## **ORIGINAL ARTICLE**

# Retrospective Evaluation of Adult Hydatid Cyst Cases Erişkin Kist Hidatik Vakalarının Retrospektif Değerlendirilmesi

<sup>1</sup>Mehmet Çelik 📵, <sup>2</sup>Ali İrfan Baran 📵, <sup>3</sup>Deniz Altındağ 📵, <sup>4</sup>Yusuf Arslan 📵, <sup>5</sup>Tayyar Tarcan 📵, <sup>6</sup>Mahmut Sünnetçioğlu 📵, <sup>7</sup>Sevil Alkan (

<sup>1</sup>Harran Üniversitesi Tıp Fakültesi Enfeksivon Hastalıkları ve Klinik Mikrobiyoloji ABD, Şanlıurfa

<sup>2</sup>YYÜ Tıp Fakültesi Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji, Van

<sup>3</sup>Cizre Dr. Selaháttin Cizrelioğlu Devlet Hastanesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji, Şırnak

<sup>4</sup>Batman Eğitim ve Araştırma Hastanesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji, Batman <sup>5</sup>Bitlis Devlet Hastanesi, Enfeksiyon

Hastalıkları ve Klinik Mikrobiyoloji, Bitlis <sup>6</sup>YYÜ Tıp Fakültesi Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji, Van

<sup>7</sup>Çanakkale Onsekiz Mart Üniversitesi Tip Fakültesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Anabilim Dalı, Çanakkale

#### Correspondence

Mehmet Celik, Karsıvaka Mah. 498.Sk. Tema Yesilvadi Sitesi A-Blok: Kat.6 No:12 Haliliye/Sanlıurfa

E-Mail: dr.mcelik12@gmail.com

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## **ABSTRACT**

Aim: The aim of this study was to evaluate the characteristics of adult patients followed up for

Aim: The aim of this study was to evaluate the characteristics of adult patients followed up for hydatid cysts disease.

Method: Patients over the age of 18 years who were diagnosed with hydatid disease, between January 2015 and September 2021 were included in the study. The clinical, laboratory and radiologic characteristics of the patients were evaluated retrospectively.

Results: The study included 66 patients. Of the patients 59.1% were female and the mean age was 40.9±15.60 years. The most common presenting symptom was abdominal pain (42.4%). The most common sites of involvement were the liver (78.8%) and lung (18.2%). The majority of patients had solitary cysts (84.8%). The most common finding in laboratory tests was elevated total IgE (74.1%). The indirect hemagglutination test was positive in 77.4% of the patients tested.

Conclusion: In our study, it was concluded that hydatid cysts are most commonly seen in the liver, often with single organ involvement, and that elevated total IgE in laboratory diagnosis may be helpful in the diagnosis of hydatid cyst disease although it does not make a definitive diagnosis.

Keywords: Hydatid cyst, liver, cystic echinococcosis, parasitic infection

#### Ö7

Amaç: Bu çalışmanın amacı kist hidatik nedeniyle takip edilen erişkin hastaların özelliklerini değerlendirmektir.

degenerialirinekiii. Y**öntem:** Çalışmaya Ocak 2015-Eylül 2021 tarihleri arasında kist hidatik tanısı konan 18 yaş üstünde hastalar dahil edildi. Hastalara ait klinik, laboratuvar, radyolojik özellikler retrospektif olarak

deăerlendirildi.

aegerienairildi. Bulgular: Çalişmaya 66 hasta dahil edildi. Hastaların %59,1'i kadın cinsiyette olup, yaş ortalaması 40,9±15,60 yıldı. Hastaların en sik tarifledikleri başvuru semptomu karın ağrısıydı (%42,4). En sik tutulum yeri sırasıyla karaciğer (%78,8) ve akciğerdi (%18,2). Hastaların büyük çoğunluğunda soliter kist (%84,8) vardı. Laboratuvar tetkiklerinde en sik saptanan bulgu total IgE yüksekliğiydi (%74,1). İndirekt hemaglütinasyon testi, test edilen hastaların %77,4'ünde pozifif olarak saptandı.

