provinces along the Dicle River Basin, which cover southeastern Anatolia (Diyarbakir, Mardin, Siirt, Batman, and a portion of Şanlıurfa) (Figure 1). It examined patients who had been admitted to the hospital in the last nine years with one or more symptoms of the disease.

Patients and Methods

The Dicle University Research and Application Hospital recruited individuals who displayed one or more symptoms of fascioliasis, such as weight loss, weakness, fever, sweating, chest pain, cough, headache, nausea, vomiting, abdominal pain, urticaria, liver mass, hypereosinophilia, or liver enzyme elevation, as the subjects of this study. A total of 640 patients were recruited, aged 7-75 years of age, 610 of whom were adults and 30, children. Moreover, 340 of the patients were women, and 300 were men. In addition, a questionnaire was administered to the patients, in which they were asked for their demographic information, complaints, and history of eating aquatic plants.

A 3-cc blood serum and a hazelnut-sized stool sample were taken from each of the patients. The stool samples were examined on the same day, and the blood serums were stored at –20°C until their analysis every 15 days to detect IgG antibodies using an enzyme-linked immunosorbent assay (ELISA) kit (DRG International, Inc., Springfield, NJ, USA). Fasciola extract or secretory antigens were used with the ELISA kit. The results were read photometrically using a Tec-

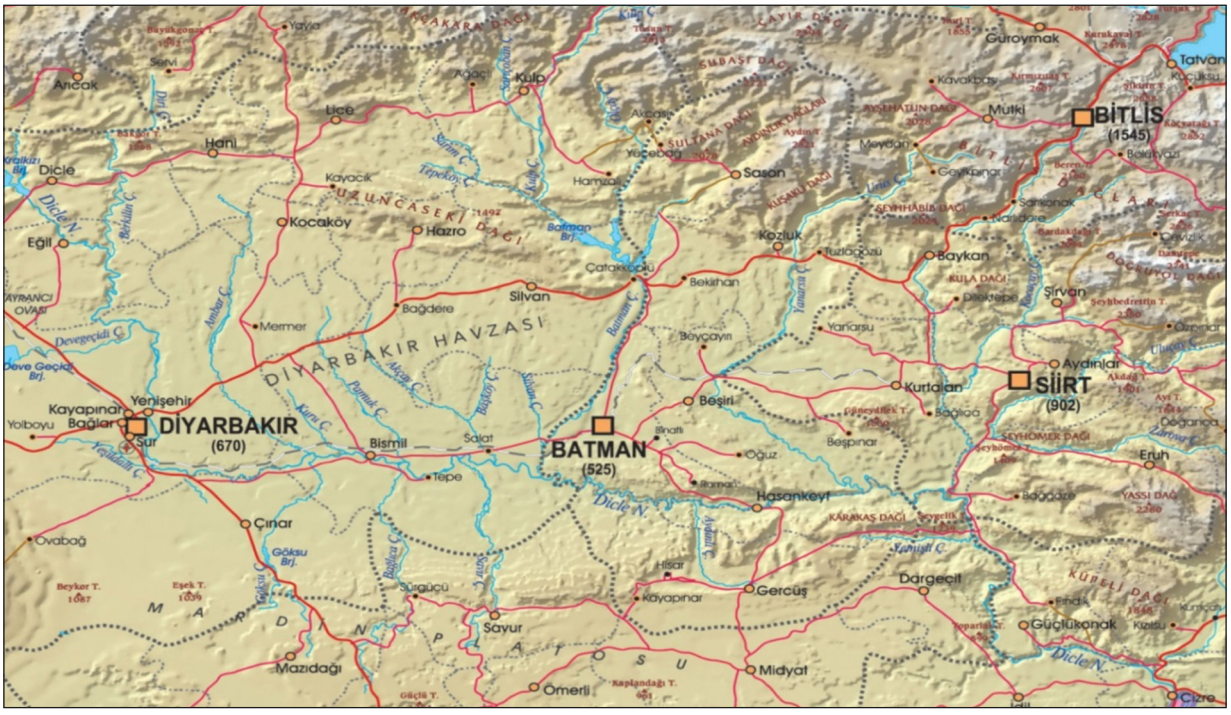

Figure 1. Dicle Basin of Turkey, where this study was conducted.

an Sunrise absorbance microplate reader (Tecan Group Ltd., Männedorf, Switzerland) at 450-620 nm. The cut-off value of the kit was 10; patient sera with a >11.0 DRG units = DU/mL [DU = patient absorbance value × 10 / cut-off (C1 + C2 / 2)] were determined to be seropositive. Abdominal USG and CT were performed for some of the positive patients. First, the stool analysis was performed for three consecutive days in mini Parasep fecal parasite concentrator tubes (DiaSys Ltd., Berkshire, England) using the native-lugol and sedimentation methods. Then, after sedimentation with the parasite concentrator tube, a search was conducted to determine the presence of parasite eggs. After obtaining ELISA and microscopy results for all patients, statistics were performed for patients who tested positive in both ELISA and microscopy according to age, gender, living places, and history of eating watercress.

