



Evaluation of Patients Diagnosed with Fascioliasis: How Can We Diagnose Without Serology?

Fasiyoliyazis Tanılı Hastaların Değerlendirilmesi: Serolojisiz Nasıl Tanı Koyabiliriz?

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ABSTRACT

Introduction: Fascioliasis is a trematode infestation caused by *Fasciola hepatica* and *Fasciola gigantica*. In this study, we aimed to investigate the etiological factors, clinical findings and diagnostic methods in patients with fascioliasis.

Materials and Methods: Patients who were diagnosed with fascioliasis between 01.06.2022 and 31.09.2022 at Gaziantep University Faculty of Medicine Infectious Diseases Clinic and Dr. Ersin Arslan Training and Research Hospital Infection Clinic were selected and analyzed retrospectively. Analyses were performed with the SPSS 22.0 software, $p < 0.05$ was considered significant.

Results: In our study, 23 cases of fascioliasis were identified. Of the 23 cases, 10 (43.5%) were male and 13 (56.5%) were female. The mean age was 44.35 ± 13.59 (19-68) years. When the symptoms at admission were evaluated, there were constitutional symptoms such as abdominal pain in 15 (65.2%) cases, fever in eight (34.8%) cases, nausea and vomiting in three (13%) cases, weakness and fatigue in seven (30.4%) cases. ROC analysis was performed to assess the availability of eosinophil levels. The diagnostic value of eosinophil levels of $>790/\text{mm}^3$ for fascioliasis, was calculated as 93.75% sensitivity and 85.71% specificity at 95% confidence interval. Patients from Yavuzeli were compared with other patients. Patients had significantly higher levels of eosinophils, WBC, and ALP ($p = 0.007$; $p = 0.013$; $p = 0.037$).

Conclusion: The diagnosis of fascioliasis should also be considered in the differential diagnosis of patients presenting with abdominal pain, fever, leukocytosis and eosinophilia and living in an endemic region for *Fasciola hepatica*.

Key Words: Abdominal pain; Eosinophilia; Fascioliasis; *Fasciola hepatica*; Fever



ÖZ

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Giriş: Fasiyoliazis; *Fasciola hepatica* ve *Fasciola gigantica*'nın neden olduğu bir trematod enfeksiyonudur. Bu çalışmada fasiyoliazisli hastalarda etiyolojik faktörler, klinik bulgular ve tanı yöntemlerini araştırmayı amaçladık.

Materyal ve Metod: Gaziantep Üniversitesi Tıp Fakültesi İnfeksiyon Hastalıkları Kliniği ile Dr. Ersin Arslan Eğitim ve Araştırma Hastanesi İnfeksiyon Kliniğinde 01.06.2022 ile 31.09.2022 tarihleri arasında fasiyoliazis tanısı alan hastalar seçilerek retrospektif olarak incelendi. Analizler SPSS 22.0 programı ile yapıldı, $p < 0.05$ anlamlı kabul edildi.

Bulgular: Çalışmamızda fasiyoliazis tanısı alan 23 başvuru tespit edildi. Yirmi üç olgunun 10'u (%43.5) erkek, 13'ü (%56.5) kadındı. Ortalama yaş 44.35 ± 13.59 (19-68) idi. Başvuru yakınmaları değerlendirildiğinde 15 (%65.2) olguda karın ağrısı, sekiz (%34.8) olguda ateş, üç (%13) olguda bulantı-kusma, yedi (%30.4) olguda halsizlik gibi konstitütif semptomlar mevcuttu. Eozinofilinin cut-off düzeyini değerlendirmek için ROC analizi yapıldı. Fasiyoliazis için $>790/mm^3$ eozinofili düzeyinin tanılarda değeri %95 güven aralığında, %93.75 duyarlılıkta ve %85.71 özgüllükte hesaplandı. Yavuzeli'den gelen hastalar diğer hastalarla karşılaştırıldı. Eozinofil, lökosit ve ALP seviyeleri Yavuzeli'den gelen hastalarda anlamlı olarak daha yüksek tespit edildi ($p = 0.007$; $p = 0.013$; $p = 0.037$).

