



## Seroprevalence of human fascioliasis in Van province, Turkey

### LIVER/BILIARY

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### ABSTRACT

**Background/Aims:** *Fasciola hepatica* is a rare zoonotic parasite that infects the liver of many mammals including humans. The aim of this study was to determine the seroprevalence of fascioliasis in Van province by ELISA (antibody detection) on the assumption that not all cases could be detected by stool examination alone.

**Materials and Methods:** A total of randomly selected 1,600 patients, directed from affiliated outpatient clinics to Yüzüncü Yıl University Medical Faculty Parasitology Laboratory, were enrolled in the study. Their mean age was 44.44±19.00 years. Blood samples were collected from all the patients, and their stool samples were examined. For the stool examination, native-lugol and sedimentation (in formalin-ethyl acetate) methods were employed. ELISA for *F. hepatica* was performed on the blood samples from all patients. Seropositive patients were treated with triclabendazole.

**Results:** *F. hepatica* was detected by ELISA in 89 (5.6%) of the 1,600 patients, but eggs were identified on the stool examination in only 29 (1.8%) patients. The prevalence of *F. hepatica* was higher in females (7.2%) than in males (4.2%) and was higher in the ≥36-year age group (6.7%) than in the ≤35-year age group (4.4%). Abdominal pain (93.3%), fatigue (88.8%), and weight loss (69.7%) were the most common symptoms. Eosinophilia was present in 89.9% of the patients. All seropositive patients had a history of eating raw aquatic plants.

**Conclusion:** Stool examination alone is not sufficient to diagnose *F. hepatica*. Serological tests such as ELISA must be used together with stool examination.

**Keywords:** *Fasciola hepatica*, humans, seroepidemiological study, Van, Turkey

### INTRODUCTION

The liver fluke *Fasciola hepatica* was first described in 1379 by Brie, who identified the parasite in sheep. Approximately 400 years later, Palas found that humans could also be infected by *F. hepatica*. In different studies, it is estimated that 2.4-17 million people worldwide are infected with *F. hepatica* (1-6).

The pathogenesis of fascioliasis, which is caused by *F. hepatica*, and the clinical presentation vary according to the infectivity of the metacercariae, number of metacercariae ingested, type of host, immunity of host immunity, and presence of parasites in the liver parenchyma or bile ducts (2,4-6). In humans, the clinical pic-

ture of fascioliasis can range from asymptomatic infections to secondary biliary cirrhosis and death. Typically, the infection is characterized by fever, eosinophilia, and abdominal pain (5-7). *F. hepatica* is usually transmitted to humans by ingestion of aquatic plants containing metacercariae or by drinking water containing metacercariae (4,5).

Although typical clinical findings are usually present in the early stages of fascioliasis, diagnosis of the disease can be difficult. The most commonly used methods to diagnose *F. hepatica* infection in humans are direct parasitology, serology, and other non-invasive diagnostic

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investigations. Recently, it was reported that serological methods can be used as the main diagnostic tool in all stages of fascioliasis, including the acute period before the presence of adult parasites in the host. Studies conducted in a number of countries, including Turkey, have indicated that ELISA has high sensitivity and specificity for the diagnosis of *F. hepatica* infection (6,8).

The aim of this study was to determine the seroprevalence of fascioliasis in Van province by ELISA (antibody detection) on the assumption that not all cases could be detected by stool examination alone.

## MATERIALS AND METHODS

The gross national product per capita and urbanization rate in Van province (urban and rural human population is 1,070,113 in 2013; Figure 1) are below the average for Turkey. However, the population growth rate is above average (9).

A total of randomly selected 1,600 patients, directed from affiliated outpatient clinics to Yüzüncü Yıl University Medical Faculty Parasitology Laboratory between May 2008 and December 2010, were enrolled in the study. Of the 1,600 patients, 727 were females (45.4%; mean age, 42.23±18.57 years; range, 15-85 years), 873 were males (54.6%; mean age, 47.54±19.41 years; range, 15-88 years), 776 (48.5%) were 35 years or younger, and 824 (51.5%) were 36 years or older. The mean age was 44.44±19.00 years (range 15-88 years). Yüzüncü Yıl University Medical Faculty Scientific Research Ethics Committee approved the study protocol. Written informed consent was obtained from all patients.

Blood samples were collected from all 1,600 patients, and their stool samples were examined for three consecutive days. The stool samples were examined using native-lugol and sedimentation (in formalin-ethyl acetate) methods (6,10). To eliminate false parasitism, patients with *F. hepatica* eggs detected in the stools were asked whether they had eaten liver during the previous week. ELISA for *F. hepatica* was performed on the blood samples of all 1,600 patients (*F. hepatica* IgG ELISA; DRG International, Inc., USA). A single oral dose of 10 mg/kg triclabendazole (Egaten; Novartis, Basel, Switzerland) was used to treat seropositive patients (2,6). After treatment, the patients underwent regular follow-up.

