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Evaluation of serological, biochemical and imaging findings with hydatid cyst patients

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Abstract

Aim: Hydatid cyst is a serious disease caused. The liver (50-70%) and, less frequently, the lungs (18-35%), are affected most. Diagnosis is made by evaluating the patient's clinical history, imaging findings, and serologic and immunologic tests together. Ultrasonography, computed tomography, and magnetic resonance imaging are used as imaging methods. Most classifications are made according to imaging findings. We aimed to present our experience by evaluating the relationship between age, sex, location and size of cysts, stage, indirect hemagglutination test, and laboratory and imaging findings in patients with hydatid cyst.

Materials and Methods: Retrospectively, we have evaluated the demographic data, laboratory examinations and imaging from 60 patient with diagnosis of hydatid cyst. These results were analyzed to assess and compared with each other.

Results: The most commonly affected age group was 25-45 years. The most frequently involved lobe was the right lobe and segment 6. No caudate lobe involvement was detected. There was no elevation of eosinophil count in patients with extrahepatic involvement.

Conclusion: The combination of clinical history, radiological and serological test results is valuable in the diagnosis of hydatid cyst. In addition, the presence of multiple cysts should be investigated in patients with high eosinophil value. The possibility of multiple cysts in the liver should be kept in mind in hydatid cyst patients with elevated aspartate transaminase level.

Introduction

Hydatid cyst (HC) is a serious disease caused by the larvae of Echinococcus Granulosus (EG). It is an endemic health problem in certain parts of the world [1].

The liver (50-70%) and, less frequently, the lungs (18-35%), are affected most. The involvement rate of other organs is approximately 8-10% [1-3]. People infected with EG usually remain asymptomatic for a long time. The patient's clinic is determined by the size and location of the lesions, the involved organ, compression on neighboring organs, complications secondary to infections, and anaphylaxis as a result of the rupture of the cysts [1].

Eosinophilia is an expected laboratory finding in all patients [2,4]. Serologic tests show a positivity rate of 25%. Diagnosis is made by evaluating the patient's clinical history, imaging findings, and serologic and immunologic tests together [4,5]. Imaging methods vary according to the involved organ [6,7].

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Imaging findings of HC can vary from a simple cystic appearance to solid lesions [4,8]. Ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI) are used as imaging methods [9-12]. Ultrasonography is the most commonly used imaging method for diagnosing, staging, and monitoring patients [13].

Most HC classifications are made according to imaging findings and features [10]. Gharbi et al. developed the first widely accepted classification of HC based on ultrasonography in 1981. Later, other classifications were produced but not widely used [13].

In this study, we aimed to present our experience by evaluating the relationship between age, sex, location and size of cysts, stage, indirect hemagglutination (IHA) test, and laboratory and imaging findings in patients with HC.

Materials and Methods

The records of 60 patients who were treated and followed up with a diagnosis of HC in our hospital between January 2018 and December 2022 were retrospectively scanned. The study protocol was approved by the

Ethics Committee of our institution (Firat University Non-Interventional Clinical Research Ethics Committee, approval date: 07/06/2022, approval number 2022/08-33).

This research is a single-centre, retrospective, cross-sectional, single-blinded, simple randomised study. The study was used sampling non-probable method.

Sample size was determined according to imaging method, Indirect Hemagglutination Assay (IHA) tests and laboratory results.

Demographic data (age and sex) and laboratory examinations (hematologic parameters, liver function tests, and serology) of the patients were evaluated retrospectively through the patient information system.

Diagnosis was made using imaging studies and IHA testing.

Patients with missing laboratory data, imaging, and IHA tests were not included in the study. As a serological test, IHA test values below 1/32 were considered negative, and values between 1/32 and 1/64 were considered moderate [14]. Patient images (Ultrasonography, computed tomography, and magnetic resonance imaging) were evaluated by a radiologist experienced in the field using the hospital PACS system, with organ locations, lesion sizes, and lesion numbers. Staging was performed according to the Gharbi's Classification. The localization of the cyst was recorded in patients with HC findings in at least one radiological imaging report.

