



ORIGINAL ARTICLE

Echinococcosis: A 15-year epidemiological, clinical and outcome overview



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KEYWORDS

Hydatidosis;
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Abstract

Objective: To analyze the epidemiological and clinical characteristics and mortality of patients with cystic echinococcosis (CE) in northern Spain.

Patients and methods: A retrospective study of the medical records of patients diagnosed with CE and hospitalized from 1997 to 2011 in a University Hospital.

Results: A total of 76 patients (44 men) were diagnosed with CE. The mean age was 57.8 years (SD: 19.1 years; range: 14.9–92.7). The yearly average incidence was 1.08 cases/100,000 inhabitants. The highest incidence was registered in patients aged 70–79 years (22.7% of all cases). Liver was the main organ involved (92.1%), followed by lung (6.6%) and peritoneum (1.3%). Fifty-five patients (72%) received treatment: 2 (3.6%) medical treatment with albendazole, 27 (49%) surgical treatment, 3 (5.4%) medical treatment combined with cyst drainage, and 23 (42%) combined medical and surgical treatment. Eight patients had a recurrence. Twenty-four (31.2%) patients died. No patient's death was attributed directly to hydatidosis, though mortality was significantly higher in the untreated vs. the treated patient group (57% vs. 22%, $p=0.003$).

Conclusions: Hydatidosis treatment and diagnostic approaches remain heterogeneous. The liver continues being the main organ affected. Mortality was higher in patients who did not receive treatment. However, this result might have been influenced by other factors, mainly age.

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PALABRAS CLAVE

Hidatidosis;
Equinococosis;

Equinococosis: epidemiología, clínica y resultados en una panorámica de 15 años

Resumen

Objetivos: Analizar las características epidemiológicas y clínicas y la mortalidad de los pacientes con equinococosis quística (EQ) en el norte de España.

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Enfermedades
zoonóticas
parasitarias

Pacientes y métodos: Estudio retrospectivo de las historias clínicas de los pacientes diagnosticados de EQ, ingresados entre los años 1997 y 2011 en un Hospital Universitario.

Resultados: Se diagnosticaron de hidatidosis un total de 76 pacientes (44 varones). La media de edad fue de 57,8 años (DE: 19,1 años; rango: 14,9–92,7). El promedio de incidencia anual fue de 1,08 casos/100.000 habitantes. La incidencia más alta se registró entre los pacientes con una edad comprendida entre 70 y 79 años (22,7% de los casos). El hígado fue el principal órgano afectado (92,1%), seguido del pulmón (6,6%) y el peritoneo (1,3%). Recibieron tratamiento 55 pacientes (72%): 2 (3,6%) tratamiento médico (albendazol), 27 (49%) tratamiento quirúrgico, 3 (5,4%) tratamiento médico combinado con drenaje del quiste y 23 (42%) tratamiento médico y quirúrgico combinados. Presentaron recurrencias 8 pacientes, y fallecieron 24 (31,2%). Ninguno de los pacientes falleció por una causa atribuible a hidatidosis, aunque la mortalidad fue significativamente mayor en el grupo de los no tratados respecto al de los tratados (57% vs. 22%, $p=0,003$).

Conclusiones: La aproximación diagnóstica y terapéutica de la hidatidosis continúa siendo heterogénea. El hígado sigue siendo el principal órgano afectado. La mortalidad fue mayor en los pacientes que no recibieron tratamiento, si bien este resultado puede estar influido por otros factores, principalmente la edad.

