Özgün Araştırma

# *Fasciola hepatica* Diagnosis: Clinical and Laboratory Clues from A University Hospital Experience

Fasciola hepatica Tanısında Klinik ve Laboratuvar İpuçları: Bir Üniversite Hastanesi Deneyimi

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Cite this article as: Sağmak Tartar A, Aşan MA, Bozdağ A, Bahçecioğlu İH, Akbulut A, Demirdağ K. *Fasciola hepatica* diagnosis: clinical and laboratory clues from a university hospital experience. Turkiye Parazitol Derg. [Epub Ahead of Print]

## ABSTRACT

**Objective:** Fascioliasis is a trematode infection caused by *Fasciola hepatica* or *Fasciola gigantica*. Diagnosis of fascioliasis is often delayed. This study aims to contribute to reducing the incidence of the disease by determining regional epidemiology and guiding public health measures, as well as increasing awareness among physicians through the examination of clinical, laboratory, and imaging findings.

**Methods:** Patients diagnosed with fascioliasis at the Infectious Diseases Clinic and Gastroenterology Clinic of Firat University Hospital between 2011 and 2022 were included in the study. Demographic information, clinical findings, complete blood count, biochemical parameters, radiological imaging reports, treatment, and prognosis were examined. Patient data were obtained from the hospital automation system, files, and epicrisis.

**Results:** Of the 19 patients followed, 15 (78.9%) were female. The mean age was 62.36±12.30 years. Fifteen patients (78.9%) lived in rural areas. Seven patients (36.8%) were involved in animal husbandry. Twelve patients (63.2%) had a history of consuming watercress. The most commonly observed symptoms were loss of appetite, right upper quadrant pain, nausea-vomiting, and night sweats. All patients were treated with triclabendazole without any side effects. Statistically significant differences were found in the levels of eosinophilia, alanine transaminase, gamma-glutamyl transferase, alkaline phosphatase, total bilirubin, and direct bilirubin between the beginning of treatment and 1 month in our patients (p<0.05). One patient was lost due to intervening cardiac problems.

**Conclusion:** Fascioliasis is also present in our region, and a significant history of watercress consumption is noteworthy epidemiologically. *Fasciola hepatica* should be considered in patients presenting with abdominal pain accompanied by peripheral eosinophilia. Increasing awareness among physicians will contribute to preventing delays in diagnosis and treatment. **Keywords:** Fascioliasis, *Fasciola hepatica*, eosinophilia, watercress

# ÖΖ

**Amaç:** Fascioliasis, *Fasciola hepatica* veya *Fasciola gigantica*'nın neden olduğu trematod enfeksiyonudur. Fasiyoliyazis tanısında sıklıkla gecikme olur. Bu çalışmada bölgesel olarak epidemiyolojinin belirlenmesi ile, alınacak halk sağlığı önlemlerine yön vererek hastalık insidansının azaltılmasına katkı sağlanması, klinik, laboratuvar ve görüntüleme bulgularının irdelenmesiyle ise hekimler arasında farkındalığın artırılması hedeflenmektedir.

**Yöntemler:** Çalışmaya 2011-2022 tarihleri arasında Fırat Üniversitesi Hastanesi Enfeksiyon Hastalıkları ve Gastroenteroloji Kliniği'nde fascioliyazis tanısı ile takip edilen hastalar dahil edildi. Demografik bilgileri, klinik bulguları, tam kan sayımı, biyokimyasal parametreler, radyolojik görüntüleme raporları, tedavi ve prognozları incelendi. Hasta bilgilerine hastane otomasyon sistemi, dosya ve epikrizlerden ulaşıldı.

**Bulgular:** Takip edilen 19 hastanın 15'i (%78,9) kadındı. Yaş ortalaması 62,36±12,30 olarak bulundu. Hastaların 15'i (%78,9) kırsal bölgede yaşamaktaydı. Yedi (%36,8) hasta hayvancılıkla uğraşmaktaydı. On iki (%63,2) hastanın su teresi yeme öyküsü

Received/Geliş Tarihi: 02.04.2024 Accepted/Kabul Tarihi: 20.06.2025 Epub: 03.07.2025