Results

Of the study subjects, 90 (14%) were positive for *Fasciola hepatica* IgG antibodies. Of these positive subjects helminth eggs were observed in (20%) subjects (Figure 2). Of these positive subjects, 85 (94.4%) were adults, and 5 (5.55%) were children, 73 (81.1%) were women, and 17 (18.8%) were men. The mean age of these positive subjects was 23.5 ± 17.6 (7-71) years. Other intestinal parasites were found in some of these subjects: Entamoeba coli in one. Moreover, 33 (36.6%) of these *F. hepatica*-positive subjects lived in the city center, and 57 (63.3%) lived in rural areas. 85 (94.4%) of the subjects had a history of eating watercress (Figure 3).

Fasciola gigantica was detected in only two of the subjects. Gastroenterologists made the diagnosis by examining the adult parasite that

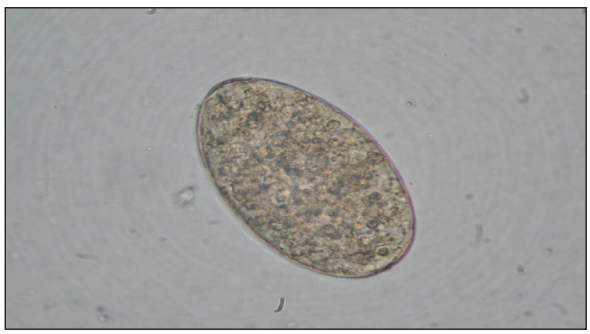

Figure 2. *Fasciola* sp. egg. Magnification: ×40.

Figure 3. Watercress consumed by the fascioliasis-positive patients.

was removed during the endoscopic retrograde cholangiopancreatography. Abdominal USG and CT were performed in the subjects with fascioliasis who were found positive for *F. gigantica via* ELISA, and the findings were reported to be consistent with those for fascioliasis.

All the subjects with fascioliasis experienced fatigue and abdominal pain. Eosinophilia was seen in 74.4%; moderate eosinophilia, in 52.2%; severe eosinophilia, in 15%; sweating, in 47.7%; headache, in 46%; fever, in 41.1%; weight loss, in 17.7%; itching, in 13.3%; nausea, in 12.2%; and vomiting, in 2.2%. These subjects were treated with 10 mg/kg of triclabendazole.

Discussion

Although fascioliasis is more common in countries where cattle and sheep are bred, it is a worldwide problem, occurring in both developed and developing countries. In the last 10 years, there has been an increase in *Fasciola* infections around the world. A study by the World Health Organization (WHO) in 1995 revealed that 2.5 million people in 61 countries were infected, and more than 180 million people were at risk[16].

The number of cases of fascioliasis has been significantly increasing since 1980, and it is considered endemic in some geographical regions of the world[17]. Esteban et al[18] conducted a study of 7,071 human fascioliasis cases (487 in Africa, 3,267 in the USA, 354 in Asia, 2,951 in Europe, and 12 in Oceania) from 51 countries over the last 25 years, in which it was reported that it caused major health problems in North Africa, Iran, and Western Europe, in addition to the Andean countries of South America. They also empha-

sized that the actual number of infected human patients worldwide was much higher than what had been reported previously. They further observed that the infection was often confused with other diseases due to its lack of specific clinical symptoms, or it was missed due to deficiencies in diagnoses, as the infection is often not sufficiently recognized by physicians.

In Turkey, 15 human cases of fascioliasis were reported between 1935 and 2000[19]. Since then, significant advances in the serological diagnosis of human fascioliasis have led to an increase in the number of reported cases in the country[14,20-22]. The disease has reportedly been seen in some provinces in the Mediterranean and eastern Anatolia.

