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The role of ELISA IgG antibodies in diagnosis of cystic echinococcosis of lung. A retrospective study of a single centre activity in Albania

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Abstract

Background Cystic Echinococcosis presents significant biological, medical, economic, and social challenges. The diagnosis of cystic echinococcosis relies on immunodiagnostic methods alongside radiological in combinations with clinical findings. In human Cystic Echinococcosis, false negative immunologic results can occur in 3–5% of patients and reach up to 35–40% in hyper endemic regions. This study aimed to assess the role of Elisa IgG CE serum antibody titres in diagnosing pulmonary Cystic Echinococcosis.

Material and methods A retrospective review of medical records for 362 CE patients diagnosed in a cohort of 20 years was conducted. Diagnosis was based on radiological and clinical data, personal and family history with confirmation by serodiagnosis or histology in surgery cases. Age, sex, cysts location, size, complications and treatment were reviewed. ELISA IgG CE was studied preoperatively in all cases with its specificity and sensitivity in all cases

Results The cohort included 362 patients of whom 51.4% males and 48.6% females, with a mean age of 40 years (range 12–80). 42 % were from rural regions. Among the cases, 112 (31%) presented with intact cysts, while 250 (69%) were complicated. ELISA IgG CE serum antibody titre tests were conducted for all cases. 350 (96.7%) underwent surgical treatment, while the remainder received conservative care. ELISA IgG CE was positive in 181 patients (50%). The sensitivity was 70% (175 patients) for complicated cases, but only 18.8% (21 patients) for uncomplicated cases.

Conclusions ELISA IgG CE has limited value in diagnosing CE. However, it may aid in identifying complicated CE. Interpretation of ELISA IgE CE results should consider clinical imaging findings. Establishing pre and postoperative surveillance protocols involving family doctors and diagnostic imaging services can enhance patient care quality.

Keywords Cystic echinococcosis, Serodiagnosis, Pulmonary echinococcosis, Albania

Background

Echinococcus species, primarily Echinococcus granulosus, are the causative agents of cystic echinococcosis, one of the most widespread zoonotic infections globally. This parasitic disease primarily affects humans and livestock, with endemic regions across South America, Africa, Eastern Europe, Central Asia, and parts of the Mediterranean, including Albania. The life cycle of Echinococcus involves a definitive host (usually dogs or other canines) and an intermediate host (commonly sheep, goats, or humans). The disease burden in endemic areas is significant due to

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its economic impact on livestock and the health system, leading to long-term disability and costly treatments. In humans, hydatid cysts commonly form in the liver (about 70% of cases) and lungs (20–30%), though they can also develop in other organs [1, 2]. Cystic echinococcosis (CE) are tissue infestations caused by the larval forms of Echinococcus granulosus, most commonly affecting the liver and lungs, the latter being the second most frequently involved organ [1, 3]. Diagnosis using a combination of clinical suspicion, imaging findings and serological tests, with or without diagnostic aspirate, has been recommended by the WHO since the early 2000s. Diagnosis include serological tests, with ELISA IgG Echinococcosis and indirect hem agglutination assay (IHA) being two key methods for identifying CE [4, 5]. While ELISA IgG was developed by Engvall and Perlmann in 1971, known for its sensitivity and reliability [6]. Serological tests with clinical, personal and family history with imagery serve for differentiating and can add CE from other masses such as simple cysts, abscesses, and tumors during imaging evaluation [7]. Despite the utility of serological testing, no single, highly sensitive, or specific test exists for detecting cystic ELISA IgG, and false negatives can occur in 3–5% of patients overall, and up to 35–40% in hyper endemic areas and Western blot as gold standard serological test [8]. Sensitivity varies with factors including cyst viability, complication, location, and parasite strains, age of patient an size of CE cysts [9, 10]. It is noteworthy that serological responses are often lower in pulmonary cases compared to hepatic ones [11]. This study aims to evaluate the utility of ELISA IgG CE in diagnosing CE.

