

# Human *Fasciola hepatica* Infection in Türkiye is More Than We Knew: A Systematic Review

## Türkiye’de İnsan *Fasciola hepatica* Enfeksiyonu Bildiğimizden Daha Fazladır: Sistematik Bir İnceleme

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### ABSTRACT

*Fasciola hepatica* is a trematode that is easily visible to the naked eye. It infects sheep and cattle, but can sometimes be an accidental host in humans. This review was carried out to review the published studies on human *Fasciola hepatica* in Türkiye and to systematically examine the data obtained from the studies. Literature search was conducted using keywords such as “*Fasciola hepatica*, Fascioliasis, Türkiye (Turkey)” from “Pubmed, Google Scholar, Google” databases. In addition, poster presentations presented at congresses of national infectious disease societies on the subject were also included in the study. Eighty-four studies published in Türkiye between 1993-2022 and 183 cases examined in these studies were included in the evaluation. In this review, it was found that *Fasciola hepatica* infection is not rare in Türkiye, but clinicians were not aware of this and did not consider this infection in the differential diagnosis. It is seen that diagnostic methods such as serological and stool microscopy are not used adequately due to the fact that *Fasciola hepatica* infection is not considered in the differential diagnosis and the diagnosis methods is not available in every center. As *Fasciola hepatica* infection is not considered in the preliminary diagnosis and these diagnostic methods are not used sufficiently, we see that cases are often confused with primary or metastatic liver tumors in abdominal imaging, and therefore unnecessary invasive procedures are performed. In regions where *Fasciola hepatica* infection is endemic, *Fasciola hepatica* infection should be considered before performing a major surgical procedure in patients with typical clinical findings, elevated liver and cholestasis enzymes, and eosinophilia, and characteristic computed tomography or ultrasonography findings, and noninvasive diagnostic methods should be used first.

**Keywords:** *Fasciola hepatica*, obstructive jaundice, eosinophilia

### ÖZ

*Fasciola hepatica* çıplak gözle kolayca görülebilen bir trematodtur. Koyun ve sığırları infekte etmekle birlikte, bazen insanlarda tesadüfi konağı olabilmektedir. Bu derleme, Türkiye’de insan *Fasciola hepatica* ile ilgili yayımlanmış çalışmaları incelemek ve çalışmalardan elde edilen verileri sistematik olarak incelemek amacıyla yapılmıştır. Literatür taraması, “Pubmed, Google Scholar, Google” veri tabanlarından “*Fasciola hepatica*, Fascioliasis, Türkiye (Turkey)” gibi anahtar kelimeler kullanılarak konu ile ilgili tarama yapıldı. Ayrıca konuyla ilgili ulusal enfeksiyon hastalıkları derneklerinin kongrelerinde sunulan poster sunumları da çalışmaya dahil edilmiştir. Türkiye’de 1993-2022 yılları arasında yayımlanan 84 çalışma ve bu çalışmalarda incelenen 183 olgu değerlendirmeye alındı. Bu derlemede *Fasciola hepatica* enfeksiyonunun Türkiye’de nadir olmadığı ancak klinisyenlerin bunun farkında olmadıkları ve ayırıcı tanı bu enfeksiyonu düşünmedikleri bulunmuştur. Ayırıcı tanıda *Fasciola hepatica* enfeksiyonunun düşünülmemesi ve her merkezde tanı imkanının olmaması gibi nedenlerle, serolojik ve gayta mikroskopisi gibi tanı yöntemlerin yeterince kullanılmadığı görülmektedir. *Fasciola hepatica* enfeksiyonunun ön tanıda düşünülmemesi ve bu tanı yöntemlerinin yeterince kullanılmaması nedeniyle, abdominal görüntülemeye olguların sıklıkla primer veya metastatik karaciğer tümörleri ile karıştırıldığını ve bu nedenle gereksiz invaziv işlemlerin yapıldığını görmekteyiz. *Fasciola hepatica* enfeksiyonunun endemik olduğu bölgelerde tipik klinik bulgusu olan, karaciğer ve kolestaz enzim yüksekliği ile birlikte eozinofili olan ve karakteristik bilgisayarlı tomografi ya da ultrasonografi bulguları olan hastalarda majör bir cerrahi girişim yapmadan önce *Fasciola hepatica* enfeksiyonu düşünülmesi ve öncelikle invaziv olmayan tanı yöntemleri kullanılmalıdır.

