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ORIGINAL PAPER

Health-related quality of life in patients with alveolar echinococcosis: a cross-sectional study

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Abstract

Purpose The Alveolar echinococcosis (AE) is a rare zoonosis caused by the parasite *Echinococcus multilocularis*. To date, nothing is known about the health-related quality of life (HRQoL) in patients with AE. The aim of the study was to evaluate the HRQoL in patients with AE in comparison of the healthy population.

Methods We used the 36-Item Short Form Health Survey (SF-36) questionnaire to evaluate the HRQoL. The SF-36 scales have a range of 0–100 (0 represents the worst and 100 the most favourable state of health). SAS Version 9.2 was used for the statistical analysis of AE-cases ($n=30$) and the healthy control group ($n=35$).

Results The analysis showed that the HRQoL in people with AE is reduced in comparison with the control population. The study group consisted of 15 (50.0%) men and 15 (50.0%) women; the control group of 16 (45.7%) men and 19 (54.3%) women. The mean age was 55.73 ± 16.65 years, while that of the control group was 54.57 ± 15.34 years. The physical quality of life in patients with AE (45.21 ± 11.42) was not significantly less than that of the control group (50.54 ± 10.52); $p=0.0568$. Nevertheless, AE-patients show lower SF-36 scores for the physical quality of life. For the mental quality of life, patients with AE had a significantly lower score (45.46 ± 10.57) than the control group (51.57 ± 9.04); $p=0.0154$.

Conclusions The HRQoL in people with AE is reduced in comparison with a control population. Assessment of the physical and mental quality of life in patients with AE may help to evaluate the patient outcome.

Keywords Alveolar echinococcosis · *Echinococcus multilocularis* · Health-related quality of life · Healthy control group · SF-36 questionnaire

Introduction

Alveolar echinococcosis (AE) is a rare, but dangerous zoonosis is caused by *Echinococcus multilocularis*. The parasite is found predominantly in temperate to cold latitudes of the northern hemisphere [1, 2]. In Europe, *E. multilocularis* is now spreading beyond the main endemic area of southern Germany, eastern France, northern Switzerland, and western Austria [1–3]. Apart from central Europe, China (especially the Tibetan plateau) and Mongolia, northern Japan, Russia (especially Siberia), parts of Turkey and parts of Canada and Alaska all have a high burden of human disease [2, 4, 5]. The largest number of cases have been reported from China [6–10]. Human disease in Germany is found predominantly in the main endemic areas of Baden-Württemberg and Bavaria [11]. The adult form of *E. multilocularis* lives in the intestines of foxes or other canids, which are the definitive hosts in the life cycle of the parasite. In southern Germany, 75% of the red foxes in parts of Baden-Württemberg carry *E. multilocularis* [3]. Small rodents as intermediate hosts and are infected by faecal–oral transmission [12, 13]. Humans are accidental intermediate hosts. In more than 98% of cases, the disease primarily affects the liver [14]. The larval tissue grows and infiltrates the tissues, leading to space-occupying lesions of malignant character [12, 13]. The most important risk factors include dog and cat ownership, having a kitchen

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garden, handling foxes, the occupation (farmer), gender, age (over 20 years) and ethnic groups (e.g., Tibetan) [3, 15–19]. For some time now, alveolar echinococcosis has been a recognised occupational disease of agricultural workers in Germany. The incubation period of AE is still not known precisely but is estimated to be between 5 and 15 years [12].

Treatment of alveolar echinococcosis

The non-specific or complete lack of symptoms means that AE is often diagnosed late or discovered as an incidental finding during a screening procedure [3, 20–22]. The malignant behaviour and progression of the disease means that, as a rule, there is always an indication for treatment [23]. About two-thirds of patients are diagnosed with local disease at a stage that is primarily inoperable. Pharmacotherapy consists of benzimidazoles (BMZ), usually albendazole (ABZ) and less often mebendazole (MBZ) [23, 24]. The introduction of benzimidazole therapy in 1976 considerably improved the prognosis [23, 24]. Benzimidazole therapy is indicated in all patients and must be continued life-long, as its effects are only parasitostatic. Not infrequently, there are problems and complaints related to taking the medication. If there is a good response to treatment with benzimidazoles, the patient's life expectancy increase [25].