Materials and methods

A retrospective analysis was conducted on 362 patients diagnosed with CE at University Hospital Shefqet Ndroqi Tirana/Albania. Which were studied in preoperative radiological and clinical diagnosis, personal and family history with add on confirmatory serodiagnosis of ELISA IgG CE and histopathologically found to have CE. Medical files of patients with final diagnosis of CE were reviewed in 20 years' cohort with the same diagnostic criteria applied. All the patients had physical examinations after the completion of personal and family medical histories. Complete blood counts, biochemical parameters, and coagulation tests were performed in all the cases. The poster-anterior (PA) chest radiograph and chest computed tomography (CT) scan with typical findings for CE evaluated by radiologist were used for preoperative diagnosis in all the cases alongside serological tests for ELISA IgG CE were conducted for all cases (Fig. 1 CT scan showing a 75×80 mm thin margin cavity in the upper lobe of the left lung with multiple folding membranes in its dependent portion in a patient with positive ELISA IgG CE). Age and sex of the cases and the cyst's location, number, size, spread to other organs outside the lungs, and condition as intact or ruptured were reviewed. (Fig. 2 CT scan showing 63×70 mm round pulmonary hypodense lesion in the lower lobe associated with a hepatic 50×50 mm lesion in a 21 year old patient with positive ELISA IgG CE). No diagnostic aspirate was performed and surgical cases diagnosis was confirmed by histology. Complications included cyst rupture, secondary infection, pneumothorax, or anaphylactic reactions. Non surgical cases were treated with albendazole 3 cycles of 28 days with 14 days apart. Non surgical were considered non fit patients for surgery and patient refusal. ELISA IgG detection was performed in centrifuged serum with Novalisa Echinococcus IgG (novatech Gmb). Descriptive statistics, ANOVA, and Chi-square tests were applied to analyze data. Sensitivity and specificity were calculated for serological tests, stratified by age, cyst location, and complication status.

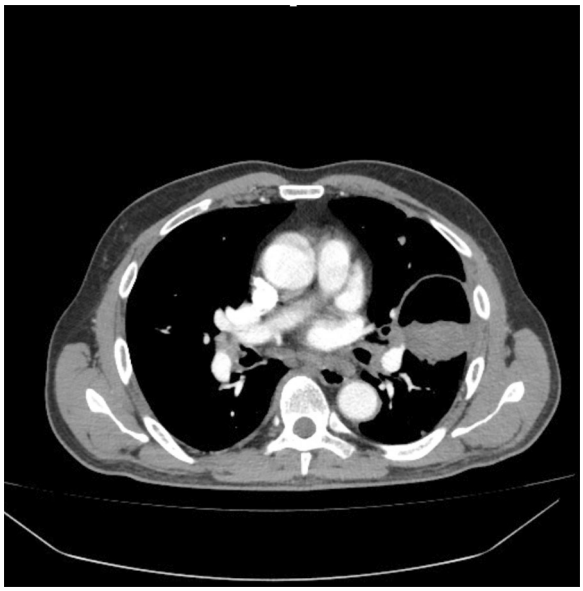

Fig. 1 CT scan showing a 75×80 mm thin margin cavity in the upper lobe of the left lung with multiple folding membranes in its dependent portion in a patient with positive ELISA IgG CE

Results

Patient demographics included 51.4% male and 48.6% female, with a mean age of 40 years (range 12–80). 42% were from rural regions. The most common symptoms included cough (76.3%), fever (31.2%), and chest pain (29.0%). Asymptomatic cases were also noted, with incidental findings on radiographs. In terms of cyst involvement, 60.2% had lung-only cysts, while 34.4% presented with both lung and liver cysts. Cysts were single in 76.3%