**Anahtar Kelimeler:** *Fasciola hepatica*, obstrüktif sarılık, eozinofili



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## INTRODUCTION

Fascioliasis has recently been recognized by the World Health Organization as an important zoonotic disease that has been neglected in humans. This disease is a parasitic zoonosis caused by two liver fluke species [*Fasciola hepatica* (*F. hepatica*), *Fasciola gigantica*] (1). *F. hepatica* is a trematode about 30 mm x 15 mm in size and easily visible to the naked eye. Although it primarily infects sheep and cattle but can accidentally infect humans due to its similar life cycle in both animals and humans (2). The socio-economic and medical significance of fascioliasis is undeniable, with an estimated global prevalence of 2.4 to 17 million infections, predominantly in Europe and Asia, with sporadic cases in other regions including North Africa, Central and South America, the Middle East, and occasionally the USA and the Caribbean (2). There is no comprehensive seroprevalence study for *F. hepatica* in Türkiye. Diagnosis can be made by serology, clinical improvement associated with reduced eosinophilia after treatment with triclabendazole, or detection of parasite eggs in stool samples. In some cases, the diagnosis is made incidentally during unnecessary procedures such as open surgery, laparoscopic cholecystectomy, or endoscopic retrograde cholangio-pancreatography (ERCP) (3). However, the diagnosis of fascioliasis can be challenging due to its many differential diagnoses and low incidence rates (4).

The main research questions in this review are:

1. Is *F. hepatica* common in Türkiye?
2. Which methods are used in the diagnosis of *F. hepatica* in Türkiye?
3. Is *F. hepatica* considered in the differential diagnosis of hepatobiliary diseases in Türkiye?

This review was conducted to examine the prevalence and regional distribution of *F. hepatica*, its clinical and laboratory findings, diagnostic methods used, treatments administered, and whether *F. hepatica* is considered in the differential diagnosis, by reviewing published studies on *F. hepatica* in Türkiye.

## METHODS

### Literature Search

Literature search was conducted using keywords such as "*Fasciola hepatica*, *F. hepatica*, Fascioliasis, Turkey" from "Pubmed, Google Scholar, Google" databases. Case reports and original human studies published in national and international journals from Türkiye were included in the evaluation. In addition, poster presentations presented at congresses of national infectious disease societies on the subject were also included in the study.

### Inclusion or Exclusion Criteria from the Study

All reported human *F. hepatica* cases and prevalence studies from Türkiye were included in the study. Cases reported from outside Türkiye, a case presented in two different places (journal or poster presentation) were not included in the study. In addition, only one of the multiple studies conducted at the same university on overlapping dates was included in the study.

### Characteristics of the Study

Between 1993-2022, 84 studies (5-88) published in Türkiye and 183 cases examined in these studies were included in the evaluation. One of these studies was a retrospective original

article including 39 cases (49), and another one was the abstract that examined 46 cases and presented at a congress (50). Seventy-six studies were case reports (5-48,57-88). Of the case reports, 59 were studies published in national and international journals, and 17 were poster presentations presented at congresses. In a case report study, there were at least one and at most 6 cases. A total of 98 cases were analyzed in these 76 case reports. Six studies were prevalence studies (51-56).

### Classification

In order to analyze the study better, the retrospective original article including 39 cases was classified as the first study (49), the summary of the papers examining 46 cases was the second study (50), and the data of 98 cases in the other 76 case studies were analyzed and classified as the third study (5-48,57-88).

### Data Analysis

Demographic characteristics, complaints, laboratory and imaging findings, parasite localization, diagnostic methods and invasive procedures, treatments and recovery status of 98 cases presented in the 76-case study were recorded in the SPSS program. Continuous variables were defined as mean  $\pm$  standard deviation and categorical variables were defined as numbers and percentages.