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vardı. En sık saptanan semptom ve bulgu iştahsızlık, sağ üst kadranda ağrı, bulantı-kusma ve gece terlemesiydi. Hastaların hepsine triklobendazol başlandı. Yan etki görülmedi. Hastalarımızın tedavi başlangıcı ve 1 ayda bakılan eozinofili, alanin transaminaz, gama-glutamil transferaz, alkalen fosfataz, toplam bilirubin ve direkt bilirubin değerlerinde istatistiksel anlamlı fark saptandı (p<0,05). Bir hasta araya giren kardiyak sorunları sebebiyle kaybedildi. Sonuç: Fascioliasis bölgemizde de görülmektedir ve epidemiyolojik olarak önemli oranda su teresi tüketme öyküsü dikkat çekmektedir. Periferik eozinofilinin

eşlik ettiği karın ağrısı ile başvuran hastalarda Fasciola hepatica düşünülmelidir. Hekimlerde farkındalığın artması tanı ve tedavideki gecikmeleri önlemeye katkı sağlayacaktır.

Anahtar Kelimeler: Fascioliasis, Fasciola hepatica, eozinofili, su teresi

# **INTRODUCTION**

Fascioliasis is a trematode infection caused by Fasciola hepatica (F. hepatica) or Fasciola gigantica (F. gigantica) (1). F. hepatica has a global distribution, while F. gigantica is predominantly seen in tropical regions.

F. hepatica is globally distributed, especially in sheep farming areas with temperate climates. Humans are accidental hosts and mainly acquire infection by consuming watercress or aquatic plants. Infection can also occur through other freshwater plants such as lettuce, mint, clover, and parsley. Outbreaks resulting from the consumption of contaminated water containing live metacercariae (2) have been described (3). Most infected individuals have mild clinical manifestations; morbidity increases with the fluke burden (4). Abdominal pain accompanied by peripheral eosinophilia should raise suspicion of fascioliasis. A careful dietary history, including consumption of watercress or potentially contaminated water-washed raw vegetables, should be obtained. Diagnosis of fascioliasis is often delayed. In a study of patients with fascioliasis in developed countries, acute infectionrelated symptoms occurred more than 1 month before diagnosis in 73% of cases (5). Another study involving patients with biliary phase fascioliasis found even longer delays (symptoms occurred 1 to 208 weeks; mean 64 weeks) (6). In this study, clinical symptoms and findings, laboratory and radiological imaging findings, treatment, and prognosis of patients followed with fascioliasis diagnosis at the infectious diseases and gastroenterology clinic between 2011 and 2021 were retrospectively examined. Determining regional epidemiology will contribute to reducing the incidence of the disease by guiding public health measures, while examining clinical, laboratory, and imaging findings aims to increase awareness among physicians.

#### **METHODS**

This study was conducted in accordance with the principles of the Helsinki Declaration. Ethical approval for the study was obtained from the Non-Interventional Ethics Committee of Firat University Faculty of Medicine (date: 21.01.2022, number: 6284). Patients diagnosed with fascioliasis at the Infectious Diseases Clinic and Gastroenterology Clinic of Fırat University Hospital between 2011 and 2022 were included in the study. Patient consent was not obtained because the study was retrospective. Demographic information, clinical findings, complete blood count, biochemical parameters, radiological imaging reports, treatment, and prognosis were examined. Patient data were obtained from the hospital automation system, files, and discharge summaries.

## **Statistical Analysis**

For statistical analysis, the IBM SPSS Statistics 22 version package program (SPSS Inc., Chicago, IL, USA) was utilized. The normality of quantitative data was examined using the Shapiro-Wilk test. Mean ± standard deviation was employed for continuous variables exhibiting normal distribution, while median (+25th-75th) was used for non-normally distributed data. Classified data were analyzed in terms of frequency and percentage. Due to the non-normal distribution of the data, the Wilcoxon signed-rank test, a non-parametric test, was used for comparisons between dependent groups. A p-value <0.05 was considered statistically significant.

#### RESULTS

Nineteen patients diagnosed with fascioliasis were followed between 2011 and 2022. Of these patients, 15 (78.9%) were female, and 4 (21.1%) were male. The mean age was determined to be 62.36±12.30 years. Fifteen patients (78.9%) resided in rural areas. Seven patients (36.8%) were involved in animal husbandry. Twelve patients (63.2%) had a history of consuming watercress. In one patient (5.3%), there was a history of contact with lakestream water. Extrahepatic involvement was not detected in any of the patients. Hepatic involvement was present in 11 patients (57.9%), while biliary involvement was present in 8 patients (42.1%). The number of flukes was unknown in 11 patients (57.9%), while single fluke was detected in 5 patients (26.3%), 2 flukes in 2 patients (10.5%), and 7 flukes in 1 patient (5.3%).