Sonuç: Çalışmamızda kist hidatiğin en sık karaciğerde görüldüğü, sıklıkla tek organ tutulumu şeklinde olduğu, laboratuvar tanısında total IgE yüksekliğinin kist hidatik hastalığı kesin tanısını koydurmasa da tanıya yardıma oldıbileçeği sonuçuna yarıldı.

da tanıya yardımcı olabileceği sonucuna varıldı.

Anahtar Sözcükler: Kist hidatik, karaciğer, kistik ekinokokkoz, paraziter enfeksiyon

## Introduction

hosts are herbivorous animals such as cattle, sheep, of adult HD patients. and humans. Transmission to humans usually occurs

Hydatid disease (HD) is one of the most important through close contact with dogs, hands contaminated parasitic diseases in terms of both human and animal with dog feces, or contaminated food (5). Humans are health and economics. It is a common disease in Turkiye, incidental intermediate hosts for Echinococcus species which is one of the countries where animal husbandry and humans cannot transmit the disease. In HD, cysts is widespread (1,2). HD affects more than one million may remain in the affected organ for years without people worldwide and causes a financial loss of more symptoms. Although symptoms related to the liver and than three billion dollars every year (3). HD is caused lungs are more common, they may vary according to by the larvae of dog and fox tapeworms (cestodes), the affected organ (6). In addition to clinical symptoms which are species of Echinococcus. Echinococcus and findings, radiologic tests including ultrasonography granulosus and Echinococcus multilocularis are the (USG), computed tomography (CT), direct radiography main species infecting humans and cause cystic and magnetic resonance imaging (MRI), serologic echinococcosis and alveolar echinococcosis in tests, and direct diagnostic and molecular methods are humans. Both clinical presentations may show a utilized in the diagnosis. Most asymptomatic patients are chronic, severe course and mortality may be observed diagnosed incidentally (7). Although many serologic as a result of inappropriate and inadequate treatment tests can be used, indirect hemagglutination (IHA) and (4). HD is most commonly found in the liver and enzyme-linked immunosorbent assay (ELISA) tests are lungs. The final host of E. granulosus is animals such preferred (8). In this study, we aimed to retrospectively as wolves, dogs and jackals, and the intermediate evaluate the clinical, laboratory and radiologic features





### Material and Methods

Patients older than 18 years of age who were followed up in the Infectious Diseases and Clinical Microbiology Clinic of Van Yüzüncü Yıl University Faculty of Medicine between January 2015 and September 2021 with a diagnosis of HD were included in the study. Information about the patients was obtained from the hospital information management system and archival records. Age, gender, clinical symptoms, radiologic imaging, laboratory tests and treatment protocols evaluated retrospectively. Biochemical values (alanine transaminase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), direct bilirubin (D.bilirubin), total bilirubin (T.bilirubin) and gamma-glutamyl transferase (GGT)) and total IgE levels of the patients were also analyzed.

In the diagnosis of HD, radiologic methods (including USG, CT, and MRI) were used in addition to serologic methods (9). Liver-localized HDs were categorized radiologically according to the Gharbi classification (10).

Statistical analysis: SPSS Statistics 23.0 package program was used for data analysis. Categorical variables were expressed as a percentage (%) and frequency (n). Mean±standard deviation values of normally distributed variables and median values of non-normally distributed variables were given. The shapiro-Wilk test was used for normality assumption.

Ethics committee approval: This study was conducted with the approval of the ethics committee of Van Yüzüncü Yıl University Non-Interventional Research Ethics Committee dated 08.11.2019 and numbered 19-141. All procedures in the study were performed according to the World Medical Association Declaration of Helsinki.