## RESULTS

### Demographic Data

In the first study; 77% of the patients were female, mean age was  $45.77 \pm 16.53$  (18-83) (49), in the second study; 60.8% of the cases were female (50), in the third study; 68.3% of the patients were female, mean age was 40.5 (4-76) (5-48,57-88) (Table 1). In the first study (49), 59% of the patients lived in rural areas, and in the third study, there was information that the patients lived in rural areas in seven cases (7,11,18,40,41,46,48).

### Epidemiology

The prevalence of *F. hepatica* varies between 0.79-10.3% in six studies reported from different provinces of Türkiye (Adana, Mersin, Isparta, Kayseri, Elazığ, Van) (Table 2) (51-56). In addition, of the 183 cases examined in this study, 33.3% were reported from the Mediterranean Region (19,23,42,50,67,69,74,76,80,81,83,87,88), 25.1% from the South East Anatolian Region (9,11,22,36,49,75,85), 15.3% from the Eastern Anatolia Region (5,7,10,17,18,20,24,48,57,60,61,63-65,71,76,84), 10.3% from the Central Anatolia Region (13,25,33,35,38,40,45,58,62,66,68,70,77-79,86), 7.1% from the Marmara Region (16,21,26,27,31,34,37,39,43,44,46,59), 6.5% from the Aegean Region (6,8,12,15,28,30,32,41,72), and 1% from the Black Sea Region (14,29) (Figure 1). In the study of Ulger et al. (49), 72% of the cases applied between March and June.

### Clinic

The mean duration of symptoms was 508 days (49) in the first study and 233 days in the third study (5-48,57-88). In the first study (49) disease stage was not reported and the most common symptoms were abdominal pain (90%), fever (28%), and weight loss (20%). In the second study (50), 54.3% of the cases were classified as acute infections and 36.9% as chronic infections. Epigastric pain was present in 61% of acute cases, fatigue in 43%,

right upper quadrant pain in 41% and fever in 40%. Epigastric pain was present in 64% of chronic cases, right upper quadrant pain in 59%, and nausea in 47%. In the third study (5-48,57-88), 48.9% of the cases were acute, 39.7% were chronic cases, and 11.2% did not report disease stage. Abdominal pain was present in 86% of acute cases, nausea and vomiting in 25%, anorexia in 33.3%, and fever in 25%. In chronic cases, 94.7% had abdominal pain, 57.8% had nausea and vomiting, 26.3% had anorexia, 23.6% had fever (Table 1). Four cases (8.6%) in the second study (50) and six cases (6.1%) (32,39,45,59,62,69) in the third study were evaluated as latent (asymptomatic) infections.

### Laboratory Finding

In the first study, 79% of the cases had eosinophilia, 38% had an increase in liver enzymes, and 1% had an increase in total bilirubin (49). In the second study, eosinophilia was found in 63% of all cases and 100% of acute cases (50). In the third study, 75.9% of all cases had eosinophilia, 43.5% had aspartate aminotransferase (AST), 40.5% had alanine aminotransferase (ALT) and 26.7% had total bilirubin elevation (Table 1) (5-48,57-88).

### Diagnosis

In the first study, enzyme-linked immunosorbent assay (ELISA) test was performed for *F. hepatica* in 12 patients and it was found positive in 11 (91.6%) patients. Diagnosis was made by clinical, laboratory and radiological findings in 27 patients (69.2%), by pathological examination of samples in 8 (20.5%) patients, and by removal of live parasites during the ERCP procedure in 4 (10.3%)