Sonuç: Karın ağrısı, ateş, lökositoz ve eozinofili ile başvuran, *Fasciola hepatica* açısından endemik bölgede yaşayan hastalarda ayırıcı tanıda fasiyoliazis tanısını da düşünülmalıdır.

Anahtar Kelimeler: Karın ağrısı; Eozinofili; Fasiyoliazis; *Fasciola hepatica*; Ateş

INTRODUCTION

Fascioliasis is a trematode infestation caused by *Fasciola hepatica* and *Fasciola gigantica*. Fascioliasis, which is mostly observed in sheep-farming regions in temperate climates, is endemic in certain geographic regions around the world. Turkey is among the endemic regions of fascioliasis. Infection occurs through the consumption of plant products such as watercress, water chestnut, lettuce, mint and parsley contaminated with metacercaria^[1].

Clinical symptoms include fever, pain in the right upper quadrant and hepatomegaly. It is often accompanied by peripheral eosinophilia^[2].

For a definitive diagnosis, it is necessary to find the eggs of the parasite from stool, duodenal aspirate, or bile samples. Serological tests are used as an alternative diagnostic method. Imaging methods such as computed tomography (CT) are also used as an aid in diagnosis^[3].

Triclabendazole is the first agent of choice in the treatment, and it has a success rate of 90%^[4].

Fascioliasis is a disease that is difficult to make a differential diagnosis, due to its infrequent occurrence, difficulty in accessing serological tests in our country, requiring experience in microscopy, presenting with different findings at different stages, and due to the similar signs and complaints that it shares with many different diseases. Analysis of regional surveillance data and being aware of the clinical spectra of the disease shall allow an early diagnosis.

MATERIALS and METHODS

Patients over the age of 18 who were diagnosed with fascioliasis between 01.06.2022 and 31.09.2022 at Gaziantep University Şahinbey Research and Training Hospital Infectious Diseases Clinic and Dr. Ersin Arslan State Hospital Infection Clinic were selected and retrospectively screened. Etiological, clinical,

laboratory, radiological findings and treatment protocols of the patients were evaluated.

Descriptive statistics of the data obtained from the study were provided with mean and standard deviation for numerical variables and frequency and percentage analysis for categorical variables. The normal distribution test of the obtained variables was examined with the Shapiro Wilk test, and it was determined that they were suitable for normal distribution ($p > 0.05$). In the comparison of these variables, independent samples t-test was used. In addition, ROC analysis was used to determine the cut-off point for some variables according to serology and stool positive/negative status. The correlation between categorical variables were analyzed with the Chi-square test. The analyses were performed with the help of SPSS 22.0 software. A significance level of $p < 0.05$ was selected.

RESULTS

A total of 23 patients diagnosed with fascioliasis were identified during the study. Of the 23 cases, 10 (43.5%) were male and

13 (56.5%) were female. The mean age was 44.35 ± 13.59 (19-68).

When the cases were evaluated according to their place of residence, the majority of the cases were from the Yavuzeli district with 15 (65.2%) cases. Subsequently, five (21.7%) cases were detected in Şehitkamil district and a total of three (8.8%) cases were detected in the Pazarcık district of Kahramanmaraş and Nizip and Araban districts. It has been determined that the cases were concentrated in Yavuzeli Üçgöl village with eight (34.7%) cases (Table 1 and Figure 1 A, B)

When the occupational distribution of the cases was examined, the disease was mostly detected among housewives with 11 (47.8%) cases. Five (21.5%) cases were detected in livestock farmers, two (8.7%) cases in retirees, two (8.7%) cases in farmers, and three (13%) cases in workers.

When the mode of transmission was examined, a history of watercress consumption was detected among 14 (60.8%) cases however, the mode of transmission was unknown for nine

Table 1. Distribution of patients by district

District	Village	n (%)
Yavuzeli	Üçgöl	8 (34.78%)
Yavuzeli	Çiltoprak	3 (13.04%)
Yavuzeli	Tokaçlı	3 (13.04%)
Yavuzeli	Merkez	1 (4.34%)
Şehitkamil	Merkez	5 (21.73%)
Other	Merkez	3 (13.04%)



Figure 1. Distribution of patients according to location.