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Introduction

Hydatidosis or cystic echinococcosis (CE) is a parasitic zoonosis caused by *Echinococcus*, whose larval stages infect various carnivores that act as definitive hosts for the parasite.¹ *Echinococcus granulosus* is the main cause of human hydatid infections.² It has a life cycle that involves dogs, sheep and sometimes other animals,^{2–5} in which the eggs of the parasite are excreted in their feces and later ingested by humans.⁶

CE has a worldwide distribution, with greater prevalence in temperate zones.^{2,7–9} In Spain, the autonomous regions of Castilla y León, La Rioja, Navarra, Aragón, and the Mediterranean coast are the areas where it is most commonly diagnosed.^{2,10} Risk factors proposed for CE acquisition include low socioeconomic level, residing in rural areas and contact with dogs, which are in turn in contact with livestock or offal of other carnivores.^{6,11}

Clinical signs and symptoms of EC may be related to the mass effect of the cyst, its superinfection or hypersensitivity reaction secondary to its rupture.^{12,13} Because of its slow growth, diagnosis is usually made in adulthood¹¹ by combining clinical symptoms with imaging tests and serological techniques.¹ Ultrasound is a key diagnostic tool due to its accessibility and safety. The World Health Organization (WHO) has proposed a classification based on ultrasound images of the cyst for diagnosis, prognosis and treatment of CE.¹⁴ Serology, which has good sensitivity but more limited specificity, provides good results in combination with imaging techniques.^{1,15} There is no universal consensus on the management of CE. Treatment is based on three pillars: medical treatment (mainly albendazole), surgery, and percutaneous drainage. The choice of the most appropriate approach is based on the patient's clinical symptoms and the characteristics of the cysts.¹

The aim of this study was to describe the epidemiological and clinical characteristics of CE diagnosed in the twenty-first century in Cantabria, an autonomous region of northern Spain, as well as to compare the outcome of patients according to whether they received treatment or not.

Materials and methods

From January 1, 1997 to December 31, 2011, the medical records of all patients diagnosed with CE during their admission to the Hospital Universitario Marqués de Valdecilla (a tertiary, 1000-bed teaching hospital, and the reference center for infectious diseases of the Region of Cantabria) were reviewed.

The following variables were collected: age, gender, nationality, address, occupation, reason for hospitalization, assigned ward and disease history, temperature, heart rate, blood pressure, symptoms and organs involved, hemoglobin levels, white blood cell count and platelet count, serum creatinine, urea, serum levels of sodium, potassium and glucose, serology and cultures, radiological examinations, type of treatment, duration of hospitalization and outcome. Follow-up time of patients after discharge was at least 1 year. Presence or absence of recurrence, complications and mortality were recorded. Recurrence was defined as readmission of the patient to the hospital for persistence or exacerbation of clinical symptoms of CE, provided that the first episode had occurred within the study period. Incidence of disease was calculated according to inhabitants served by the Hospital Universitario Marqués de Valdecilla.

Patient diagnoses were classified into the 3 categories proposed by WHO¹: (a) possible case: any patient with a compatible clinical or epidemiological history, and image findings or serology positive for CE; (b) probable case: any patient with a compatible clinical and epidemiological

history, and imaging findings and two positive serological tests, and (c) confirmed case: in addition to the above, confirmation by microscopy or molecular biology techniques of the presence of the parasite or its components in surgical or percutaneous samples, or changes in WHO staging of the cyst,¹⁴ either spontaneously or after treatment.

Statistical analysis

All data were included in the SPSS statistical software package (Statistical Package for Social Sciences, Chicago, IL, USA) for later processing. Quantitative data were expressed as mean \pm standard deviation (SD) or absolute value (percentage). Student's *t*-test or the Mann-Whitney *U* test were used to detect differences between two groups of quantitative variables, and the chi-square (χ^2) test was used to compare qualitative variables. A logistic regression analysis was performed, considering "death" as the dependent variable and including the variables showing statistical significance between the two groups (treated vs. untreated) in the univariate analysis.