The dependent variable was hydatid cyst disease. Independent variables were İHA, alanine transaminase (ALT), aspartate transaminase (AST), gamma-glutamyl transferase (GGT), eosinophil, and basophil values.

Statistical analysis

Statistical analyses were performed using the IBM SPSS software version 26.0. The variables were investigated using the Kolmogorov-Smirnov test. Descriptive analyses were presented using means and standard deviations for normally distributed quantitative variables. Frequencies and percentages were used to describe categorical variables.

Results

The records of 60 patients with a diagnosis of HC who were admitted to our hospital were obtained. Of the patients included in the study, 17 (28.33%) were males and 43 (71.66%) were females. The female/male ratio was 2.52. The mean age of the patients was 39.6±16.6 years (range, 10-80) years. The mean age of male patients was 38.41±14.8 years (range, 10-62 years) and the mean age of female patients was 40.09±17.5 years (range, 11-80 years). The most commonly affected age group was 25-45 years. The demographic characteristics of the patients are shown in Table 1.

Table 1. Demographics of the study population (n= 60).

Age	Female (%)	Male (%)	Total (%)
5-25	11 (78.57)	3 (21.42)	14 (23.33)
25-45	14 (60.86)	9 (39.13)	23 (38.33)
45-65	13 (72.22)	5 (27.77)	18 (30)
>65	5 (100)	0	5 (8.3)
Total	43 (71.66)	17 (28.33)	60

Table 2. Data of extrahepatic HC lesions (n=11).

Extrahepatic	Number	Size	Stage	Liver	IHA	Eos	Bas
Lung	1 (RUL)	70x100	1	-	1/160	0	0.1
Lung	1 (LUL)	90x115	1	-	1/640	0.18	0.04
Breast	1 (R)	30x40	4	Seg 2(1)	1/80	0.07	0.04
Breast	1 (L)	15x15	2	Seg 4,7,8	<1/16	0.02	0.01
Spleen	1 (UP)	30x40	1	-	1/1280	0.28	0.04
Spleen	1 (UP)	35x35	5	-	1/16	0.24	0.2
Spleen	1 (LP)	35x42	5	Seg 8	1/16	0.18	0.03
Spleen	1 (LP)	30x42	5	-	<1/16	0.2	0.04
Kidney	1 (R)	45x50	2	Seg 4,7,8	<1/16	0.02	0.01
Mesentery	1	30x30	2	Seg 6	1/32	0.47	0.02
Extremity	1 (L Thigh)	30x80	2	-	1/64	0.06	0.08

*IHA; Indirect Hemagglutination Assay, †Eos;Eosinofil, ‡Bas;Basofil, §RUL;Right Upper Lobe, ||LUL;Left Upper Lobe, ¶UP;Upper Pole, **LP;Lower Pole.

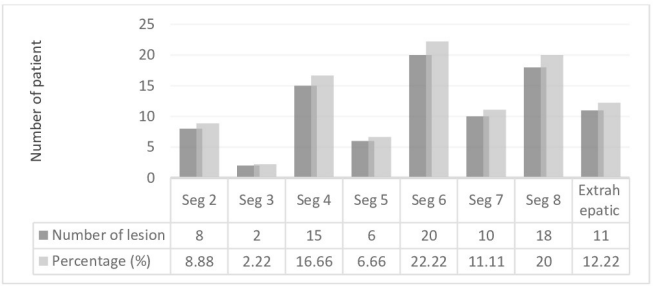


Figure 1. Liver segments and extrahepatic distribution of all HC lesions (N= 90).

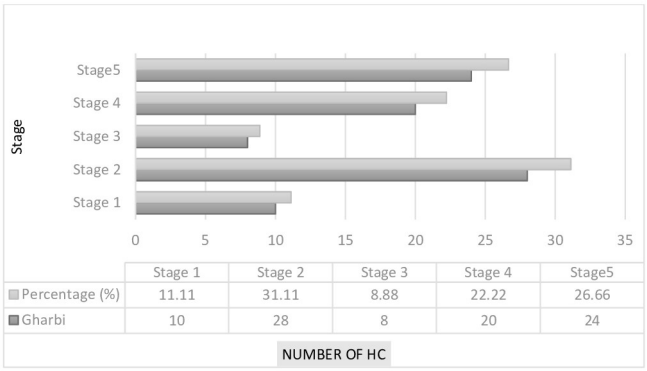


Figure 2. Distribution of all lesions according to Gharbi (N=90).