Table 2. Complaints of patients at admission

Symptom	n (%)
Abdominal pain	15 (65.2%)
Fever	8 (34.8%)
Constitutional	7 (30.4%)
Darkening of urine color	4 (17.4%)
Nausea-vomiting	3 (13%)
Pruritus	1 (4.34%)
Weight loss	1 (4.34%)
Asymptomatic	1 (4.34%)

(39.2%) cases. When the patients with unknown exposure history were examined, it was observed that four of them lived in Yavuzeli district, where the greatest number of cases were detected.

When the symptoms of the cases at the time of admittance were evaluated, the most common complaint was found to be abdominal pain in 15 (65.2%) cases. This was followed by fever in eight (34.8%) cases. Three (13%) cases presented with constitutional symptoms such as nausea and vomiting, seven (30.4%) cases with weakness and fatigue and four (17.4%) cases presented with complaints of darkening of urine color (Table 2).

In the examinations and tests, stool samples of 11 (47.8%) of the patients were examined. Fecal microscopy revealed no *Fasciola hepatica* eggs. *Fasciola hepatica* IgM ELISA was positive in 16 (69.6%) cases. There were seven cases in which no parasitic element was found in the stool sample via microscopy and ELISA

was negative. While two of these cases were diagnosed during ERCP due to existing biliary tract lesions, the other five cases were accepted as Fascioliasis, considering the presence of eosinophilia, the region in which they lived and their family and exposure history.

Abdominal USG was performed in all of the cases and imaging findings were detected in 20 of them. Abdominal CT was performed for the diagnosis of 10 (43.1%) patients, while USG was used for the diagnosis of seven (30.4%) patients, ERCP for two (8.7%) and MRI for one (4.3%) patient. The most common involvement of the liver was isolated right lobe in 11 (55%) patients, followed by the bilateral involvement in six (30%) patients, and finally isolated left lobe in three (15%) patients. When imaging results were examined, hypointense areas with peripheral irregularity contrast involvement were commonly detected on MRI, while CT revealed hypodense areas in the liver parenchyma, patchy, merging, scattered and linear line (like train tracks) areas. The parasite was observed with ERCP in two out of seven patients whose serological tests were negative (Figure 2). The remaining five patients were diagnosed with the presence of eosinophilia, complaints, imaging findings, family and exposure history.

When patients with positive and negative serological tests were compared, ALP levels and the presence of leukocytosis and eosinophilia were found to be significantly higher in serology-positive patients (Table 3). As a result of the

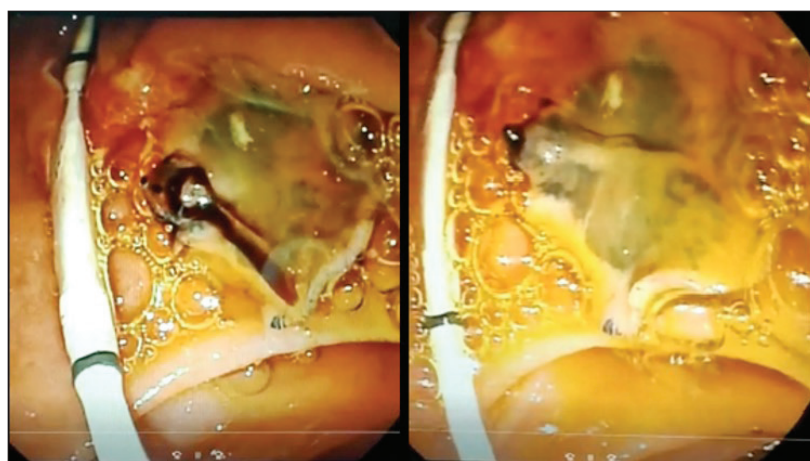


Figure 2. *Fasciola Hepatica* displayed in ERCP.