Results

A total of 76 cases of hydatidosis (58% men) were diagnosed during the study period. The characteristics of these patients are summarized in Table 1. Their mean age was 57.8 years (SD: 19.1 years; range: 14.9–92.7), and was slightly higher in women (57.4 vs. 58.4 years, $p=0.834$). The majority of diagnoses of CE were made in 2005, in which 8 cases (10.5%) were recorded. The yearly average incidence was 1.08 cases/100,000 inhabitants. Sixty-two cases (80%) were from the province of Cantabria, 5 (6%) from the rest of Spain, and 3 (4%) belonged to other nationalities. In 6 (8%) patients the origin was unknown. Within Cantabria, 29 patients (46%) were from rural areas and 33 from urban areas (54%). Hydatidosis was a casual finding in 43 patients (56%) during an imaging or surgical examination for another reason, whereas 27 patients (35.5%) presented abdominal pain as the initial symptom. Of the 76 cases of CE, 50 (65.8%) were classified as confirmed, 1 (1.3%) as probable, and 25 (32.9%) as possible.

The liver was the primary location of hydatidosis in 71 patients (94%), and the lung in five cases (6%). In 70 patients (92%) involvement was only present at the primary location. In six patients, infection had spread to other sites: in three to the lungs (4%), in two to the peritoneum (3%) and in one case to both the lungs and the vertebrae (1%). Cysts were calcified in 24 patients (31.6%).

An imaging test was performed in 74 patients (95%): ultrasound was obtained in 61 patients (80%), and computed tomography (CT) scans in 56 (74%). In 39 patients, both examinations were performed, and lesions which were undetected by ultrasonography were observed with CT in 5 patients (13%). Serology was performed in 30 patients (39%), of which 13 (43%) had a positive result. Among patients with negative serology, 13 (76%) had liver cysts and 1 (6%) had lung cysts. In 3 patients (18%) cysts were present in multiple organs.

Table 1 Characteristics of the study population.

	N=76
Age (years, SD)	57.8 (19.1)
Gender (male (%))	44 (58%)
<i>Population</i>	
Urban Cantabria	33 (44.5%)
Rural Cantabria	28 (37%)
Other places in Spain	5 (6.5%)
Foreigners	3 (4%)
Unknown	6 (8%)
<i>Clinical symptoms, n (%)</i>	
Asymptomatic	43 (56%)
Abdominal pain	27 (36%)
Fever	1 (1%)
Other	5 (7%)
<i>Location, n (%)</i>	
Liver	71 (93.4%)
Lung	5 (6.6%)
<i>Calcified cysts, n (%)</i>	
Calcified cysts, n (%)	24 (31.6%)
<i>Positive serology, n (%)</i>	
Positive serology, n (%)	13 (17.1%)
<i>Diagnosis, n (%)</i>	
Possible	25 (32.9%)
Probable	1 (1.3%)
Confirmed	50 (65.8%)
<i>Treatment, n (%)</i>	
Only medical	2 (2.6%)
Only surgical	27 (35.5%)
Medical + surgical	23 (30.3%)
Medical + drainage	3 (3.9%)
None	21 (27.6%)
<i>Recurrence, n (%)</i>	
Recurrence, n (%)	8 (10.5%)
<i>Deaths, n (%)</i>	
Deaths, n (%)	24 (31.2%)
<i>Cause of death, n (%)</i>	
Hydatidosis	0 (0%)
Pneumonia	3 (3.9%)
Neoplasm	6 (7.8%)
Other	5 (6.5%)
Unknown	10 (13%)

Treatment

Fifty-five patients (72%) received some form of treatment for CE. Of these, 2 (3.6%) patients received only medical treatment; 27 (49%) only surgical treatment; 3 (5.4%) medical treatment combined with cyst drainage; and 23 (42%) combined medical and surgical treatment. Medical treatment involved the use of albendazole, whereas the surgical technique used in all cases was pericystectomy. Of patients who underwent surgery treatment, 8 (13%) had surgical complications: 3 (5.4%) developed abscesses, 3 (5.4%) surgical site infections, 1 (1%) obstruction due to peritoneal adhesions and 1 (1%) hemorrhage.