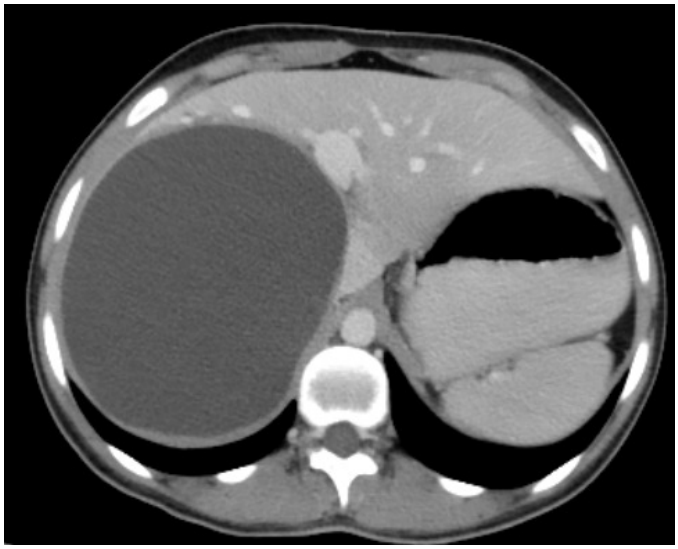
In our study, the eosinophil count was 0.5 in seven (11.66%) patients and above 0.1 in 13 (21.66%) patients. Liver enzymes levels were as follows: alanine transaminase (ALT, normal=5-45 U/L), aspartate transaminase (AST, normal=5-40 U/L), gamma-glutamyl transferase (GGT, normal for males=2-55, normal for females=2-38 U/L). Of the five (8.33%) patients with high AST levels, three had extrahepatic involvement, five had multiple cysts, and IHA tests were positive in four patients. Of five (8.33%)

patients with high ALT levels, three had extrahepatic involvement, three had multiple cysts, and IHA tests were positive in two patients.

GGT levels were above 38 U/L in only eight (13.33%) female patients. IHA tests were positive in six patients, extrahepatic involvement was found in three patients, and multiple cysts were found in four patients. AST and ALT levels were high in two of these eight patients, and both patients had extrahepatic involvement and multiple cysts.

Multiple cysts were present in four (57.14%) of seven patients with high eosinophil counts. Stage 2 cysts were detected in three (42.85%) and stage 3 (42.85%) cysts in two patients. IHA tests were 1/160 or above in six (85.71%) of them. IHA tests were negative in four (30.76%) of 13 patients with high basophil counts. There were multiple cysts in three (23.07%) of 13 patients. Basophil counts were high in three (16.66%) of 18 patients with multiple cysts, and basophil counts were high in 10 (23.80%) of 42 patients.

The IHA tests of 39 (65%) patients were above 1/64. Intermediate positivity in IHA tests was detected in eight (13.33%) patients. The eosinophil count was high in one (7.69%) of 13 patients who were IHA negative. Eosinophil counts and basophil counts were high in six (12.76%) and nine (19.14%) of 47 patients who were IHA positive, respectively. Eosinophil counts were high in four (22.22%) of 18 patients with multiple cysts and three (7.14%) of 42 patients with single cysts. Of thirteen patients who were IHA negative, six patients (46.15%) had stage 5 lesions, two patients (13.33%) had stage 4, one patient (7.69%) had stage 1, two patients (15.38%) had stage 2, one patient (7.69%) had stage 3, and one patient (7.69%) had both stage 2 and stage 3 lesions.



(a) Type 1, In the right lobe of the liver.

(b) Type 3, In the right and left lobes of the liver.

Figure 3. Contrast-enhanced axial section, Abdomen CT, Hydatid Cyst.