patients. No parasite eggs were detected in the stool of any of the patients (49). In the second study, ELISA test was positive in all patients, except for one patient who was not examined. While *F. hepatica* eggs were detected in the stools of three patients and in 3 of 4 patients who underwent ultrasonography (USG)-guided fine needle aspiration. In 5 patients who were operated on with various preliminary diagnoses, the diagnosis of *F. hepatica* was confirmed by pathological examination of the samples (50). In the third study, serological tests for *F. hepatica* were performed in 60 patients, and it was found positive in 59 (98.3%) patients (ELISA test in 38 cases, indirect hemagglutination test in 22 cases) (8,11,12,15,18,20,21,23,25,29,31-34,36-45,47,57,58,65,67-69,71-75,77,82,83,85-88). Stool microscopy was performed in 45 patients (8,11,12,18,20,21,23,28,30-32,34,36-39,41,43,45,47,57,58,65-67,69,71,73-77,79,83,84, 86), and *F. hepatica* eggs were observed in 14 (31.1%) patients (11,12,18,20,21,30,47,57,65,67,79,84), *F. hepatica* eggs were seen in the bile aspiration fluid in five patients (6,66,73,81,87), in the duodenal aspiration fluid in one patient (18), and in the colon biopsy sample in one patient (30). Pathological examination of the liver was performed in 36 of the cases yapılmış (5,7,12,17,19,20,24,25,28,30,32,34,44,57-59,61,62,64,66,67,72,76,78,81-83,85,86) and in 24 (66.6%) patients *F. hepatica* was diagnosed. ERCP was performed in 25 of the cases (5,6,9-11,14-16,22,26,27,35,46-48,61,63,65,66,70,73,81) and diagnostic findings were observed in 23 (92%) patients. The diagnostic methods used are shown in Table 3.

**Table 1.** Distribution of cases in acute and chronic phase in the third study by age, gender, symptom duration and laboratory values of fascioliasis cases between 1993-2022, Türkiye

	Acute phase (liver period), n=48	Chronic phase (biliary period), n=39	Total, n=98
Age median (min-max)	44 (4-76)	40 (9-75)	40.5 (4-76)
Gender-female (%)	67.2	69.0	71.4
Symptoms	Acute phase (liver period), n=43 (%)	Chronic phase (biliary period), n=38 (%)	Total, n=91 (%)
Stomach ache	37 (86.0)	18 (94.7)	81 (89.0)
Nausea-vomiting	12 (25.0)	22 (57.8)	36 (39.5)
Anorexia	16 (33.3)	10 (26.3)	28 (30.7)
Fever	12 (25.0)	9 (23.6)	22 (24.1)
Weight loss	11 (22.9)	8 (21.0)	23 (25.2)
Jaundice	1 (2.0)	9 (23.6)	10 (10.9)
Urticaria	4 (8.3)	2 (5.2)	7 (7.6)
Average symptom duration/day	208	311	233
Lab	Acute phase (liver period) %	Chronic phase (biliary period) %	Total %
Eosinophilia	73.3	66.0	75.9
ALP elevation	40.8	58.4	48.3
AST elevation	37.2	52.7	43.5
Leukocytosis	44.7	31.6	41.6
ALT elevation	30.3	52.7	40.5
GGT elevation	18.8	48.0	32.4
Total bilirubinemia	8.3	49.0	26.7

AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, GGT: Gamma-glutamyl transferase, ALP: Alkaline phosphatase

**Table 2.** Prevalence of *Fasciola hepatica* by provinces in between 1993-2022, Türkiye

Provinces	Year	Scope of work n	Looked test	Prevalence (%)	Source
Mersin	2009	884	ELISA	0.79	(51)
Kayseri	2008	374	ELISA/UAV	3.5	(52)
Van	2004	500	Stool microscopy	1.8	(53)
Adana	2005	291	UAV	10.3	(54)
Isparta*	2003	756	ELISA	6.1 <sup>#</sup>	(55)
Isparta*	2003	320	ELISA	0.9 <sup>a</sup>	(55)
Elazığ	2002	540	ELISA	2.78	(56)

\*: Same study, #: Included group of patients with eosinophilia, a: Included group of patients without eosinophilia, ELISA: Enzyme-linked immunosorbent assay