## **Results**

The study included 66 patients, 39 (59.1%) women and 27 (40.9%) men. The mean age of all patients was 40.9±15.60 years, the mean age of women was 41.5±15.6 years and the mean age of men was 39.8±15.75 years. The most common clinical symptoms at initial presentation were abdominal pain (n=28, 42.4%), pruritus, nausea, and vomiting (8 patients each, 12.1%). Eighteen of these patients (27.3%) had no symptoms (Table 1). The most common organ involved was the liver (n=52, 78.8%), followed by the lung (n=12, 18.2%) and kidney (n=8, 12.1%). Singleorgan involvement was observed in 58 patients (87.9%) and the most commonly involved organ was the liver (n=46, 69.7%) (Table 2). When the size of the cysts were evaluated, it was found that the cysts were 13 cm in the kidney, 12 cm in the liver, 9 cm in the lung, and 5 cm in the brain. Regarding the number of cysts seen in the organs, 56 patients (84.8%) had solitary cysts, 9 patients (13.6%) had two cysts and one patient (1.5%) had multiple cysts. The most common laboratory tests at initial presentation were total IgE (74.1%), C-reactive protein (CRP) (66.7%), and GGT elevations (41.5%) (Table 3). The hydatid cyst IHA test was positive in 77.4% of the patients tested (Figure 1).

Table 1. Distribution of HD patients' symptoms

| The initial symptoms                 | n  | %    | The initial symptoms              | n  | %    |
|--------------------------------------|----|------|-----------------------------------|----|------|
| Abdominal pain                       | 28 | 42.4 | Expectoration                     | 3  | 4.5  |
| Nausea                               | 8  | 12.1 | Sweating                          | 2  | 3    |
| Vomiting                             | 8  | 12.1 | Dysuria                           | 2  | 3    |
| Itching                              | 8  | 12.1 | New shivering or shaking (rigors) | 1  | 1.5  |
| Fever                                | 6  | 9.1  | Chest pain                        | 1  | 1.5  |
| Loss of appetite                     | 6  | 9.1  | Constipation                      | 1  | 1.5  |
| Weight loss                          | 6  | 9.1  | Abdominal swelling                | 1  | 1.5  |
| Pain in his/her back, under the ribs | 4  | 6.1  | Headache                          | 1  | 1.5  |
| Fatigue                              | 4  | 6.1  | Seizures                          | 1  | 1.5  |
| Shortness of breath                  | 4  | 6.1  | Hematuria                         | 1  | 1.5  |
| Cough                                | 3  | 4.5  | No symptoms                       | 18 | 27.3 |
|                                      |    |      |                                   |    |      |

Table 2. HD organ involvement sites

| Organ          | n  | %    | Organ           | n | %   |
|----------------|----|------|-----------------|---|-----|
| Liver (Total)  | 52 | 78.8 | Kidney (Single) | 6 | 9.1 |
| Lung (Total)   | 12 | 18.2 | Liver+Lung      | 5 | 7.6 |
| Kidney (Total) | 8  | 12.1 | Liver+Kidney    | 1 | 1.5 |
| Liver (Single) | 46 | 69.7 | Lung+Kidney     | 1 | 1.5 |
| Lung (Single)  | 6  | 9.1  | Brain           | 1 | 1.5 |

Table 3: Abnormal laboratory findings of the HD patients

| Laboratory<br>findings  | n<br>(Total) | n (+) | %    | Labo-<br>ratory<br>findings        | n (Total) | n (+) | %    |
|-------------------------|--------------|-------|------|------------------------------------|-----------|-------|------|
| Leukocytosis            | 66           | 17    | 25.8 | Increased<br>ALP levels            | 41        | 11    | 26.9 |
| Eosinophilia            | 66           | 16    | 24.2 | Increa-<br>sed GGT<br>levels       | 41        | 17    | 41.5 |
| Anemia                  | 66           | 20    | 30.3 | Increased<br>T.bilirubin<br>levels | 60        | 4     | 6.7  |
| Thrombocyto-<br>penia   | 66           | 1     | 1.5  | Increased<br>D.bilirubin<br>levels | 60        | 2     | 3.3  |
| Increased CRP<br>levels | 66           | 44    | 66.7 | Increased creatinine levels        | 64        | 0     | 0    |
| Increased AST levels    | 65           | 26    | 40   | Increased<br>Total IgE<br>levels   | 58        | 43    | 74.1 |
| Increased ALT levels    | 64           | 16    | 25   |                                    |           |       |      |
|                         |              |       |      |                                    |           |       |      |