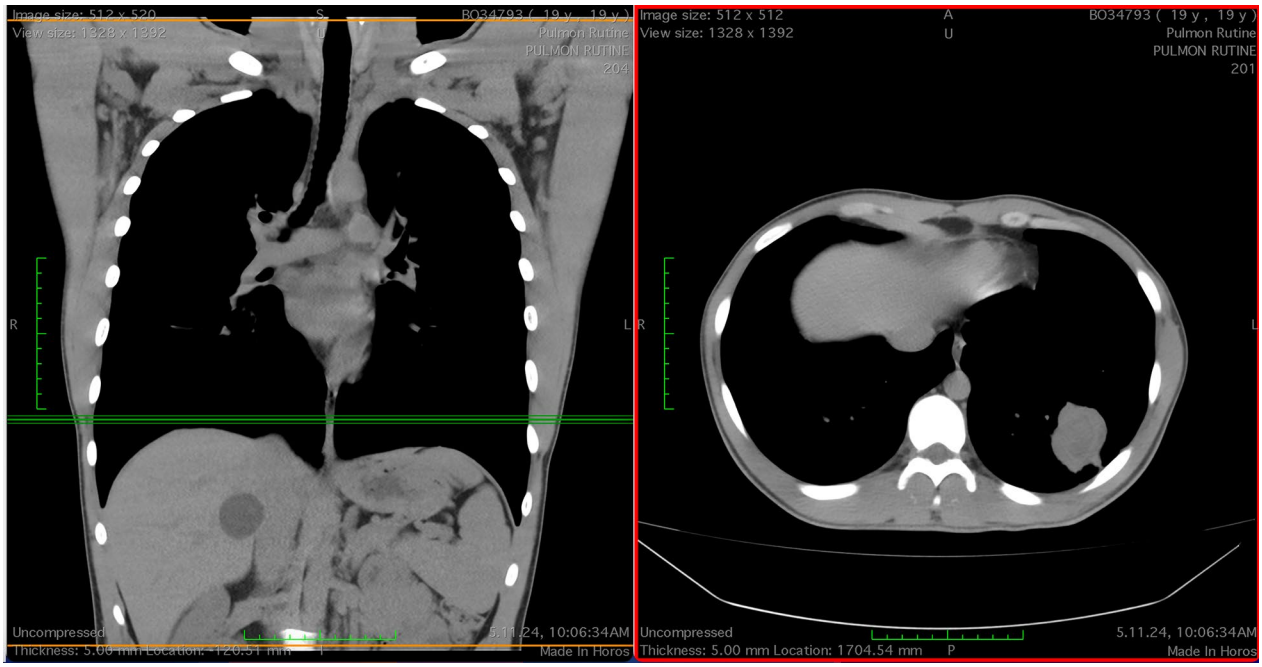

Fig. 2 CT scan showing 63 × 70 mm round pulmonary hypodense lesion in the lower lobe associated with a hepatic 50 × 50 mm lesion in a 21 year old patient with positive ELISA IgG CE

of cases, and the average diameter was 6.4 cm (Fig. 3). Out of the 362 patients reviewed were Pulmonary Cysts Only (218 patients) with Positive serology were 102 patients (46.8%) and Negative serology 116 patients (53.2%). In Hepatic Cysts Only (64 patients) had Positive serology 50 patients (78.1%) and Negative serology: 14 patients (21.9%). In Combined Pulmonary and Hepatic Cysts were (80 patients) with Positive serology 66 patients (82.5%) and Negative serology 14 patients (17.5%)

Among the cases reviewed, 112 (31%) presented with intact cysts and 250 (69%) with complicated cysts. ELISA IgG was tested in all cases, revealing a positive result in 181 patients (50%). Sensitivity was notably higher in complicated cases (70%) compared to uncomplicated ones (18.8%) (Fig. 4) and higher age sensitivity for 10–30 years was 65% (Fig. 5) .350 (96.7%) received surgical treatment, while the remainder 3.3% or 72 patients were treated conservatively with 3 cycles of albendazole for 28 days with 14 days apart each cycle. Histopathological examination confirmed hydatid cysts in all surgical patients.

The average postoperative hospitalisation duration was 12.8 ± 3.73 days. Surgical intervention resulted in complications for 34.8% of cases, with no reported fatalities.