Table 3. Comparison of patients with negative and positive serology results

	Serology				p
	Negative		Positive		
	Mean	Standard deviation	Mean	Standard deviation	
WBC	8620.00	2762.31	12027.50	2993.36	0.018*
Eos	640.00	317.54	4090.62	2519.92	0.002*
Hb	13.43	.91	12.38	1.75	0.150
ALT	23.29	11.10	26.88	13.13	0.536
AST	22.29	9.03	26.81	11.43	0.365
GGT	44.57	14.11	73.63	45.92	0.120
ALP	55.57	24.08	127.69	56.87	0.004*
T. Bil	.65	.18	.46	.12	0.007*
D. Bil	.22	.12	.17	.20	0.533
Ind. Bil	.43	.11	.34	.09	0.056
Sed	29.00	9.83	41.85	27.89	0.258
CRP	16.48	14.14	25.05	26.84	0.440

WBC: White blood cell, Eos: Eosinophil, Hb: Hemoglobin, ALT: Alanine aminotransferase, AST: Aspartate transaminase, GGT: Gamma glutamyl transferase, ALP: Alkaline phosphatase, T. Bil: Total bilirubin, D. Bil: Direct bilirubin, Ind. Bil: Indirect bilirubin, Sed: Sedimentation, CRP: C-reactive protein.

ROC analysis, we applied to evaluate the availability of eosinophilia level in the diagnosis of patients with complaints and exposure history, the diagnostic value of eosinophilia level >790/mm³ for Fascioliasis was calculated at 95% confidence interval, 93.75% sensitivity and 85.71% specificity (Figure 3).

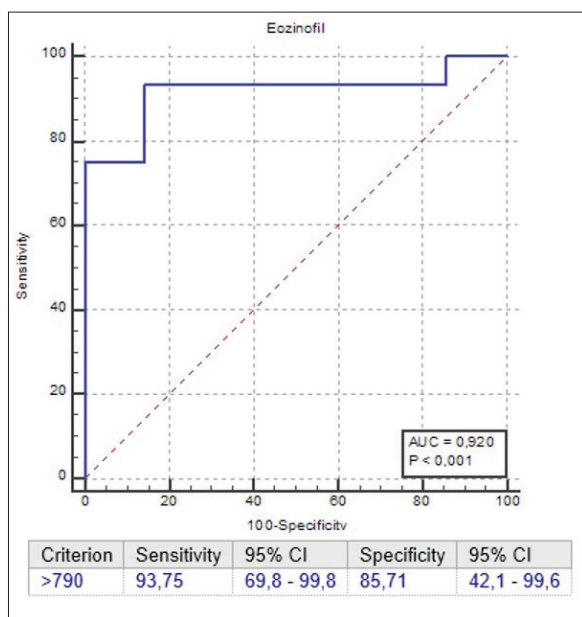


Figure 3. The usability of eosinophilia level in the diagnosis of patients.

Patients from Yavuzeli were compared with other patients. It was found that the eosinophilia level, WBC, and ALP levels of the patients were significantly higher (p= 0.007; p= 0.013; p= 0.037) (Table 4).

In all patients, 10 mg/kg of triclabendazole was administered twice daily as treatment. In the first and third months after the treatment, control tests for eosinophilia regression, inflammatory markers and liver function tests were planned. However, 15 patients were evaluated at the first-month control and six showed complete improvement in laboratory findings. At the third month of follow-up, the results of nine patients could be obtained and laboratory values improved in all but one.

DISCUSSION

Fascioliasis is a parasitic infectious disease that is seen all over the world. However, it has a high prevalence, especially in some regions^[5]. In the study conducted by Boşnak et al. in 2016, where patients with fascioliasis who were admitted to our hospital were also reported, 22 cases in total were detected in a six-year period, while in our study, it is noteworthy that there were 23 cases in just a four-month period^[6].

Table 4. Comparison of patients in Yavuzeli district with patients in other regions

	Serology				p
	Other		Yavuzeli		
	Mean	Standard deviation	Mean	Standard deviation	
WBC	8960.00	2505.42	12295.71	3107.71	0.013*
Eos	1278.89	1528.40	4172.86	2620.44	0.007*
Hb	12.68	1.51	12.71	1.71	0.967
ALT	19.89	7.96	29.57	13.50	0.066
AST	21.89	5.44	27.71	12.78	0.213
GGT	54.33	38.04	71.50	42.74	0.338
ALP	76.11	42.69	124.79	61.86	0.037*
T.Bil	0,53	0,13	0,51	0,18	0.769
D.Bil	0,16	0,09	0,20	0,22	0.562
Ind. Bil	0,37	0,07	0,36	0,12	0.808
Sed	33.00	21.82	40.25	25.37	0.517
CRP	19.10	20.41	24.56	26.05	0.605

WBC: White blood cell, Eos: Eosinophil, Hb: Hemoglobin, ALT: Alanine aminotransferase, AST: Aspartate transaminase, GGT: Gamma glutamyl transferase, ALP: Alkaline phosphatase, T.Bil: Total Bilirubin, D. Bil: Direct Bilirubin, Ind. Bil: Indirect Bilirubin, Sed: Sedimentation, CRP: C-reactive protein.