\*ALT: Alanine transaminase; AST: Aspartate aminotransferase; ALP: Alkaline phosphatase; **D.bilirubin:** Direct bilirubin; **T.bilirubin:** Total bilirubin; **GGT:** Gamma-glutamyl transferase

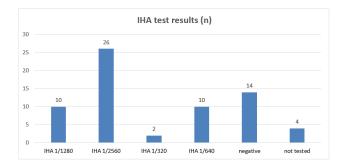


Figure 1. IHA test results of the patients

Of the cysts located in the liver, 39 (75%) were categorized according to the Gharbi classification. The cysts were mostly classified as type 1 (n=11, 28.2%) and type 2 (n=10, 25.6%) (Table 4).

Table 4. Gharbi classification of liver hydatid cysts

| Gharbi classifi-<br>cation | n  | %    | Gharbi classifi-<br>cation | n | %    |
|----------------------------|----|------|----------------------------|---|------|
| Type 1                     | 11 | 28.2 | Type 5                     | 4 | 10.3 |
| Type 2                     | 10 | 25.6 | Type 1-2                   | 1 | 2.6  |
| Type 3                     | 8  | 20.5 | Type 3-4                   | 1 | 2.6  |
| Type 4                     | 4  | 10.3 |                            |   |      |

Patients with liver involvement mostly underwent PAIR (percutaneous aspiration, injection, and re-aspiration) (19.7%) while lung and other organ involvement underwent open surgical intervention (Table 5). All patients were treated with albendazole 2x400 mg for an average of 3-6 months in non-surgical patients and one week before and one month after the procedure in surgical patients.

Tablo 5. Summary of treatments for HD patients

| Method           | n  | %    | Method                                   | n  | %   |
|------------------|----|------|--|----|-----|
| PAIR*            | 13 | 19.7 | Wedge resection (Lung)                   | 1  | 1.5 |
| Cystectomy       | 8  | 12.1 | Decortication, Cystotomy<br>+ Capitonage | 1  | 1.5 |
| PAIR+ Cystectomy | 4  | 6.1  | Treatment refusal                        | 4  | 6.1 |
| Nephrectomy      | 2  | 3    | Only medical treatment                   | 31 | 47  |
| Lung lobectomy   | 2  | 3    |  |    |     |

\*PAIR: percutaneous aspiration, injection, and re-aspiration

Relapse was detected in three patients (4.5%). One of these patients had been previously followed up and surgically treated for liver HD, but two years later lung HD was detected and albendazole and surgical treatment were repeated. In two patients with liver HD (one of them underwent PAIR and the other underwent cystectomy in the first follow-up), the surgical procedure was repeated due to relapse.

## **Discussion**

According to the data of the Ministry of Health of the Republic of Turkiye, there has been an increase in the number of reported cases of HD, which is one of the notifiable infectious diseases in our country. While the number of cases was 408 in 2008, it reached 1,867 by the end of 2019. While the number of cases reached the highest rate, especially between 2016-2017, it is seen that the number of cases reported after 2016 exceeded 1,700. However, it is thought that this increase is not a real increase and is related to the 2015 year-end regulation of the surveillance of infectious diseases mandatory to be notified by the Ministry of Health (1). Although it has been shown that HD can be observed at any age, it has been reported that the disease usually becomes symptomatic years after contact in childhood (6). In the HERACLES study, it was found that the prevalence of HD increased gradually with age in Turkiye (11). Güreser et al. (12) reported that 75% of the patients were over 40 years of age. In the study by Türkoğlu et al. (13), the mean age of the patients was found as 40.6 years. In our study, 59% of the patients were female and 41% were male. The mean age of all patients was 40.9 years and the result is similar to the literature.