In Antalya, the disease was observed in 3.0% of patients[23] in Mersin, in 1.93% of patients with a family history of the disease, and in 0.55% of patients without a family history[21]; in the city center of Isparta, it was detected in 2.4% of patients[20] , and in patients with eosinophilia, the rate was 6.1%, whereas, in patients without eosinophilia, it was 0.9%[24]; in rural areas, the prevalence was 9.3% of patients[20]; in Elaziğ, it was observed at a rate of 2.7% in healthy-looking individuals[25], and in Van, the disease was found in 26% of 92 individuals from the same family and 30 individuals in the control group with a history of eating watercress[8], in 1.8% of 1,600 patients[22], and in 5.5% of 817 individuals over eight years[26]. Saba et al[27] reported the clinical and demographic characteristics of 53 cases; Kabalioğlu et al[28], the magnetic resonance imaging findings of 29 patients; and Sezgin et al[29], the radiological and clinical findings of 9 cases. In the current study, fascioliasis seropositivity was found in 14% of the 640 subjects.

In this study, we reported a higher incidence of fascioliasis in Turkey than in previous studies[30-35]. We attribute the higher rate of positivity for fascioliasis in this study to the choice of investigation group from individuals with complaints. On the other hand, our findings showed that this disease is endemic in Turkey. The reason for this is that the Dicle River passes through this region, and the dams built on the river have increased the number of irrigation areas therein, making it suitable for the establishment of intermediate mansions and for the growth and farming of more wildwater plants, such as watercress. However, the tropical climate of the region and the typical occupation of sheep breeding therein can be considered factors of the prevalence of the disease.

Fasciola sp. is transmitted to humans through oral ingestion of metacercariae, the infective form of the parasite found in freshwater and aquatic plants[17]. The daily consumption of watercress was found to be the cause of a *Fasciola* outbreak in two families[36]. Twenty-seven of 37 fascioliasis patients consumed watercress[37], and 17 of 18 fascioliasis patients ate commercially grown watercress[15]. Kaya et al[20] reported that most of the fascioliasis patients in Isparta had consumed uncooked and poorly washed watercress. Karahocagil et al[8] reported an outbreak in a family in Van, in which all the patients regularly consumed wild watercress that had been collected from the fields where the animals grazed. In a study that examined the family history of *Fasciola* in Mersin, Özturhan et al[21] stated that 5 of 7 positive patients had a history of eating greens.

In the current study, 87 of the 90 patients had a history of eating watercress. This rate is compatible with those in the aforementioned studies. Thus, consumption of watercress has been determined as the most important factor of the infection. The use of dams on the Dicle river basin for irrigation has led to an increase in watercress and its areas of growth. It is believed that the collection of watercress, which is wild, and its selling in local markets enables individuals to obtain this plant faster and accelerates the spread of the infection.

In Hatami et al[38], 18 of the 34 fascioliasis patients were female, 16 were male, and their average age was 21.65 years, with 59% of them aged 20 years or less. In Cosme et al[37], 23 of the 37 fascioliasis patients with were male and 14 were female, and their ages ranged from 19 to 71 years. In Karahocagil et al[8], 21 of the 24 fascioliasis patients were women, 3 were men, 16 were adults, and 8 were children. In Saba et al[27], 32 of the 53 fascioliasis patients were women, 21 were men, and their average age was 42 years. In Özturhan et al[21], 5 of the 7 fascioliasis patients were female, 2 were male, and all the patients were adults.

In the current study, 73 of the positive patients were women, 17 were men, 85 were adults, and 5 were children. Thus, this disease is more common in women and adults than in other provinces in Turkey. It has been reported that in contrast to South American countries, in hyperendemic countries such as Egypt and Iran, fascioliasis has been detected at a higher rate in women than in men[38,39]. Based on these data on fascioliasis in Turkey, the high rate seen in women is similar to that in Iran and Egypt. It

is believed that these regions might have been exposed to a higher rate of contamination with metacercariae due to factors such as the sociocultural structure, the living conditions, the diet of the women, and their hygiene status. Kaya et al[20] found that fascioliasis was more seroprevalent in rural areas than in the Isparta city center. Indeed, other studies have reported that fascioliasis is more common in rural populations in countries such as Egypt and Iran[38,40]. In the current study, 57 (63.3%) of the fascioliasis patients lived in a rural area, and 33 (36.6%) lived in the city center. The higher seroprevalence of the disease in rural areas is attributed to the ease of access of the local people to aquatic plants and the fact that this type of nutrition has become a way of life for them.

In Mailles et al[15], 89% of fascioliasis patients had fatigue, 67% had fever, 61% had muscle pain, 61% had abdominal pain, and 39% had itching. Cosme et al[37] reported that the most common symptoms of fascioliasis were malaise and weight loss (75.6%) and abdominal pain (72.9%). In Karahocagil et al[8], all the fascioliasis patients reported fatigue, weakness, loss of appetite, and abdominal pain, in addition to weight loss at 75%, headache at 45.8%, sweating in 41.7%, fever in 33.3%, respiratory distress in 25%, itching in 16.7%, and nausea and vomiting in 3%. In Demirci et al[24], abdominal pain was the most common symptom in 16 patients, followed by weight loss (12), fever (9), and urticaria (4). In the current study, fatigue and abdominal pain were observed in all the patients, in addition to sweating at 47.7%, headache at 46%, fever at 41.1%, weight loss at 17.7%, itching at 13.3%, nausea at 12.2%, and vomiting in 2.2%.