**Figure 1.** Regional distribution of cases fascioliasis between 1993-2022, Türkiye

**Table 3.** Diagnostic methods used for diagnosis of fascioliasis between 1993-2022, Türkiye

	n=98 (%)	Diagnostic finding rate
<b>Serology*</b>	60 (61.2)	59/60 (98.3%)
<b>Stool microscopy</b>	45 (45.9)	14/45 (31.1%)
<b>ERCP</b>	25 (25.5)	23/25 (92.0%)
<b>Pathology</b>	36 (36.7)	24/36 (66.6%)

\*: ELISA test in 38 cases, IHA test in 22 cases, ERCP: Endoscopic retrograde cholangio-pancreatography, ELISA: Enzyme-linked immunosorbent assay

**Imaging Findings**

In the cases reported in the first arm of the study, diagnostic imaging modalities were USG in 94.8%, abdominal computed tomography (CT) in 74.3%, magnetic resonance imaging (MRI) in 59%. The most frequently reported radiological finding was the appearance of masses with irregular borders around the bile ducts in the subcapsular area of the liver (49). In the third arm of the study, USG was performed in 78.5%, abdominal CT in 51%, and abdominal MRI in 22.4%. The most frequently reported USG findings were enlargement of the common bile duct (31.1%), cholelithiasis (22%), hypoechoic appearance in the liver (20.7%), and heterogeneous appearance in the liver (12.9%).

The most common abdominal CT findings were hypodense nodule in the liver (40%), enlargement of the common bile duct (18%) and heterogeneous appearance in the liver (16%), and the most common abdominal MRI findings were hypodense nodule in the liver (50%) and enlargement of the common bile duct (45.4%) (5-48,57-88).

**Treatment**

All patients in the first arm of the study were given triclabendazole for two consecutive days. While clinical and laboratory findings of the patients were generally improved in the 1<sup>st</sup> month, improvement in the radiological findings was observed after the 3<sup>rd</sup> month. After 12 months of treatment, 88.6% of the patients showed radiological improvement in liver lesions, and 11.4% did not change the size of the lesions. Five (12.8%) patients showed no clinical or laboratory improvement in their follow-up, and therefore triclabendazole was given again (49). In the third arm of the study, triclabendazole was given to 73 patients (5,6,8,10-13,15,16,18,20,23,25-27,29-34,36-48,57,58,60-64,67-69,71,74,75,77,81-83,86-88), bithionol to four patients (9,35,65,72), praziquantel to four patients (28,66,73), metronidazole to two patients (59,79), albendazole to two patients (76), ornidazole to one patient (78), and emetine chlorohydrate to one patient (66). Eleven cases (7,14,17,24,70,80,84,85) had no treatment information. There was no improvement in one patient (47) receiving triclabendazole, and two patients (76,77) had no treatment response information, while all other patients improved.

## DISCUSSION

*F. hepatica* is a liver parasite that has been infecting humans for over 5,000 years (89). It is a rare parasitic infection that spreads mostly in tropical, subtropical and temperate climate regions of the world and is frequently reported from sheep and cattle breeding countries (90). The main source of infection is the consumption of raw vegetables contaminated with metacercariae. Familial and regional outbreaks have been reported in the literature due to watercress consumption (91-94). The non-embryonic eggs excreted with the feces of the host become embryonic when they come into contact with water, then return to the form called "miracidium" and invade the snail tissue. In the snail tissue, respectively; they revert to sporocyst, redia and cercaria forms. Then they float freely in aquatic plants in the form of cercariae in cysts. The metacercariae form in aquatic plants is eaten by humans and transmission occurs (3). Fascioliasis has recently been recognized by the World Health Organization as an important zoonotic disease that has been neglected in humans (1). But, increased focus on human fascioliasis over the past 30 years has led to the discovery of major endemic regions in China, Southeast Asia (such as Vietnam), Egypt, Türkiye, and northern Iran (89). The prevalence of *F. hepatica* varies between 0.79-10.3% in 6 studies reported from different provinces of Türkiye (Table 2) (51-59). When we examine the reported cases, we see that *F. hepatica* cases have been reported from every region of Türkiye. The cases were mostly reported from the two neighboring regions, the Mediterranean and Southeastern Anatolia Regions (Figure 1). These studies show that *F. hepatica* infection is not very rare in our country. Comprehensive serological studies should be conducted in different regions of Türkiye to determine the exact prevalence of the disease.