The symptoms and findings of the patients are provided in Table 1. Various laboratory parameters at the time of admission and at the 1<sup>st</sup> month of treatment are presented in Table 2.

Table 1. Patients' symptoms and findings			
Symptom	n	(%)	
Night sweats	7	36.8	
Nausea-vomiting	13	68.4	
Anorexia	19	100	
Diarrhea	1	5.3	
Weight loss	4	21.1	
Myalgia	1	5.3	
Bloating	1	5.3	
Cough	1	5.3	
Right upper quadrant pain	17	89.5	
Jaundice	5	26.3	
Hepatomegaly	4	21.1	
Cholelithiasis	5	26.3	
Urticaria	1	5.3	

<b>Table 2.</b> Various laboratory parameters detected at the time of admission and at 1 <sup>st</sup> month of				
Parameter	Median (interquartile range) at admission	Median (interquartile range) at 1 <sup>st</sup> month	p-value	
WBC (mm <sup>3</sup> )	9.51 (6.61-13.23)	6.27 (4.66-8.26)	0.117	
Eosinophil (mm³)	9.6 (2.3-44)	5.3 (2.4-9.4)	0.01*	
Hemoglobin (g/dL)	13 (11.4-14.1)	12.1 (11.6-13.1)	0.610	
Platelet (mm³)	275,000 (223,000-339,000)	265 (239-321)	0.530	
Alanine aminotransferase (U/L)	34 (27-160)	25 (17.5-37)	0.019*	
Aspartate aminotransferase (U/L)	28 (23-91)	23 (18-28.5)	0.066	
Alkaline phosphatase (U/L)	165 (96-232)	95 (75-103)	0.028*	
Gamma-glutamyl transferase (U/L)	79 (47-194)	26 (20.5-41.5)	0.011*	
Total bilirubin	0.7 (0.4-2.3)	0.4 (0.35-0.65)	0.017*	
Direct bilirubin	0.2 (0.1-1.5)	0.1 (0.1-0.15)	0.011*	
*: p<0.05 was considered statistically significant, WBC: White blood cell				

No parasite eggs were detected in the stool of any patient. Imaging findings were obtained form 12 patients. Magnetic resonance imaging (MRI) was used for 7 patients (58.3%), computed tomography (CT) for 4 patients (21.1%), and no significant findings were found in one patient (8.3%). Eight patients (42.1%) were diagnosed with endoscopic retrograde cholangiopancreatography (ERCP), and 2 patients (10.5%) were diagnosed with biopsy. One patient underwent serological testing, which yielded a positive result.

All patients were initiated on triclabendazole. No side effects were observed. One patient was lost due to intervening cardiac problems. Eighteen patients were discharged with recovery.

#### DISCUSSION

*F. hepatica* is endemic in Central and South America (especially Bolivia and Peru), Europe (especially Portugal, France, Spain, and Türkiye), Asia (especially China, Vietnam, Taiwan, Korea, and Thailand), Africa, and the Middle East. Globally, 180 million people are at risk (6,7). In Türkiye, the incidence rates of cases vary according to regional distribution. The actual number of fascioliasis cases in our country is likely higher than the detected case numbers due to the asymptomatic course of cases, difficulties in considering the disease, especially in rural areas, and delays in diagnosis. In previous studies published in our province, the prevalence of fasciola hepatica immunoglobulin G positivity was found to be 2.78% (8).

Sheep and cattle are the most important definitive hosts of F. *hepatica*; goats, buffaloes, horses, donkeys, camels, pigs, deer, and rabbits can also be infected. Snails are intermediate hosts. Humans are accidental hosts and usually acquire infection by ingesting watercress or water chestnut grown in sheep farming areas. Infection can also be transmitted by other freshwater plants such as lettuce, mint, clover, and parsley. Humans can acquire infection by ingesting contaminated water containing live metacercariae. Outbreaks have been described to develop in this way (9,10). The incidence of animal and human infection increases in rainy years due to the increase in snail numbers and the longer survival of encysted cercariae (11). In our patients, a history of watercress consumption was present in 12 (63.2%) patients, and a history of animal husbandry was present in 7 patients. It can be said that watercress is the most significant

item in the epidemiological history in our region. A careful dietary history, including the consumption of raw vegetables washed in contaminated water, should be obtained.