Time and again during initial treatment and follow-up, patients complain about the burdensome aspects of medication, as well as about echinococcosis-associated problems and mental stress. The assessment of the health situation is gaining in importance especially in chronic diseases as well as neglected tropical diseases (NTDs), which also includes alveolar echinococcosis. Health metrics such as Disability-Adjusted Life Year (DALY) and Quality-Adjusted Life Year (QALY) are worldwide recognised techniques which are used consistently to assess the situation of helminthic diseases and especially of echinococcosis [4, 26]. In particular, DALY was evaluated for echinococcosis as part of the Global Burden of Diseases 2010 Project. These health metrics are commonly used in cost-benefit analysis in national and global health policy discussions on the allocation of health resources [26, 27]. However, these methods and techniques show limitations [26, 27]. A limitation and weakness of these procedures is that they do not reflect the individual situation of the patient. The measurement of quality of life is a suitable tool to evaluate the individual situation and to initiate possible preventive measures.

To date, nothing is known about the health-related quality of life (HRQoL) in patients with AE. Pertinent questions have still to be answered and evaluated. It is well known, however, that rare diseases may also considerably reduce both the physical and the mental quality of life of those affected in comparison with general population norms.

Health-related quality of life

Even though it is often difficult to give a precise definition, medical, health science and epidemiological research uses the term 'quality of life (QoL)' as a multidimensional subjective construct of social, physical, and mental components, including both positive and negative aspects of individual perception. In 1949, the World Health Organization (WHO) described quality of life as the physical, mental, and social condition of the individual based on the definition of health [28–30]. WHO later recognised quality of life as a major target of health promotion in the Bangkok Charter for health promotion in a globalized world revised in 2005 [31].

The original focus in medicine was to measure the epidemiological relevance of a disease to a population by determining mortality, but this approach has altered greatly in recent years. Demographic shifts, increasing life expectancy, and improved treatment outcomes create more chronic diseases and thus determine the spectrum of morbidity. Quality of life as an indicator of health has become more relevant and will probably continue to play an increasingly important role. The medical origins of quality of life research can be traced back to oncology and palliative care [28, 29]. Its range of use has since become much wider, and many different general and disease-specific tools for measuring the quality of life have been developed in recent years. Quality of life research now has a key role in oncology, palliative care and allergology and is increasingly being used for population-specific studies in rehabilitation medicine, epidemiology, and public health [28, 29]. Quality of life is also being used more and more to evaluate the quality of different treatments, hospitals, and medical centres.

The aim of our study was therefore to investigate and evaluate whether the health-related quality of life in patients with alveolar echinococcosis differs from that of a normal healthy population with respect to both physical and mental aspects.

Methods

Inclusion and exclusion criteria

The study included patients with alveolar echinococcosis. Cases with insufficient data for the definition of AE according to the WHO Informal Working Group on Echinococcosis (WHO-IWGE) were also excluded. The case definition categorises an infection/disease as 'confirmed', 'probable' or 'possible', based on defined imaging features

and serology. All cases considered only 'possible' were excluded. A "possible" case definitions means that there is only positive serology or imaging. "Probable" case definition includes a positive serology and a positive imaging. And "confirmed" cases means that there is a histological confirmation of the diseases [32]. The study on health-related quality of life was conducted in the infectious disease outpatient department between June 2017 and February 2018, using the 36-Item Short Form Health Survey (SF-36).

SF-36 questionnaire

The health-related quality of life (HRQoL) was measured with the 36-Item Short Form Health Survey (SF-36). The SF-36 was developed by the Research and Development Corporation (RAND) as part of the Medical Outcome Study (MOS) [28, 29]. This non-disease-specific questionnaire has been validated internationally and is now used worldwide to determine the health-related quality of life in medical, health science and epidemiological research.