A statistically significant correlation has not been found between ELISA IgG with patient age, cyst diameter and site of involvement which resulted respectively $P < 0.243$; $P < 0.400$; $P < 0.111$

Discussion

CE, as explored in this study, is often asymptomatic until cysts reach a large size or rupture, leading to potentially serious complications such as secondary infections, pneumothorax, and anaphylaxis. [2] In our study, the overall sensitivity of serum antibody titres Echinococcus IgG for diagnosing CE was found to be 50%, with a notable sensitivity of 70% in complicated cases but only 18.8% for uncomplicated cysts Given the low sensitivity of antibody testing in uncomplicated cases, the study emphasises the importance of imaging techniques such as chest X-rays and CT scans as the primary diagnostic tools for CE. Further age, cyst diameter, cyst location, extra pulmonary involvement does not affect ELISA IgG CE positivity. The study highlights that while ELISA IgG offers a valuable tool for detecting Echinococcus antibodies, its sensitivity especially in pulmonary involvement lags behind other diagnostic approaches such as more sensitive radiological techniques like CT scans, which remain the gold standard in identifying hydatid cyst morphology and complications. This study has its limitations due to dependence on clinical records and is retrospective with also cases whom refused surgery which give confounding results in sensitivity and specificity of the serological test. Other studies have reported varying sensitivities for serological tests in diagnosing CE disease. For instance a study [2] found that the sensitivity of ELISA for CE ranged from 54 to 75%, indicating a higher overall

Category	Details
Total Patients	362
Male	165 (Mean age: 27.6 ± 16.32 years)
Female	221 (Mean age: 32.7 ± 17.8 years)
Overall Mean Age	30.15 ± 16.93 years
Age Group	55.7% aged between 10 and 30 years
Agricultural Workers	34%
Residence	Rural Areas: 42%
Dog Ownership	53.2%
Previous Surgeries (Household Members)	15 (9 pulmonary cysts, 6 liver cysts)
Previous Surgeries (Patients)	25 (14 pulmonary, 10 liver, 1 brain)
Common Symptoms	Cough, Hemoptysis, Chest Pain
Sudden cough with expectoration	19.8%
Fever and purulent sputum	31% (119 patients)
Allergic episodes	3% (12 patients)
Pleural effusion	0.7% (3 patients)
Hydropneumothorax	0.2% (1 patient)
Asymptomatic	2.3%
Eosinophilia	24.8%
Chest Radiographs	All abnormal findings
Well-defined round cysts	52.2%
Lung abscess	20.3%
Perivesicular pneumocysts/crescent signs	11.2%
Iceberg/water-lily sign	14.2%
Translucent cyst resembling bulla	1.3%
Pleural effusion	3.4%
Hydropneumothorax	0.2%
Calcification of cyst wall	0.7% (2 patients)
Lung-Localized Disease	218 patients
Extrapulmonary Cysts	64 Hepatic
Cyst Characteristics	Unique cysts: 74.4% (286 cases), Multiple cysts: 5.1% (20 cases), Bilateral cysts: 5.8% (21 cases)
Lung Predilection	Right lung: 56.8%, Lower lobes: 59%
Bronchoscopy Findings	White gelatinous material in 21 patients confirming echinococcus
Total Complications	44 patients (11.8%)
Prolonged air leaks	9
Atelectasis needing bronchoscopy	2
Aspiration pneumonia	11
Empyema	4
Operative Deaths	2 (Cardiac arrest: 1, Respiratory failure: 1)

Fig. 3 Descriptive analysis in number and percentage of data in the study

detection rate compared to your findings, particularly in complicated cases. In contrast, the sensitivity increased significantly (70%) in cases where cysts were complicated (ruptured or leaking) [10, 12]. This suggests that serological tests may be more effective when the immune system has been activated by antigen leakage, typically seen in complicated cases [13]. The lower sensitivity observed in pulmonary hydatid cysts is consistent with findings from other studies, which have consistently shown that hepatic cysts tend to elicit a stronger serological response