It is seen that the cases examined in this study are mostly women (5-50,57-88). Similarly, in other previous studies, it was found that *F. hepatica* was more common in women (95,96). However, Parkinson et al. (97) did not find a significant relationship between infection and gender in their study in Bolivia. Another study of more than 21,000 children in Egypt showed that *F. hepatica* infection was more common in women (98). This situation may be related to cultural, hygiene and behavioral factors such as more contact with raw water plants, as well as an unexplained physiopathological mechanism that increases the susceptibility of women to this infection. Comprehensive studies are needed to explain this situation.

Fascioliasis is divided into two main stages, acute (liver stage) and chronic (biliary stage), each showing different clinical signs and symptoms (99). Some authors consider asymptomatic *F. hepatica* infection as a latent infection apart from the chronic stage (32,39,45,50). However, asymptomatic infection is generally considered in the chronic stage (3,99,100). The acute stage (liver period) begins 3-5 months after infection, it is the period when immature forms in the duodenum reach the liver and finally, they pass into the bile ducts. The chronic stage (bile duct period) begins after about the sixth month and is the period when the parasites mature in the bile ducts. This stage can last for several years (>10 years) and half of the patients are asymptomatic (3). When the reported cases were examined, most of the cases were in the acute stage (48.9%, 54.3%) (5-48,50,57-88). However, in a study of 24 cases by Karahocagil et al., (94) most of the cases were evaluated as chronic stage (54%). *F. hepatica* is a parasite

that usually settles in the liver and biliary system, but cases with atypical localization have also been reported. It was reported that *F. hepatica* was localized in the colon in three cases (30,36,44), both in the colon and liver in 2 cases (17,24), in the peritoneum in one case (86), in the ovary in one case (83), and in the lung in another case (85). Abdominal pain, nausea-vomiting, weakness, fever are the most common in both stages, and diarrhea, weight loss, urticaria, jaundice, itching, headache, and sweating have also been reported (5-50,57-88,94).

The most common laboratory finding of *F. hepatica* is eosinophilia (5-50,57-88,93,94). Eosinophilia is an important laboratory finding in fascioliasis. Saba et al. (50) reported the percentage of eosinophilia as 100% in acute patients. Karahocagil et al. (94) reported eosinophilia in 70.8% of 24 seropositive patients. However, normal eosinophil count does not exclude the diagnosis. Turhan et al. (101) reported that only 11% of seropositive patients had eosinophilia. In addition, AST, ALT, total bilirubin, gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP) elevation and leukocytosis can be seen (5-50,57-88,94). Hyperbilirubinemia is a more common finding in the chronic stage because the parasite obstructs the bile duct (5-48,57-88). The presence of eosinophilia along with elevated bilirubin and cholestasis enzymes (ALP, GGT) or elevations of AST and ALT in the endemic area should suggest *F. hepatica* infection.

Fascioliasis has no specific signs and symptoms. Diagnosis and treatment are not easy because physicians rarely encounter this disease, and effective drugs are not available in many countries. However, patients with a history of living in an endemic area and eating watercress, as well as symptoms such as abdominal pain, nausea-vomiting, weakness, fever, diarrhea, weight loss, urticaria, jaundice, and eosinophilia should be evaluated for *F. hepatica* infestation with parasitological, radiological and serological tests. Definitive diagnosis of fascioliasis is made by detection of *F. hepatica* eggs in stool or gallbladder sample or radiological findings suggestive of fascioliasis together with a positivity of serological test (102). Serology has been the fastest and most effective diagnostic method in the diagnosis of fascioliasis in recent years. Antibodies are detectable 2 to 4 weeks after initial exposure, undetectable in approximately 65% of patients one month after successful treatment, but low levels of positive titers may persist for years in some patients (2). ELISA is the most commonly used serological diagnosis method, in the literature it is stated that the sensitivity of this method is 78.9-100% and the specificity is 97% (103,104). ELISA positivity was reported to be 91.6% in the case series of Ulger et al., (49) and 100% in two studies by Saba et al. (50) and Karahocagil et al. (94). Stool microscopy is another useful diagnostic method still used in the diagnosis of chronic infections in countries with scarce resources. An adult *F. hepatica* parasite can lay more than 20,000 eggs per day. Because this release is intermittent, multiple stool samples should be examined (2). It takes 5 to 7 weeks after initial infection for adult worms to mature enough to produce eggs, so there are no eggs in the stool in the acute phase of infection, so serological testing is of greater importance (2). In the 39 case study of Ulger et al., (49) it was stated that stool microscopy of all patients was examined and no parasite eggs were observed. In the 46-case study of Saba et al. (50), parasite eggs were found in the stool of only 3 cases. In the 24-case study of Karahocagil et al. (94), parasite eggs were observed in the stool of 11 patients. The presence of *F. hepatica* eggs in the stool is diagnostic, but