Primary infection is always asymptomatic initially. Small

cysts may remain asymptomatic for years although not permanently. The incubation period in HD is uncertain and probably lasts for months or years. The disease becomes symptomatic when the cysts rupture or show mass effect. More than 90% of cysts are found in the liver, lungs, or both. Symptomatic cysts can be found in kidney, spleen, peritoneal cavity, skin and muscles (2-3%) and more rarely in heart, brain, vertebral column and ovaries (≤ 1%). The clinical presentation depends not only on the organ involved but also on the size of the cysts, their location within the organ, mass effect and complications due to cyst rupture and secondary infection. Common complications include rupture of the biliary tract and secondary cholangitis, biliary obstruction, intracystic or subphrenic abscess formation, intraperitoneal rupture (with or without anaphylaxis), rupture of the bronchial tree and broncho-biliary fistula development (14). Alveolar echinococcosis presents later than the cystic form. Liver and mostly right lobe involvement is observed in 99% of HD patients. Multiorgan involvement is seen in 13% of the cases as lung, brain, and spleen involvement in addition to liver. Although HD is rarely multivesicular, it is generally unilocular (1). Clinically, epigastric pain and cholestatic jaundice are observed in one-third of the patients, and faint symptoms such as fatigue and weight loss are also observed (4). In a multicenter study conducted in Turkiye, it was reported that the most common presenting complaints were abdominal pain, nausea, and vomiting and 18.2% of the patients were asymptomatic. It was shown that the majority of patients were diagnosed between 2-6 months after the onset of complaints. Also, in this study liver involvement was the most common (90%), 89.4% of patients had single-organ involvement, and 50% of patients with multiple-organ involvement had lung involvement together with the liver (6). Türkoğlu et al. (13) found that 75.6% of the patients were symptomatic and abdominal pain (65.6%), cough (23.3%), chest pain (19.4%) and nausea and vomiting (14.4%) were the most common symptoms. It was observed that 73.1% of the patients had single organ involvement and 26.9% had multi-organ involvement, liver (64.3%) and lung (29.3%) were the most commonly involved organs, and bone, kidney, omentum, mesentery, brain, spleen, bladder, muscle, and adrenal gland were also involved. Öztürk-Durmaz et al. (15) determined that 80.2% had solitary cysts and 19.8% had more than one cyst, 87.4% involved the liver, 4.9% the spleen, 3.9% mesenteric adipose tissue, 1.9% the kidney and 1.9% the lung. In a study conducted in Italy, it was reported that 57% of 10,682 patients who underwent surgical procedures with a diagnosis of HD between 2001 and 2012 were over the age of 60, and the cysts were found in the liver (83.6%) and lung (8.4%) (16). In an observational study conducted in Iran, it was stated that 61% of cysts were in the liver and 20% in the lung, 53% had solitary cysts, 18% had two cysts, 7% had three cysts and 8% had more than three cysts (17). In our study, 72.8% of the patients were symptomatic and 27.2% were asymptomatic. Abdominal pain (42.4%) was most commonly described at the initial presentation. The most commonly involved organ was the liver (78.8%) while the lung (18.2%) and kidney (12.1%) were the other commonly involved organs. Single organ involvement was present in 87.9% of the patients and the liver (69.7%) was the most commonly affected organ, and the cysts were mostly solitary (84.8%). It is noteworthy that kidney involvement was higher than in the current literature, especially in terms of organs with cysts.

Serologic tests are used together with radiologic imaging such as USG, CT, MRI, and direct radiography to make the diagnosis of HD. If HD is suspected on radiologic imaging, serologic tests must be performed (5). The sensitivity of serologic tests is reported to be 88-96% in liver cysts, 50-56% in the lung, and 25-26% in other organ involvement. The most commonly used serologic tests are IHA, ELISA, IFA and immunoblotting tests. IHA is important in both diagnosis and monitoring of treatment and is used to monitor the efficacy of treatment in the postoperative period (18). In the study by Türkoğlu et al. (13), serologic tests (IHA and/or IFA) were performed in 66% of the patients, and positivity was found in 70.7% of the patients. In the study of Öztürk-Durmaz et al.(15), 52 (50.4%) of 103 patients underwent the IHA test, and positivity was established in 27 (51.9%). In the study of Akkaya Işık et al. (6), IHA test positivity was 81.8%. In our study, the hydatid cyst IHA test was performed in 93.9% of the patients and 77.4% were positive and this rate is similar to the literature.