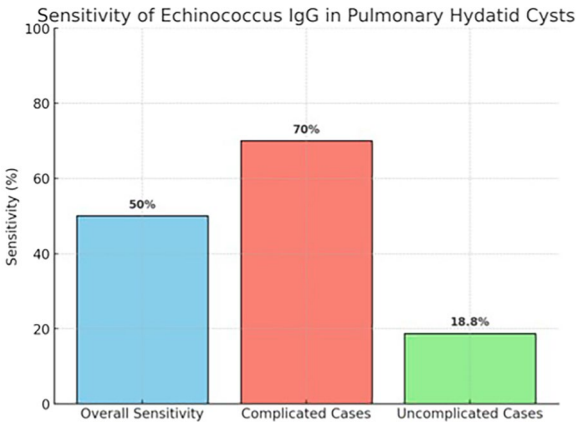

Fig. 4 Sensitivity of echinococcus IgG in diagnosing CE

[14]. This discrepancy may be attributed to the anatomical and immunological differences between the liver and lungs, with the liver often having a higher antigen load and greater immune accessibility. This highlights the anatomical differences in immune response to hydatid cysts and the need for tailored diagnostic approaches based on cyst location, diameter, age does not affect the positivity of Echinococcus IgG. In our study no statistical significance was noted for age, diameter and cyst location in comparison with ELISA IgG positivity. Age can also affect the serodiagnostic reactivity. In particular, children aged 3–15 years may exhibit minimal antibody response [15]. Complications significantly enhance the sensitivity of serological tests, with 70% sensitivity in complicated cysts. This observation aligns with studies [16] where the sensitivity of ELISA was reported to be higher in patients with ruptured cysts or secondary infections, suggesting that complications lead to increased antigen exposure. Conversely, patients with intact cysts exhibited a poor serological response, a finding also reported in multiple studies [17]. It highlights the value of serological testing as a supportive tool in these instances, though not as a standalone diagnostic method. Compared to indirect hem agglutination assays (IHA), which are also widely used, ELISA is generally more sensitive but still falls short when cysts are intact or localised in the lungs [18]. In resource-limited settings where access to advanced imaging is restricted, ELISA provides a more accessible and less invasive option, but its limitations suggest that it should be used in conjunction with other methods rather than as a standalone diagnostic tool. In our cohort, common symptoms included cough (76.3%), fever (31.2%), and chest pain (29.0%), which are typical presentations for pulmonary hydatid cysts. This mirrors findings from other studies [19] where cough and chest pain were reported in 70% of cases. However, our study noted a significant number of asymptomatic cases, highlighting the need for imaging studies in endemic areas to detect incidental findings, a point echoed in other literature [20] as serological test may not always pick up on early stage or uncomplicated cysts, particularly in asymptomatic individuals.

Conclusion

In conclusion this study contributes valuable data regarding the diagnostic limitations of serological tests for CE, and highlights the challenges posed by cyst location, complications, and the variable sensitivity of diagnostic approaches. The comparative analysis underscores the necessity of a multimodal diagnostic strategy, combining serological tests with imaging and clinical studies, to improve the detection and management of CE in endemic regions considering the limitations of this retrospective study. Future research could focus on integrating newer diagnostic technologies like PCR-based tests, which have demonstrated higher sensitivity and specificity by detecting Echinococcus DNA. Additionally, exploring immunological biomarkers that could provide earlier detection of cyst rupture or antigen leakage might further enhance serological diagnostic approaches. Expanding research into these areas could significantly improve the early diagnosis of CE, particularly in endemic regions.

Age Group	Total Patients	ELISA Sensitivity (%)
10–30 years	215	65
31–50 years	90	50
51+ years	81	40

Fig. 5 Age group vs ELISA IgG sensitivity

Author contributions
FC: Participated substantially in conception, design, and execution of the study; also participated substantially in the drafting and editing of the manuscript. ET: Participated substantially in conception, design, and execution of the study; also participated substantially in the drafting and editing of the manuscript. AT: Participated substantially in conception, design, and execution of the study; also participated substantially in the drafting and editing of the manuscript. AM: Participated substantially in conception, design, and execution of the study; also participated substantially in the drafting and editing of the manuscript. VG: Participated substantially in conception, design, and execution of the study. IS: Participated substantially in conception, design, and execution of the study. ST: Participated substantially in conception, design, and execution of the study. SB: Participated substantially in conception, design, and execution of the study. ON: Participated substantially in conception, design, and execution of the study. FR: Participated substantially in conception, design, and execution of the study. All authors have read and approved the submission of the final manuscript.

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Availability of data and materials
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Ethical approval was requested and obtained from the Ethical Committee of University Hospital "Shefqet Ndroqi" of Tirana.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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