The fact that cases were often concentrated in non-central districts suggests that there may be a lack of supervision of agricultural and livestock activities in these regions. Again, in order to raise awareness for the people living in this region about this infectious disease, it is necessary to provide relevant education to children and adult age groups and to avoid contaminated food and water consumption.

When the geographical conditions of the regions where the cases were concentrated were examined, it was determined that an arid climate prevailed and water resources were not widespread, and these findings were incompatible with the literature. Although no living history was determined in patients presenting with suspicious clinical and laboratory findings under predisposing climatic conditions, the diagnosis of fascioliasis should be kept in mind^[7].

The frequent consumption of watercress in the mode of transmission is consistent with the literature, and it is necessary to ensure appropriate hygiene conditions for the production and consumption of these foods. For this purpose, methods such as preventing contamination with sewage water, ensuring

water sanitation, controlling intermediate hosts such as snails, will be effective in the relevant regions. As personal precautions, methods such as avoiding suspicious foods, washing with plenty of clean water, soaking in boiling water, keeping in 60°C water or soaking in 6% vinegar water mixture for 5-10 minutes are also effective^[8].

The fact that the majority number of cases were detected among housewives can be linked to locals being widely involved in animal husbandry and farming. As in many studies in the literature, another study conducted in our own clinic revealed that fascioliasis is more common among women, especially housewives, and that the reason for this may be that housewives have relatively more water contact^[6,9].

In developed countries, the presence of eosinophilia in the blood and a history of watercress consumption or another freshwater plant in the anamnesis are helpful in diagnosing fascioliasis^[10]. In the cases encountered in Yavuzeli district and especially in Üçgöl village, the fact that eosinophilia values were significantly higher suggests that the parasite in that region could be more virulent with a higher transmission load and other accompanying parasitic infections,

however it is necessary to investigate with samples taken from the relevant region.

In endemic areas, the prevalence decreases from children and young adults to adults. Taking into account that the lifespan of the parasite in humans ranges from 9 to 13.5 years, it was considered that most adults in endemic areas could be in the biliary phase. However, acute lesions resulting from recurrent infections also appeared to be superimposed on chronic disease with relative frequency. Thus, the acute period could be prolonged and overlap with both latent and biliary periods^[9]. In our study, in patients with positive serology, both the presence of eosinophilia and the elevation of cholestasis enzymes suggested that an acute infection may have developed on top of the chronic disease, or that the disease may be in the transition phase to the biliary period.

Computed tomography findings detected in the study by Koç et al. are flat or branched hypodense lesions detected in subcapsular or peripheral regions of the liver and concomitant periportal, peridiaphragmatic lymphadenopathy^[11]. Computed tomography findings detected in the study by Han et al. are multiple hypodense lesions with peripheral contrast^[12]. In our study, although the CT findings used for diagnostic purposes were consistent with the literature, the diagnosis was not performed via CT for all the patients. Some of the patients were diagnosed via USG, MRI and ERCP.

In our study, there was a lack of access to treatment for the patients diagnosed in our study. First of all, in patients with suspicious clinical and laboratory findings, fascioliasis should be considered and for diagnostic purposes, imaging methods and serological examinations should be requested. In our country, the diagnostic process is being disrupted because the serological tests used for this purpose are being studied in limited medical centers. For this purpose, the number of laboratories that can perform serological tests should be increased nationwide. When diagnosed, access to treatment can also be difficult, since the supply of the drug with the active ingredient triclabendazole is mostly obtained from sources abroad. To ensure easy access to treatment, it

is necessary to increase the number of centers where this medicine is constantly available.

In our study, the number of cases was limited, and parametric measurements could not be made. It is necessary to conduct studies with a larger sample group. In our retrospective study, treatment follow-ups could not be made at frequent intervals.