### Statistical analysis

The Z-test was used to compare proportions of the categorical variables. All statistical analysis was performed using the MINITAB (ver: 14.1, Minitab Inc., USA) statistical package program. The level of statistical significance was set at 5%.

## RESULTS

Evidence of *F. hepatica* infection was detected by ELISA in 89 (5.6%) of the 1,600 study patients. However, eggs were found in the stools of only 29 (1.8%) of the 1,600 patients, i.e., in 32.6% of the 89 seropositive patients. Fascioliasis was detected in 7.2% of the 727 females, 4.2% of the 873 males, 4.4% of the 776 pa-



Figure 1. Location of Van province, Turkey (original).

tients aged 35 years or younger, and 6.7% of the 824 patients aged 36 years or older.

The most frequent clinical findings in the seropositive patients were abdominal pain (93.3%), fatigue (88.8%), and weight loss (69.7%). Eighty seropositive patients (89.9%) had eosinophilia (mean eosinophil %, 21.11±11.86; range, 6%-60%; normal range, 0%-5%) with rates of ≥20% in 46.3% of these patients. Hepatomegaly was detected in four patients (Table 1). All the seropositive patients reported a history of consumption of green aquatic plants such as watercress.

On the follow-up examinations of the seropositive patients approximately 1 month after treatment, complaints associated with fascioliasis had decreased or completely disappeared. No *F. hepatica* eggs were detected in the stools of seropositive patients who attended the follow-up.

The differences in the incidence of *F. hepatica* infection between males and females and between the two age groups were statistically significant ( $p < 0.05$ ). However, there were no statistically significant differences between the genders and age groups of the patients in terms of the incidence of eosinophilia.

## DISCUSSION

The incidence of human fascioliasis has increased together with advances in diagnostic procedures. In recent years, cases of fascioliasis have been reported with increasing frequency in many countries, thus changing the perspective of the disease (4,5).

Large-scale studies of fascioliasis in endemic areas around the world have determined a very low prevalence (hypoendemic; <1%) in Basse Normandie and Corsica in France and the Chile-7 region; moderate prevalence (mesoendemic; 1-10%) in Porto in Portugal, Alexandria, Nile Delta, and Sharkia in Egypt, Corazal in Puerto Rico, and Cajamarca in Peru; and high prevalence (hyperendemic; >10%) in Puno, Puno-Asillo, and Mantaro Valley in Peru and Altiplano within Peru and Bolivia (1,3,4,11,12).

**Table 1.** The laboratory and clinical findings of ELISA positive patients (n=89)

	Gender				Total		Age groups			
	(n=52)		(n=37)		n=89		≤35 (n=34)		≥36 (n=55)	
	Nr.	%	Nr.	%	Nr.	%	Nr.	%	Nr.	%
<b>Laboratory findings</b>										
Egg in the stools	18	34.6	11	29.7	29	32.6	13	38.2	16	29.1
Eosinophilia	46	88.5	34	91.9	80	89.9	29	85.3	51	92.7
<b>Clinical findings</b>										
Abdominal pain	48	92.3	35	94.6	83	93.3	31	91.2	52	94.5
Fatigue	46	88.5	33	89.2	79	88.8	30	88.2	49	89.1
Weight loss	38	73.1	24	64.9	62	69.7	22	64.7	40	72.7
Lack of appetite	36	69.2	20	54.1	56	62.9	20	58.8	36	65.5
Fever	21	40.4	8	21.6	29	32.6	13	38.2	16	29.1
Nausea	13	25	12	32.4	25	28.1	8	23.5	17	30.9
Urticaria	11	21.2	4	10.8	15	16.9	5	14.7	10	18.2
Chest pain	10	19.2	4	10.8	14	15.7	7	20.6	7	12.7
Constipation	8	15.4	6	16.2	14	15.7	4	11.8	10	18.2
Diarrhea	6	11.5	5	13.5	11	12.4	4	11.8	7	12.7
Jaundice	5	9.6	--	--	5	5.6	1	2.9	4	7.3
Hepatomegaly	3	5.8	1	2.7	4	4.5	1	2.9	3	5.5

♀: females, ♂: males, Nr: number

In three previous studies performed in Van province, *F. hepatica* eggs were detected in the stool specimens of 5 (2.4%) of 206 people in the town of Ercis (13), in 2 (0.68%) of 293 students in the 7–15 age group (14), and in 1 (0.03%) of 3,534 people aged 14 years and above in Van city (15). In the present study, the eggs were detected in the stool samples of 29 (1.8%) of 1,600 patients (Table 1).