The SF-36 has a wide range of use, in both sick and healthy people over the age of 14 years. In North America, this non-disease-specific instrument is used frequently, not only in somatic medicine but also for people with mental health issues [28, 29]. Its fields of application in Germany range from oncology and palliative care to orthopaedics and rehabilitation research, finding a place in virtually all medical specialties.

The SF-36 questionnaire consists of 36 items that tap eight subjective health concepts and can be combined to give a physical and a mental summary score designating the physical and mental quality of life. Each of the eight SF-36 scales has a range of 0–100, where 0 represents the worst possible state of health and 100 the most favourable state of health [28, 29].

Following the scoring algorithms made available by the developers, the 36 questions of the SF-36 questionnaire provide overall physical and mental summary scores (Table 1).

Healthy control population

An age- and gender-specific control population of healthy subjects is available for the SF-36 questionnaire. The physical and mental component summary scores of the general population norms can be used as a control group. The developers of the SF-36 have described the corresponding scoring algorithm [29].

Statistical analysis

The validated statistics software SAS Version 9.2 was used for the analysis. The SF-36 scale scores were obtained according to the developers' algorithms [29]. The *t* test was used to compare the means. Analysis of variance (ANOVA) and multivariate analysis of variance (MANOVA) were used for the dependant variables. The null hypothesis (H_0) is the assumption that the patients with AE show no differences in quality of life from the healthy control population. The alternative hypothesis (H_1) assumes that the cases of AE show a difference in quality of life from the healthy control population. The level of significance was set at $\alpha = 0.05$. p values < 0.05 were considered to be statistically significant.

Results

The study population consisted of 30 patients ($n = 30$) with alveolar echinococcosis on treatment with surgery, benzimidazoles or during a break in therapy. Data for the health-related quality of life were recorded in the period from June 2017 to February 2018, using the SF-36 health questionnaire. The control group consisted of 35 healthy people ($n = 35$) from general population norms of the algorithms supplied by the developers (Fig. 1).

The study group consisted of 15 (50.00%) men and 15 (50.00%) women; the control group of 16 (45.71%) men and 19 (54.29%) women. The mean age of the patients was 55.73 ± 16.65 years, while that of the control group was

Table 1 SF-36 scales

Scale	Number of items	Questions	Quality of life
Physical functioning	10 items	Questions 3a–j	Physical quality of life
Role limitations due to physical health	4 items	Questions 4a–d	
Bodily pain	2 items	Questions 7, 8	
General health	5 items	Questions 1, 11a–d	
Emotional well-being	5 items	Questions 9b,c,d,f,h	Mental quality of life
Role limitations due to emotional problems	3 items	Questions 5a–c	
Social functioning	2 items	Questions 6, 10	
Energy/fatigue	4 items	Questions 9a,e,g,i	

The table shows the eight scales and their composition [29]