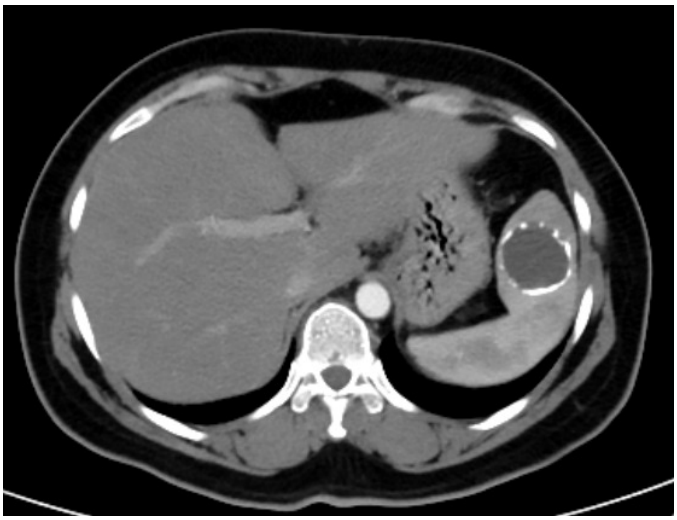
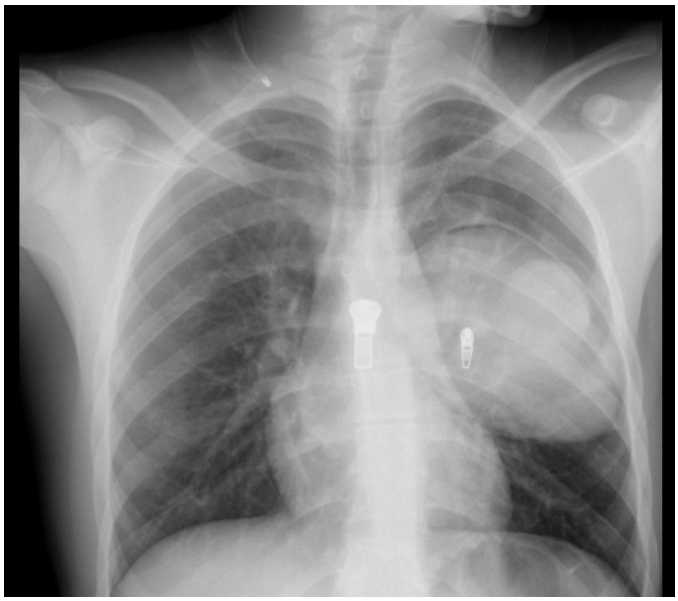


Figure 4. Axial Contrast-enhanced CT, Type 5 Hydatid Cyst in spleen upper pole.

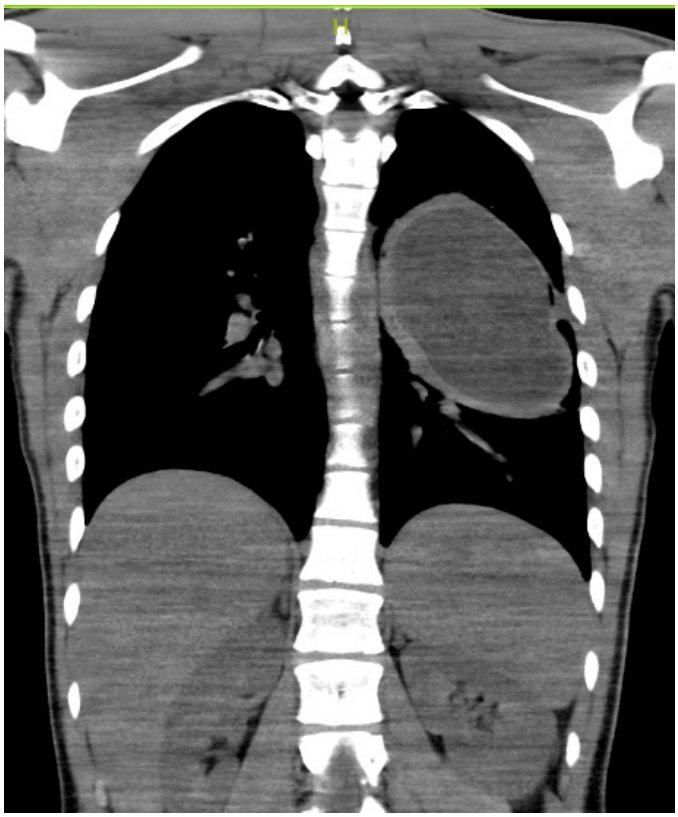
US, CT, and MRI were the imaging methods used in the scans of our patients. A single HC lesion was detected in 42 (70%) of our entire patient cohort, and more than one lesion was detected in 18 patients (30%). Isolated hepatic involvement was found in 50 patients (83.33%), extrahepatic involvement in 10 patients (16.6%), isolated extrahepatic involvement in six patients (10.00%), and both hepatic and extrahepatic involvement in four patients (6.66%). HC lesions were present in both the right and left lobes in 12 (20%) of 60 patients, in the left lobe in 12 (20%), and in the right lobe in 30 patients (50%). There were multiple cysts in the liver in 15 patients (25%). The most frequently involved lobe was the right lobe and segment 6. No caudate lobe involvement was detected. Liver segment distributions of the lesions are summarized in Figure 1. The smallest size of all HC lesions was located in segment 5 (6 mm) and the lesion with the largest size was located in segment 6 (102 x 130 mm). The mean size of all HC lesions was 41.02 x 52.62 mm.