Eosinophilia is the most important guiding laboratory finding for fascioliasis in patients with an appropriate clinical picture. Especially in the acute phase, it often exceeds the 5% limit[15]. In Demirci et al[24], 6.1% of 756 individuals with eosinophilia were positive for *Fasciola*, and there was a statistically significant relationship between eosinophilia and fascioliasis. In Dauchy et al[41], all the patients had eosinophilia at a rate above 30% in half of the patients. In Saba et al [27], eosinophilia was found at a rate of 100% in acute patients and in 21% in chronic patients. In Karahocagil et al[8], eosinophilia was in 70% of the patients, and the rate of eosinophilia was >20% in 58% of the patients. In the current study, eosinophilia was observed in 74.4% of the patients and in 52.2% of the fascioliasis patients at a rate of >15%.

Serological methods more effectively determine fascioliasis infection because no eggs are seen in the feces in the first 3-4 months. In the ELISA test, extractive and secretory antigens called cathepsin L1 are used[42,43]. Rokni et al[42] found that the sensitivity and specificity of the ELISA prepared with these antigens were 100% and 98%, respectively. In Turkey, Karahocagil et al. 8 reported that all their patients were positive, as determined by the ELISA test, whereas those in the control group were negative. They also identified three cases when the clinical findings and the ELISA test were used without the radiological findings. Sakru[44] reported the sensitivity and specificity of the ELISA test as 100% and 97%, respectively. In the current study, all the patients were positive according to the ELISA test, and the sensitivity and specificity of ELISA were 100% and 98%, respectively. Although the radiological findings of two patients showed that they were positive for fascioliasis, they were negative according to the ELISA test. Further examinations showed that the patient did not have fascioliasis. These findings showed the value of the ELISA test for the early diagnosis of fascioliasis infection, especially in the acute phase, before clinical signs of infection appear.

Limitations

Our study has a limitation, such as the fact that it is a monocenter study.

Conclusions

Fascioliasis was detected in 14% of the subjects in this study. According to the epidemiological classification for the disease by Mas-Coma[17], the Dicle Delta, where this study was conducted, is a hyperendemic region.

Of the patients found to be positive, 94.4% stated that they had consumed watercress. For this region, the source of the disease is watercress.

The ELISA test is a reliable and specific method of diagnosing fascioliasis both in its early phase and in its acute phase when the eggs are no longer seen in the stool. The test can be used both as a routine test and a screening test.

Although the clinical and laboratory findings of fascioliasis varied, it should be considered in individuals with symptoms such as abdominal pain, fever, sweating, weight loss, eosinophilia, and elevated liver enzymes in the upper right quadrant in areas where the disease is endemic.

Since this disease is foodborne, it can infect entire families. Therefore, family screenings are essential.

It is our opinion that the disease will become less prevalent if raw water plants such as watercress are consumed only if they have been washed very well to prevent diseases if the sale of watercress in markets is prohibited, and if water plants that have been collected from pastures where animals graze are never consumed.

We believe that educating the public about this disease and informing specialist physicians about its prevalence and symptoms are of great importance, as with many other diseases.

Conflict of Interest

The authors declare that they have no conflict of interests.

Ethics Approval

The Ethics Committee of Dicle University gave its approval for the study with number 24-26-0510.

Informed Consent

Blood serum and feces of the patients were used in this study. Before the samples were taken, patients were informed that serum and stool samples and some laboratory analysis results would be used as research data. Consent forms were obtained from all patients.

Availability of Data and Materials

The data used for publication can be accessed through the corresponding author.

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Authors' Contribution

Muttalip Çiçek, Kendal Yalçin: conceptualization, methodology, software, data curation, writing- original draft preparation. Alican Bilden, Fatih Çakir: visualization, investigation. supervision, software, validation. Muttalip Çiçek, Nezahat Akpolat: writing- reviewing and editing.

ORCID ID

Muttalip Çiçek: 0000 0003 4807 4482
Kendal Yalçin: 0000-0003-2137-7934
Alican Bilden: 0000-0003-1119-3859
Fatih Çakir: 0000-0002-9808-4366
Nezahat Akpolat: 0000-0002-9808-4366

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