Among the 21 (28%) patients who did not receive any treatment, 16 (76%) did not have clinical symptoms at the time of diagnosis, and 5 (24%) had comorbidities that contraindicated medical or surgical treatment. There were no

Table 2 Characteristics of patients with hydatidosis according to whether they received specific treatment or not.

	Treatment <i>n</i> = 55	No treatment <i>n</i> = 21	<i>p</i> value
Age (years, SD)	51 (17)	76 (11)	<0.0001
Sex (male [%])	29 (53%)	15 (71%)	0.140
Prior hydatidosis, <i>n</i> (%)	5 (9%)	1 (5%)	1.000
Asymptomatic patients, <i>n</i> (%)	32 (58%)	5 (24%)	0.007
Liver cysts, <i>n</i> (%)	51 (93%)	20 (95%)	0.576
Calcified cysts, <i>n</i> (%)	9 (16%)	15 (71%)	<0.0001
Positive serology, <i>n</i> (%)	11 (50%)	2 (25%)	0.496
Confirmed diagnosis, <i>n</i> (%)	49 (89%)	1 (5%)	<0.0001
Recurrence, <i>n</i> (%)	8 (15%)	0 (0%)	0.09
Death, <i>n</i> (%)	12 (22%)	12 (57%)	0.003

differences in age, gender, degree of diagnostic confirmation and calcification between both groups.

There were 8 (11.8%) cases of recurrence. Of these, 6 (75%) patients had received medical and surgical treatment, whereas 1 (12.5%) had received only surgical treatment, and another (12.5%) combined medical and surgical treatment.

Outcome

During the 15-year-period covered by the study, 24 (31.2%) patients with CE died, with a mean age of 69 years (SD: 15.3; range: 25–87 years). Those patients had been older than those still living (53 years; SD: 18.6; range: 15–92 years) ($p < 0.0001$). Average survival after diagnosis of those patients who died was 6.4 years (SD: 10.8; range: 1.5–56 years). The main known causes of death were neoplasms in 6 (25%) patients and pneumonia in 3 (12.5%). In 10 of the 24 patients who died (42%), the cause of death was not determined. Hydatidosis could not be established as the cause of death in any case.

Mortality was significantly higher in the untreated vs. the treated patient group (57% vs. 22%, $p = 0.003$). Treated patients were significantly younger (51 vs. 76 years, $p < 0.001$) and with a higher percentage of symptomatic cases (58% vs. 24%, $p = 0.007$). There was also a predominance of men (71% vs. 53%, $p = 0.140$) (Table 2). Of the patients who received treatment, 9 (16%) had calcified cysts, a characteristic that was also observed in 15 (71.4%) of the patients who did not receive treatment ($p < 0.0001$).

Absence of hydatidosis treatment was correlated to mortality in the non-adjusted analysis, as well as other characteristics such as the presence of calcified cysts and recurrence of disease (Table 3). All were more frequent in older patients. After adjustment by age, gender, recurrence,

Table 3 Factors associated with mortality.

Variable	OR (CI)	<i>p</i> value
Age	1.06 (1.02–1.10)	0.002
Male gender	2.25 (0.80–6.33)	0.125
Symptomatic patients	0.51 (0.19–1.38)	0.188
Confirmed diagnosis	0.28 (0.10–0.78)	0.015
Calcified cysts	3.33 (1.20–9.31)	0.022
Recurrence	0.70 (0.13–3.74)	0.637
Hydatidosis treatment	0.21 (0.07–0.61)	0.004

OR: odds ratio; CI: confidence interval.

degree of diagnostic confirmation and calcification, the differences were not significant (OR: 0.83; CI: 0.09–7.50; $p = 0.867$).