the absence of parasite eggs does not exclude infection. In addition, diagnosis can be made by detecting *F. hepatica* eggs in the bile fluid obtained through invasive procedures performed with various preliminary diagnoses (66,73,80,81). Sometimes the diagnosis is made as a result of invasive procedures such as open surgery, laparoscopic cholecystectomy and ERCP. Live adult *F. hepatica* parasite can be detected in the biliary tract during ERCP in patients with biliary obstruction (5,6,9-11,14-16,22,26,27,35,46-49,61,63,65,66,70,73). In addition, *F. hepatica* can be identified in open surgical operation and pathological examination of biopsies (5,7,17,19,20,24,28,30,34,44,49,50,58,59,61,64,67,72,78,82,83,85).

The differential diagnosis of *F. hepatica* includes liver abscess, malignancy, viral hepatitis, cholecystitis, cholangitis, ruptured hydatid cyst, toxocariasis, acute schistosomiasis, ascariasis, and strongyloidiasis (2,105-107). The diagnosis of fascioliasis may be overlooked due to the many differential diagnoses and low incidence (4). The most common diagnostic imaging modalities are abdominal USG, CT, and MRI, respectively (5-50,57-88). USG findings are focal areas of the liver with increased echogenicity, multiple nodules of varying echogenicity, irregular lesions or a single complex mass, enlargement of the common bile duct, and cholelithiasis (Table 4). The most common liver CT or MRI findings are heterogeneous appearance and hypodense nodule in the liver, enlargement of the common bile duct, and multiple metastasis-like lesions (Table 4) (5-50,57-88,94). The most common mistake in the interpretation of imaging methods is confusion with malignancy. As a result of the evaluation of the imaging, we see that *F. hepatica* is often confused with malignancy (8,17,19,22-25,30,34,36,39,40,44,57-59,61,62,72,75,81-83,94),

in one case (61) chemotherapy was given considering liver metastasis of colon cancer, and hepatobiliary diseases such as liver abscess (31,49), choledocholithiasis (6,10,14,20,27,66), cholecystitis (13,57,66,75) and cholangitis (7,9,15,16,65) are considered in the preliminary diagnosis. With these preliminary diagnoses, we see that 82 of 183 cases (44.8%) underwent at least one invasive procedure such as ERCP, open surgery, and liver biopsy (5-50,57-88).

Appropriate treatment for both stages is triclabendazole 10 mg/kg daily for 2 days. The cure rate is 90% (2). The first drug therapy recommended by the CDC for fascioliasis since 1998 is triclabendazole. The recovery rate was reported as 79.4% in the first dose and 94% in the second dose (108). In another study, similar cure rates of 79.2% at the first dose and 100% at the second dose were reported (103). In the study conducted by Ulger et al., (49) 2 doses of triclabendazole were given to 39 patients and treatment response was obtained in 34 patients (87.1%). There are also other medical treatment options other than triclabendazole. It has been reported in the literature that some cases were successfully treated with alternative drugs such as bithionol, praziquantel, albendazole, metronidazole and ornidazole (9,28,35,59,65,66,72,73,76,78,79). When a patient is diagnosed with fascioliasis, other family members should be checked with serological testing. When the patient has a positive test, treatment should be given regardless of whether he is symptomatic or not (94).