Eggs are not observed in the stools of all infected individuals. Therefore, serology is the preferred diagnostic method for the diagnosis of *F. hepatica*. Using serology, infection can be identified, even in the acute phase, and the response to treatment can be monitored. Serology is also the most appropriate method to determine the regional prevalence of fascioliasis. ELISA for *F. hepatica* has a high sensitivity (83%–100%) and specificity (63%–97.8%; 5,6).

In Turkey, previous ELISA studies on the seroprevalence of fascioliasis have determined a prevalence of 3.01% in Antalya province (5), 2.4% in Isparta center, 9.3% in a village in Isparta province (16), 0.55% in patients with no family history of fascioliasis and 1.93% in patients with a family history of fascioliasis in Mersin province (17), and 2.78% of 540 randomly selected healthy people in Elazığ province (18). In a recent study conducted in Van province, 24 of 92 people with a seropositive family member were found to be seropositive (19). In the present study, ELISA detected fascioliasis in 89 (5.6%) of the 1,600 randomly selected individuals.

The effects of *F. hepatica* on the host are related to the mechanical and toxic effects and to blood loss. Clinically, the infection is most frequently characterized by fever, eosinophilia, and abdominal pain (2,5,6). Kaya et al. (20) reported that 59% of 22 patients with fascioliasis had fever, 14% had nausea, 18% had tremor, 18% had weight loss, 5% had itching and urticaria, 100% had abdominal pain, and 27% had hepatomegaly. Karahocagil et al. (19) reported that all 24 patients positive for *F. hepatica* in their study had weakness, fatigue, loss of appetite, and abdominal pain and that 75% had weight loss, 45.8% had headache, 41.7% had sweating, 33.3% had fever and dyspnea, 25% had nausea and vomiting, 16.7% had itching, and 8.3% had jaundice. In that study, eosinophilia was detected in 70.8% of patients, with eosinophilia >20% in 14 (58.3%) patients. In a study by Mailles et al. (21), asthenia was reported in 89% of 18 patients with fascioliasis, fever in 67%, myalgia in 61%, right upper quadrant abdominal pain in 61%, and itching in 39%.

In the present study, abdominal pain (93.3%), fatigue (88.8%), and weight loss (69.7%) were the most common clinical findings. Eosinophilia was detected in 89.9% of the 89 seropositive patients, with eosinophilia ≥20% in 46.3% of these patients (Table 1).

In the present study, fascioliasis was more prevalent in females than in males and in patients aged 36 years or older than in those aged 35 years or younger. There was a significant rela-

relationship between the incidence of infection and both age and gender ( $p < 0.05$ ). All seropositive patients had a history of consuming green aquatic plants such as watercress, similar to the findings of another study conducted in Van province (19). The higher fascioliasis rate in females compared with that in males may be attributed to females eating green aquatic plants more frequently than males. The higher rate of infection in people older than 35 years may reflect the increased possibility of encountering the parasite with aging.

Triclabendazole, albendazole, and praziquantel are the most commonly used agents for the treatment of fascioliasis. In a number of studies, triclabendazole had to be used because eggs were detected or a full symptomatic recovery was not achieved after treatment with albendazole or praziquantel (5,6,19,22,23). Based on these previous studies, in the present study, the patients were directly commenced on a standard dose (2,6) of 10 mg/kg triclabendazole. After treatment, the patients clinically improved, and the symptoms of the infection had disappeared. Therefore, fascioliasis can be successfully treated with 10 mg/kg triclabendazole as a single dose.

In conclusion, the eggs of *F. hepatica* were detected by stool examination in only 32.6% of the 89 seropositive patients. Therefore, many cases of fascioliasis could be overlooked based on the clinical and stool examinations alone. The results of this study confirmed that stool examination alone is not sufficient to identify all cases of fascioliasis and that serological tests such as ELISA should be used together with stool examination. The prevalence of *F. hepatica* was 5.6% based on ELISA and 1.8% based on the stool examination. Eosinophilia was also important for the diagnosis of *F. hepatica* infection. In endemic areas, in patients with symptoms such as abdominal pain, fatigue, and weight loss, fascioliasis should be considered in the differential diagnosis.

**Ethics Committee Approval:** Ethics committee approval was received for this study from Scientific Research Ethics Committee of Yüzüncü Yıl University Medical Faculty.

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

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