According to the Gharbi's classification [9], of all the HC lesions are shown on Figure 2. In Gharbi stage 2, the mean AST level was found above normal.

Of the patients with extrahepatic involvement, nine (90%) were females and one (10%) was male. The female-to-male ratio was 9/1. The mean age was 40.7±18.7 (range, 19-80) years. The distribution and laboratory values of extrahepatic cysts are shown in Table 2. Of the extrahepatic lesions, 6.66% were located in the lung, 3.33% in the breast,



(a) PA chest X-ray.



(b) Coronal Unenhanced CT.

Figure 5. Type 1 Hydatid Cyst in the upper lobe of the left lung.

Figure 6. Axial Contrast-enhanced CT, Type 2 Hydatid Cyst in left breast.

6.66% in the spleen, 1.66% in the kidney, 1.66% in the mesentery, and 1.66% in the extremities (Table 2). There was no elevation of eosinophil count in patients with extrahepatic involvement. The basophil count was high in two patients.

Discussion

Hydatid cyst is a chronic parasitic zoonosis that is endemic in sheep-raising [13-16]. It is among the most neglected diseases [13]. Orally ingested eggs hatch in the intestines and reach the liver via the portal vein. Sometimes they spread to all other internal organs by crossing the liver barrier, where they turn into cysts [6,17].

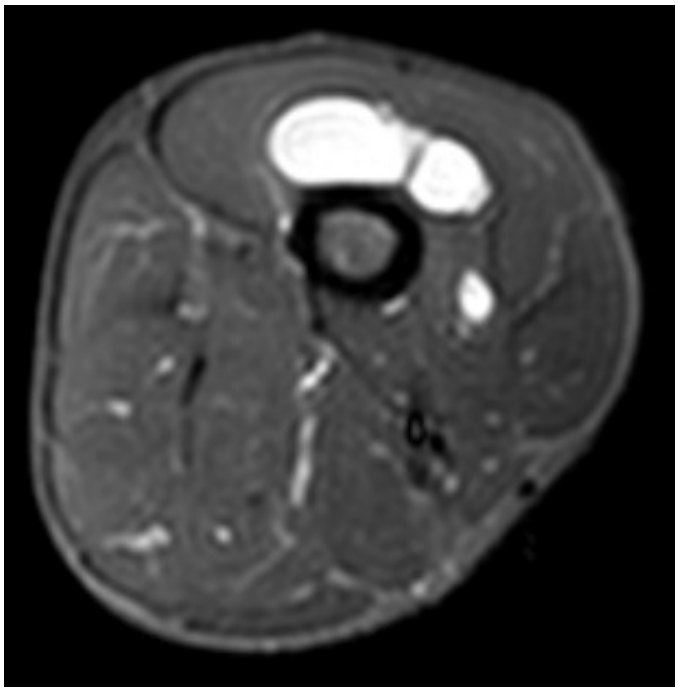
In the study conducted by Venkumar et al [18], the most frequently affected age group was 25-29 years (50%), followed by the 35-39 years (46.7%) age group. The most frequently affected age group in our patients was 25-45 years (38.33), which was consistent with Venkumar et al.'s findings. In the study of Bartin et al [19], 75% of the patients were females and 25% were males. In another study, 53.3% were females and 46.7% were males. In our study, the rate of women was 71.66% and the rate of men was 28.33%, consistent with other studies [19].