In the relevant region, asymptomatic cases can also be detected with serological scans and real seroprevalence can be determined as such. It may be possible to determine whether the infection occurs endemically or in the form of an epidemic in the region in question. Thus, it will be possible to diagnose patients with eosinophilia who present with non-specific complaints such as fever, abdominal pain, and also to dominate regional surveillance and to reduce the time to diagnose and morbidity.

CONCLUSION

This study, which was conducted upon the detection of a high number of cases in a period of about three months, draws attention to the fact that the diagnosis of fascioliasis should be considered in patients presenting with abdominal pain, fever, leukocytosis, and eosinophilia in the relevant geographical region. To confirm the diagnosis, imaging and serological tests may be necessary and steps should be taken to make the appropriate treatment available.

ETHICS COMMITTEE APPROVAL

This study was approved by Gaziantep University Clinical Research Ethics Committee (Decision no: 2019/268, Date: 19.06.2019).

CONFLICT of INTEREST

None of the authors had conflict of interest.

AUTHORSHIP CONTRIBUTIONS

Concept and Design: AÖM, AŞ, EE, EG

Analysis/Interpretation: AÖM, KK, EE, AŞ

Data Collection or Processing: EG, SB, EE, KK

Writing: AÖM, KK, İK, AŞ

Review and Correction: İK, EG, SB, KK, AŞ

Final Approval: İK, SB

REFERENCES

1. Mas-Coma S. Epidemiology of fascioliasis in human endemic areas. *J Helminthol* 2005;79:207-16. <https://doi.org/10.1079/JOH2005296>
2. El-Shabrawi M, El-Karaksy H, Okasha S, El-Hennawy A. Human fascioliasis: Clinical features and diagnostic difficulties in Egyptian children. *J Trop Pediatr* 1997;43:162-6. <https://doi.org/10.1093/tropej/43.3.162>
3. Espino AM, Finlay C. Sandwich enzyme-linked immunosorbent assay for detection of excretory secretory antigens in humans with fascioliasis. *J Clin Microbiol* 1994;32:190-3. <https://doi.org/10.1128/jcm.32.1.190-193.1994>
4. Keiser J, Utzinger J. Chemotherapy for major food-borne trematodes: A review. *Expert Opin Pharmacother* 2004;5:1711-26. <https://doi.org/10.1517/14656566.5.8.1711>
5. Lopez M, White Jr AC, Cabada MM. Burden of Fasciola hepatica infection among children from Paucartambo in Cusco, Peru. *Am J Trop Med Hyg* 2012;86:481. <https://doi.org/10.4269/ajtmh.2012.11-0448>
6. Boşnak VK, Karaoğlan I, Sahin HH, Namiduru M, Pehlivan M, Okan V, et al. Evaluation of patients diagnosed with fascioliasis: A six-year experience at a university hospital in Turkey. *J Infect Dev Ctries* 2016;10:389-94. <https://doi.org/10.3855/jidc.6681>
7. Arjona R, Riancho JA, Aguado JM, Salesa R, González-Macías J. Fascioliasis in developed countries: A review of classic and aberrant forms of the disease. *Medicine* 1995;74:13-23. <https://doi.org/10.1097/00005792-199501000-00002>
8. Centers for Disease Control and Prevention. Prevent and controls 2018. Available from: <https://www.cdc.gov/parasites/fasciola/prevent.html>.
9. Mas-Coma S, Valero MA, Bargues MD. Fascioliasis. *Adv Exp Med Biol* 2019;1154:71-103. https://doi.org/10.1007/978-3-030-18616-6_4
10. Mas-Coma S, Bargues MD, Valero MA. Diagnosis of human fascioliasis by stool and blood techniques: Update for the present global scenario. *Parasitology* 2014;141:1918-46. <https://doi.org/10.1017/S0031182014000869>
11. Koç Z, Ulsan S, Tokmak N. Hepatobiliary fascioliasis: Imaging characteristics with a new finding. *Diagn Interv Radiol* 2009;15:247-51. <https://doi.org/10.4261/1305-3825.DIR.1851-08.2>
12. Han J, Han D, Choi B, Han M. MR findings in human fascioliasis. *Tropical Med Int Health* 1996;1:367-72. <https://doi.org/10.1046/j.1365-3156.1996.d01-43.x>

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