Discussion

During a 15-year-period, 76 patients diagnosed with CE were recorded in a university hospital. Patients were predominantly male and had a mean age of almost 58 years. When these results were compared with other studies, it was found that distribution by gender varied widely in the different publications. Thus, two studies conducted in other Spanish regions showed similar proportions to ours, and mean ages also agreed.^{12,16} However, other series found no differences by gender,^{10,17} or even a trend to a higher proportion of women, as occurs in a study conducted in Yemen,¹⁸ where the patients were also much younger. These authors point out that the variation in distribution by gender found in the different publications may have been influenced by social and cultural factors as the person usually in charge of the animals transmitting the disease was obviously more exposed.

Most of the patients studied were from Spain, with anecdotal cases of hydatidosis in foreign patients, unlike other Spanish publications where the number of foreigners is much larger.¹⁶ It is striking that there were more patients from urban than rural areas, contrary to what is suggested by the epidemiology of the disease^{6,11} and other studies published in Spain.¹² However, this was also reported in a study published in Romania,¹⁷ where the distribution of the disease was slightly higher in the urban area, despite a much higher incidence rate of the disease in the rural area (5.1 vs. 2.5/100,000 inhabitants).

More than half of the diagnosed cases of hydatidosis were made coincidentally in the context of imaging or surgical examinations done for other reasons, as in the study by Pardo et al.¹⁰ Less than half of the patients had clinical symptoms, the most common being abdominal pain, one of the most characteristic symptoms.^{12,16}

The main diagnostic tool of CE was imaging testing, as confirmed in other studies.¹⁶ Ultrasound was the most commonly used technique, though it sometimes failed to detect lesions visible on CT. Nearly all patients had cysts at a single location, the liver being the most frequently affected organ. Both characteristics are consistent with published studies.^{1,2,10,12,16–18} Cysts were calcified in a third of our patients, suggesting they were inactive.

A third of patients received no treatment and in those who did (72%), treatment was mainly surgical, alone or in

combination with medical treatment (49% and 42% of total treatments initiated, respectively). These figures are higher than those published in other studies, which in many cases do not reach two thirds of patients who received surgical treatment.^{12,16} In our case, the main reasons for not initiating treatment were the absence of clinical symptoms or excessive comorbidity. This difference is shown when the treated and untreated patient groups are compared, as the latter had a significantly older mean age and a higher proportion of asymptomatic patients.

During the 15-year study period, 31.2% of the patients diagnosed with hydatidosis died. Mean age was significantly higher in those who did. The primary causes of death were neoplasms and pneumonia. In nearly a third of patients, the reason for death was unknown, and in none of the cases was the cause of death attributed to hydatidosis. This is probably why our mortality rate is higher than in other studies, where no deaths¹⁷ or very few¹² were recorded. A recent study has reported a considerable mortality, but it is very low in comparison to our results.¹⁹ These differences may be related to total observation time for each study. Our study included mortality for any cause and over a very long follow-up period, while in the other studies the observation period was limited to the time of diagnosis and the postoperative period. However, although mortality in our patients was significantly higher in the untreated patient group, the logistic regression study indicated that this result might have been influenced by other factors, primarily age. That seems also to be the explanation for why some factors, such as the presence of calcified cysts or recurrences, theoretically linked with a better prognosis, were related to death. These characteristics were more frequent in older patients, and we were evaluating mortality for any cause.

This study has several limitations. First, its retrospective nature. Secondly, all our patients were admitted to the same hospital; this could be a selection bias because our series may not represent the situation of all patients with hydatidosis which prevents establishing the actual incidence of the disease. However, ours represents one of the largest series analyzing the epidemiological, clinical and outcome during this century.

In summary, echinococcosis, a disease of mandatory declaration in our country, still represents a high economic burden. Our study reveals that surgery is the most used treatment. The mortality of patients in our series was high, but not directly related to hydatidosis. There were fewer deaths in treated patients, though their younger age should be taken into account. Our results suggest the need to design current multicenter prospective studies to determine the actual risk of hydatidosis in developed countries and establish definite indications of treatment.

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