The diagnosis of HC is made by the combination of the patient's history, serologic tests, and imaging findings [2,4,5,14]. Routine laboratory tests are not specific [1]. Biochemically, there is usually eosinophilia [4,19]. IHA, The one of the methods used for the diagnosis of the disease [11,14,20]. Eosinophil counts were high in 11.66% of our patients. Only two (3.33%) patients in whom the levels of all three enzymes (AST, ALT, GGT) were high had both extrahepatic involvement and multiple cysts. Multiple cysts were found in 57.14% of patients with elevated eosinophil counts and IHA positivity was found in 85.71%. Patients presenting with HC usually have very low antibody levels. In this case, cut-off values should be considered to increase the probability of detecting antibodies in these patients [14].

Primary infection is often caused by a cyst [11,14,18]. Multiple cysts are present in 20% to 40% of patients and may affect one or more organs [14]. Multiple cysts were present in 18 (%30) patients, consistent with literature. Most patients with HC are asymptomatic in the early stages of infection [14,21]. Some cysts may collapse spontaneously and disappear or become calcified. Sometimes constantly increase in size, press on tissues and organs, and may become complicated [11,14,21].

In a study by Venkumar et al [18], single cysts were found in 93% of patients, multiple cysts in 7%, cysts were found

(a) Axial T2 MRI.



(b) Sagittal T2 MRI.

Figure 7. MRI, Type 2 Hydatid Cyst in left thigh.

in the right lobe in 83.3%, the left lobe in 10%, and both lobes in 6.7% [18]. Botezatu et al [1] detected involvement of the right lobe in more than 50% of their patients and both lobes in 9% of their patients. In addition, the most frequently involved segments in the liver were 6,7, and 8. This was followed by segments 3 and 4 by 12% each. The rarest was segment 1. In most patients, two segments of the liver were involved [1]. The rate of multiple cysts was 30% (n=18) in our patients and the rate of single cysts was 70% (n=42), concordant with the literature. Of the liver-localized cysts, 25 (31.64%) were in the left lobe, 54 (68.35%) in the right lobe, and 12 (15.18%) in both lobes. The frequency of liver segments involved was 6, 8, 4, 7, 2, and 3, respectively. No segment 1 involvement was detected (Graph 2).

US, CT and MRI are frequently used in diagnosis [9-12]. The first classification was developed by Gharbi based on US findings [9, 13, 22]. Although a well-contoured anechoic cystic lesion is usually detected, it may vary according to the stage of the disease [22]. According to Gharbi, five subtypes were defined [9, 22]. Type 1 constitutes 25-40% of all cysts. It is difficult to distinguish from a simple cyst [9]. In type 5, it shows hyperechoic calcified and usually dead HC [22]. Partial cyst calcification does not indicate that the parasite is dead. It can be assumed to be inactive [4].

The CT is indicated when US is inadequate due to patient-related difficulties. CT has be high sensitivity (94%). It is a diagnostic imaging method used to detect vascular, biliary, or extrahepatic involvement and complications such as rupture and infection [4]. HC is detected as a well-circumscribed, round-oval homogeneous opacity [1]. The air inside the cyst and enlargement of the pericyst on contrast-enhanced CT may show the development of annular enhancement and infection. In case of detachment of the membranes, dense linear areas within the cyst are detected. Daughter vesicles show peripheral alignment and are more hypodense than cyst fluid [3,4]. Calcification of the cyst wall is easily detected [2,4].

MRI is a diagnostic imaging modality that shows cystic lesions, floating membranes, detached membranes, and biliary system involvement. The characteristic image is daughter cysts seen as structures adherent to the germinal layer and they appear hypointense with respect to the cyst fluid. Membranes appear hypointense in all sequences [4].