## CONCLUSIONS

Contrary to popular belief, *F. hepatica* is not rare in Türkiye and is more common in all regions of Türkiye, especially in the Mediterranean and Southeastern Anatolia regions. When we examine the reported cases in Türkiye, we see that diagnostic methods such as serological examinations and stool microscopy are not sufficiently used due to the fact that *F. hepatica* infection is not considered in the differential diagnosis and diagnostic facilities are not available in every center. As a result of not considering *F. hepatica* infection in the preliminary diagnosis and the insufficient use of these diagnostic methods, we see that patients are often misdiagnosed as having primary or metastatic liver tumors based on abdominal imaging. Consequently, invasive procedures or even open surgery have been performed on these patients for diagnostic purposes. This is an unacceptable situation, both for the patients and considering the economic burden it places on the country. In areas where *F. hepatica* infection is endemic, *F. hepatica* infection should be considered in patients with clinical findings, elevated liver and cholestasis enzymes along with eosinophilia, and characteristic CT or USG findings, before major surgical intervention. Non-invasive diagnostic methods such as stool microscopy and serological tests should be used first. The most appropriate treatment for *F. hepatica* is triclabendazole at 10 mg/kg daily for 2 days. However, triclabendazole is not available in Türkiye and must be obtained from abroad. To prevent *F. hepatica* infection, especially in endemic areas, individuals should avoid consuming raw water plants and stay away from areas where food and water may be contaminated or where hygiene conditions are inadequate.

**Table 4.** Radiological findings of the fascioliasis cases between 1993-2022, Türkiye

<b>USG findings (77 patients)</b>	<b>n (%)</b>
Enlargement of the common bile duct	24 (31.1)
Cholelithiasis	17 (22)
Hypoechoic appearance in the liver	16 (20.7)
Heterogeneous appearance in the liver	10 (12.9)
Intrahepatic bile duct dilatation	9 (11.6)
Cholecystitis	6 (7)
<b>Abdominal CT findings (50 patients)</b>	<b>n (%)</b>
Hypodense nodule in the liver	20 (40)
Enlargement of the common bile duct	9 (18)
Heterogeneous appearance in the liver	8 (16)
Mass appearance in the colon	7 (14)
Stone in the choledoch	4 (8)
Hypoechoic appearance in the liver	2 (4)
Normal view	3 (6)
<b>Abdominal MRI findings (22 patients)</b>	<b>n (%)</b>
Hypodense nodule in the liver	11 (50)
Enlargement of the common bile duct	10 (45.4)
Intrahepatic bile duct dilatation	4 (18.1)

USG: Ultrasonography, CT: Computed tomography, MRI: Magnetic resonance imaging

1. *F. hepatica* infection is not uncommon in Türkiye, and *F. hepatica* infection should be considered in patients with elevated liver and cholestasis enzymes along with eosinophilia and characteristic imaging findings, and non-invasive diagnostic methods (stool microscopy and serological tests) should be used first.
2. In Türkiye, serological tests for *F. hepatica* are performed in certain reference laboratories. However, *F. hepatica* is an endemic infectious disease in Türkiye. Therefore, providing serological diagnostic facilities in healthcare centers will increase awareness and diagnosis rates of *F. hepatica*.
3. The unavailability of triclabendazole, the primary treatment option for *F. hepatica* infection, in Türkiye can cause difficulties for clinicians in treatment and patient followup, leading to patient suffering. Therefore, healthcare administrators should pay more attention to this issue.

### \*Authorship Contributions

Concept: N.M., F.C., A.T.Ö., Design: N.M., F.C., A.T.Ö., Data Collection or Processing: N.M., F.C., A.T.Ö., Analysis or Interpretation: N.M., F.C., A.T.Ö., Literature Search: N.M., F.C., A.T.Ö., Writing: N.M., F.C., A.T.Ö.

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