In endemic areas, the likelihood of infection in very young children and women is higher. Studies conducted in our country also emphasize female dominance (12). Sheep, cattle, or humans acquire infection by ingesting vegetation containing metacercariae. Metacercariae exit the duodenum and migrate to the bile ducts through the intestinal wall, peritoneal cavity, and liver parenchyma, where they mature into adults. In humans, this takes three to four months. Adult flukes are found in the larger bile ducts of mammalian hosts. Adult flukes can partially obstruct the bile ducts and cause thickening, dilation, and fibrosis of the proximal bile duct (13).

Liver damage is associated with the parasite burden. The number of adult flukes reaching the biliary tree is usually low. The estimated lifespan of adult *F. hepatica* flukes in humans is 9 to 13 years. Many infections are mild; morbidity increases with fluke burden (14). Among the forms of infection are the acute (hepatic) phase, chronic (biliary) phase, ectopic fascioliasis, and pharyngeal fascioliasis. In this study, while the number of flukes was unknown in 11 (57.9%) patients, single fluke was detected in 5 (26.3%) patients, 2 flukes in 2 (10.5%) patients, and 7 flukes in 1 (5.3%) patient. Extrahepatic involvement was not detected in any of the patients. Hepatic involvement was present in 11 (57.9%) patients, while biliary involvement was present in 8 (42.1%) patients.

Symptoms in the acute (hepatic) phase generally begin 6 to 12 weeks after ingesting metacercariae. The early phase of hepatic migration is usually associated with fever, right upper quadrant pain, and hepatomegaly. Jaundice is occasionally observed. Other symptoms include anorexia, nausea, vomiting, weight loss, myalgia, cough, and urticaria. Prominent peripheral eosinophilia is almost always present. The acute phase can be complicated by hemobilia or subcapsular hepatic hematomas (9). In most cases, acute symptoms typically resolve about six weeks later, but widespread hepatic parenchymal necrosis can occur in very severe infections.

Extrahepatic symptoms can also occur in the acute phase, possibly due to an immunological or allergic mechanism (11). A Loeffler-like syndrome or right-sided pleural effusion containing eosinophils may be observed (6,15). Urticaria may be associated with itching and dermatographia (16). Pericarditis, cardiac conduction abnormalities, meningeal symptoms, focal neurological changes, or seizures have also been described but are rare.

The chronic phase (biliary phase) typically begins approximately six months after the primary infection and may persist for around ten years or even longer. Although often asymptomatic, patients may present with epigastric and right upper quadrant pain, diarrhea, nausea, vomiting, weight loss, and hepatomegaly. It may cause biliary obstruction, leading to complications such as gallstone formation, cholangitis, obstructive jaundice, and, through obstruction of the pancreatic duct, recurrent episodes of pancreatitis. Prolonged and/or severe infection may also result in sclerosing cholangitis and biliary cirrhosis. Peripheral eosinophilia may or may not be present during the biliary phase (5).

Ectopic fascioliasis remains unknown whether extrahepatic involvement in ectopic fascioliasis results from hematogenous dissemination of the parasites or their migration through soft tissues. Ectopic fascioliasis leads to eosinophilic and mononuclear infiltration, accompanied by secondary tissue damage. The most frequently affected site is the subcutaneous tissue of the abdominal wall. Other organs that may also be involved include the lungs, heart, brain, muscles, genitourinary system, skin, and eyes.

Pharyngeal fascioliasis is a form of fascioliasis observed in the Middle East, typically transmitted through the consumption of undercooked viscera—particularly liver—from infected animals. The live parasite may attach to the upper respiratory tract or proximal segments of the gastrointestinal tract, leading to allergic pharyngitis characterized by edema and obstruction. In severe cases, airway compromise and asphyxiation may occur.

In this study, the most commonly detected symptoms were anorexia, right upper quadrant pain, and nausea-vomiting. Five of the cases were evaluated as being in the chronic phase, presenting with cholangitic findings. The symptoms and clinical features of the remaining patients were consistent with the hepatic phase. Similar to our study, abdominal pain and anorexia were the most frequent symptoms in the study by Binici.