There are no biochemical and hematologic diagnostic tests specific to HD. Elevated bilirubin and transaminases may be observed in patients with liver involvement and biliary obstruction. In patients with cyst leakage or rupture, eosinophilia may be observed in the hemogram or peripheral smear, unlike in patients with cyst membrane integrity (19). In the study by Akkaya Işık et al. (6), the most common laboratory finding was anemia (25.3%) while eosinophilia was detected in 19%, AST in 15%, ALT in 19% and elevated T.bilirubin in 11%. In the study of Güreser et al. (12), GGT (28%), ALT (16%), AST (16%), and ALP (13%) elevations and eosinophilia were found in 19%. In our study, elevated total IgE (74.1%), CRP (66.7%), and GGT (41.5%) levels were especially prominent at the first presentation to the clinic. Eosinophilia was present in 24.1% of the patients.

While surgery was the only option in the treatment of HD until the 1980s, the combination of chemotherapy with benzimidazole compounds (albendazole 10-15 mg/kg/g, mebendazole 40-50 mg/kg/g) and the PAIR method gained priority (4). After the widespread use of benzimidazole compounds, it has been observed that one third of the patients receiving treatment recovered completely, and 30-50% had a significant regression in cyst size (20). In HD, if the cyst is intact, complete recovery can be achieved with surgery. Complete removal of the cyst is extremely important in terms of prevention of scattering of cyst contents and prevention of complications. Pericystectomy, marsupialization, capitonage and resection may be

necessary depending on the location of the cyst. In patients who cannot be operated, PAIR can be performed in solid or multiple cysts located in the liver, spleen, kidney, abdominal cavity and bone (4). Chemotherapeutic agents can be used as an adjuvant to surgical treatment before surgery, after surgery, or both. A course of chemotherapy before the surgical procedure sterilizes the cysts and facilitates the surgical procedure by reducing their tension while a short course of chemotherapy after surgery reduces the risk of recurrence (21). In a study conducted in India, only 9.4% of patients who used albendazole before surgery and 96.9% of patients who did not use albendazole before surgery had live cysts during surgery. In the same study, the recurrence rate was found as 18.75% in patients who did not receive albendazole treatment and 4.2% in those who did (22). In a study conducted in Turkiye, recurrence was in only one of 98 patients (1.02%) who received preoperative and postoperative albendazole (23). In a meta-analysis by Smego et al. (24), 769 patients who underwent PAIR with albendazole/mebendazole (ALB/MBZ) treatment were compared with 952 patients who underwent surgery alone and it was concluded that PAIR with ALB/MBZ treatment was more effective, had lower morbidity and mortality rates, lower risk of recurrence and shorter hospital stay. In our study, the PAIR procedure was performed the most (19.7%). While 12% of the patients underwent cystectomy, 47% did not require any surgical intervention. All of the patients were given albendazole treatment, which was started one week before the procedure and continued until one month after the procedure in patients who did undergo surgery and for 3-6 months in patients who did not undergo surgery. Recurrence developed in three patients followed up clinically, so these patients were given albendazole treatment and the surgical procedure was repeated.

## Conclusion

HD remains an important health problem in Turkiye. The diagnosis may be missed due to the lack of symptoms for a long time. In our study, it was observed that HD was most commonly seen in the liver and mostly in the form of single-organ involvement and that elevated total IgE was helpful in the laboratory diagnosis, although not diagnostic. HD should be kept in mind in patients presenting with abdominal pain and elevated total IgE.

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Ethical aspects of the research: This study was conducted with the approval of the ethics committee of Van Yüzüncü Yıl University Non-Interventional Research Ethics Committee dated 08.11.2019 and numbered 19-141. All procedures in the study were performed according to the World Medical Association Declaration of Helsinki.

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