The spread of HC may be by lymphatics, retrograde migration from the vena cava, hematogenous, or peritoneal fluid circulation spread throughout the peritoneal fluid [2].

HC most frequently involves in the liver (50-70%) (Figure 3) followed by the lung (10-40%), spleen, kidneys, and brain [1,9-11,14,16,17,19]. Consistent with the literature, liver involvement was seen most frequently in 54 (90%) of our patients. Lung involvement was present in two (3.33%) of our patients, less frequent than in the literature. All organs and systems can be affected [9,11,14,19] and two organs can be affected simultaneously in 5-13% of patients [2]. In 10 of our patients (16.66%), there was simultaneous involvement of two organs, compatible with the literature.

Splenic involvement is seen at a rate of 2-2.5%. There may be primary/hepatic and multiple organ involvements [2]. Spleen involvement (6.66%) was not compatible with the literature (Figure 4). Renal involvement is rare (1-3%). Cysts are usually unilateral and located in the upper/lower pole [2]. Consistent with the literature, renal involvement was seen most frequently in 1 (1,66%) of our patients.

The lung is the most common location in the pediatric population. The cyst grows faster due to negative pressure. Calcification (0.7%) is rare in pulmonary HC. It is rarely symptomatic and detected incidentally on X-ray [16]. An uncomplicated HC is detected as a homogeneous opacity with smooth contours on chest radiographs. The lower lobes (60%) and especially the right basal lobe are

frequently involved; 30% tend to be more than 1 and 20% tend to be bilateral [16]. In our pediatric population, four patients did not have lung involvement, but all had liver involvement. There was lung involvement in two of our adult patients, and the lesions were located in the left upper lobe of the left lung in both patients (Figure 5). It was not compatible with the literature.

Breast involvement is detected at a rate of 0.27%. Breast involvement is detected in women aged 30-50 years. The screening method is mammography (MG), US, and MRI. It appears homogeneous and well-defined in MG. Breast HC should be included in the differential diagnosis of breast masses, especially in endemic regions [23,24]. Among our two (3.33%) patients, 1 was located in the right (age 45) and 1 in the left breast (age 46) (Figure 6).

Muscle localization is rare (0.7-0.9%), even in endemic countries. HC should be differentiated from soft tissue tumors. Intramuscular HCs have been reported in the chest wall muscles and pectoralis major, sartorius, quadriceps, and gluteus muscles (Figure 7a,b) [17]. Quadriceps muscle involvement was present in one (1.66%) of our patients.

The incidence of peritoneal cavity involvement is approximately 2% [2]. Only one (1.66%) patient had mesenteric involvement and accompanying liver multiple cysts, all of which were stage 2 cysts according to the Gharbi's classification.

Up to 91.6% of our cases were detected by imaging methods (US, CT and MRI). All cases diagnosed by imaging were type 2, 3, 4 and 5 hydatid cysts. In Type 1 HC, the IHA values were above 1/160. Serological testing completed imaging methods by 8.33%.

Conclusion

Hydatid cyst disease should be considered in the differential diagnosis of cystic lesions, especially in patients who have spent time in endemic areas. The combination of clinical history, radiological and serological test results is valuable in the diagnosis of HC. According to our study, imaging methods are more valuable in the diagnosis of hydatid cyst disease than laboratory findings and serological tests. In addition, the presence of multiple cysts should be investigated in patients with high eosinophil value. The possibility of multiple cysts in the liver should be kept in mind in hydatid cyst patients with elevated AST level.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Ethical approval

The Non-Interventional Clinical Research Ethics Committee of Firat University granted the ethics committee approval for the current research (Decision No.2022/08-33, Dated: 07/06/2022).

Competing interest

No competing interest was declared by the authors.

Acknowledgement

None

Authors' contribution

PGB: Conception and designing of the study, creating the study plan, data processing, and writing the manuscript, design of the work and critical revision of the manuscript, the acquisition, analysis, and interpretation of data for the work, all the authors have approved the final version of the manuscript to be published.

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