Fascioliasis should be considered in patients presenting with abdominal pain and hepatomegaly accompanied by peripheral eosinophilia.

Diagnosis can be established by identifying eggs in stool, duodenal aspirates, or bile samples. Eggs may not be detected in feces during the acute phase of infection or in ectopic fascioliasis. Since egg shedding may be intermittent, examination of multiple specimens may be required; negative stool examinations do not exclude the diagnosis. In this study, no parasite eggs were detected in the stool of any patient.

The diagnosis may be made during surgery or endoscopy for biliary obstruction when adult flukes are found in the biliary tree. On ERCP, adult flukes may appear as small, radiolucent linear, elliptical, or crescent-like shadows, with jagged, irregular margins in the gallbladder or dilated bile ducts. Laparoscopy may also demonstrate nodules in the liver capsule.

Serology generally becomes positive early in the hepatic migration phase; therefore, it is useful for diagnosis before eggs appear in the stool. It is also useful in ectopic diseases when eggs are not detected in the stool. Serological tests include indirect hemagglutination, complement fixation, counterimmunoelectrophoresis, immunofluorescent tests, and enzyme-linked immunosorbent assay. The sensitivity of these tests is good, but their specificity is not optimal. Cross-reactions occur with other parasitic infections. In this study, serological testing was performed in one patient, and it was positive.

Real-time polymerase chain reaction on stool is emerging as an alternative diagnostic technique with high sensitivity, but is not yet commercially available.

Useful radiographic tools for fascioliasis include CT, ultrasonography, cholangiography, ERCP, and MRI (17). Ultrasonography, cholangiography, and ERCP are useful in the biliary phase of infection (18).

The treatment of fascioliasis consists of antihelminthic therapy. Additional intervention may be required depending on the nature of the clinical picture. The preferred treatment is triclabendazole; bithionol and nitazoxanide are alternative options (19,20). Triclabendazole is an imidazole derivative. It is effective against all stages of fascioliasis with a cure rate of over 90% (21). The dosage consists of orally administering 10 mg/kg for one or two days. The drug is relatively well tolerated; absorption is preferably increased by postprandial administration following a fatty meal.

The mechanism of resistance of triclabendazole against Fasciola is not known (22). Treatment failures have been reported in humans and may be due to resistance; however, some studies have shown improvement after repeated triclabendazole doses (23-25).

Triclabendazole prolongs the QTc interval. The primary complication of treatment is biliary obstruction due to dead parasites, which may occur three to seven days after treatment and may require removal by ERCP. In this study, no side effects or complications related to triclabendazole were observed in any of the patients.

Post-treatment follow-up should include resolution of eosinophilia, clearance of eggs in stool, and a decrease in serology titers. However, difficulties in detecting eggs in stool and accessing serological tests limit the role of these parameters in follow-up. Resolution of biliary tract findings on ultrasound after treatment may also be beneficial (26).

# **CONCLUSION**

In conclusion, Fascioliasis is the most widely distributed vectorborne parasitic disease known, with the widest latitude, longitude, and altitude distribution. It is also seen in our region, and a significant history of watercress consumption epidemiologically stands out. *F. hepatica* should be considered in patients presenting with abdominal pain accompanied by peripheral eosinophilia. Increasing awareness among physicians will contribute to preventing delays in diagnosis and treatment.

## \*Ethics

**Ethics Committee Approval:** This study was conducted in accordance with the principles of the Helsinki Declaration. Ethical approval for the study was obtained from the Non-Interventional Ethics Committee of Firat University Faculty of Medicine (date: 21.01.2022, number: 6284).

**Informed Consent:** Patient consent was not obtained because the study was retrospective.

#### Footnotes

#### \*Authorship Contributions

Surgical and Medical Practices: A.S.T., M.A.A., A.B., İ.H.B., A.A., K.D., Concept: A.S.T., İ.H.B., K.D., Design: A.S.T., A.A., Data Collection or Processing: A.S.T., M.A.A., Analysis or Interpretation: A.S.T., M.A.A., A.B., İ.H.B., A.A., K.D., Literature Search: A.S.T., M.A.A., A.B., Writing: A.S.T., M.A.A.

**Conflict of Interest**: No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study received no financial support.

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