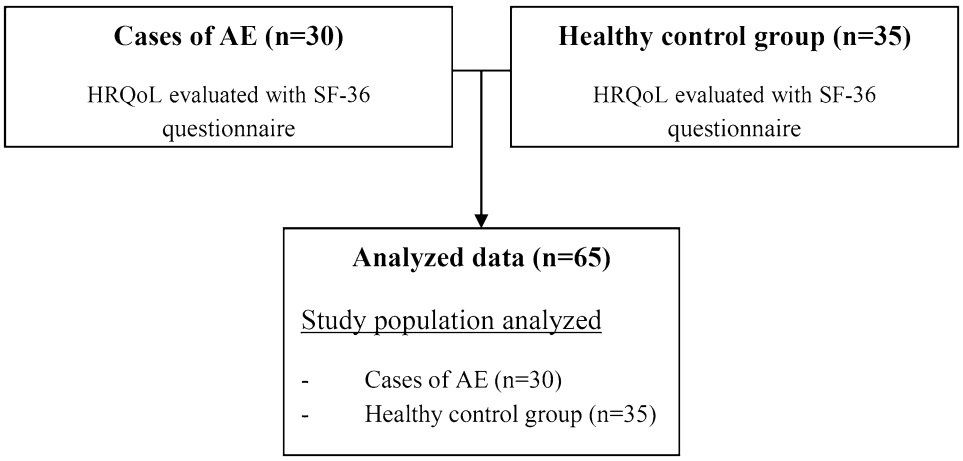

Fig. 1 Flow chart showing the included patients with alveolar echinococcosis and the control population screened with the SF-36 questionnaire (AE = alveolar echinococcosis)

54.57 ± 15.34 years (Table 2). At the time of analysis, 14 (46.67%) patients were younger than 55 years, 13 (43.33%) were aged between 55 and 75, and the other three (10.00%) were over-75 s. The mean body mass index (BMI) in the study group was 24.58 ± 3.74. The BMI was < 25 in 19 (63.33%) patients, between 25 and 30 in eight (26.67%) patients, and > 30 in three (10.00%) patients. At the time of the study, the mean duration of AE in the study group was 120 ± 117 months (range: 4–385 months). The average duration of disease was 110 months in the female patients, and 130 months in the male patients (Table 2).

Analysis of the SF-36 scales in accordance with the developers' algorithms gave the scores for the control and study groups shown in Table 3. Comparison of the means of the scale scores between the study group and the control group gave statistically significant differences for physical functioning, general health, energy/fatigue, social functioning, and role limitations due to emotional problems (Table 3; Fig. 2). There were no significant differences between patient and control groups for the scales of role limitations due to physical health, bodily pain, and emotional well-being ($p > 0.05$). The summary score of the physical quality of life comprises the scales of physical functioning, role limitations due to physical health, bodily pain and general health, while the mental quality of life summary score is obtained from the scales of energy/fatigue, social functioning, role limitations due to emotional problems, and emotional well-being (Tables 1, 3).

Overall, the physical quality of life in patients with alveolar echinococcosis (45.21 ± 11.42) was not significantly less than that of the control group (50.54 ± 10.52); $p = 0.0568$. For the mental quality of life, however, patients with AE had

Table 2 Characteristics of the study and control groups

n	Study group		Control group	
	n = 30	%	*n* = 35	%
Gender				
Male	15	50.00	16	45.71
Female	15	50.00	19	54.29
Age				
< 55 years	14	46.67	17	48.57
55–75 years	13	43.33	16	45.71
> 75 years	3	10.00	2	5.71
Body mass index (BMI)	24.58 ± 3.74			
BMI < 25	19	63.33		
BMI 25–30	8	26.67		
BMI > 30	3	10.00		
	M	SD	Min	Max
Duration of disease (in months)	120	117	4	385

M mean, *SD* standard deviation, *BMI* body mass index, *n* sample size

Table 3 Means and standard deviations of the SF-36 scales in the study and control populations

SF scale	Study population Mean ± SD	Control group Mean ± SD	*t*	*p* value
Physical functioning	74.50 ± 24.89	88.14 ± 21.42	2.38	0.0206*
Role limitations due to physical health	65.00 ± 42.85	81.42 ± 36.55	1.67	0.1002
Bodily pain	74.20 ± 28.37	79.82 ± 28.13	0.80	0.4262
General health	51.10 ± 21.37	70.21 ± 20.73	3.65	0.0005*
Energy/fatigue	49.16 ± 22.70	63.18 ± 22.13	2.50	0.0152*
Social functioning	72.91 ± 26.48	87.14 ± 24.90	2.23	0.0293*
Role limitations due to emotional problems	67.77 ± 40.57	93.33 ± 23.98	3.14	0.0026*
Emotional well-being	67.60 ± 17.89	74.51 ± 18.56	1.52	0.1330
Physical summary score	45.21 ± 11.42	50.54 ± 10.52	1.94	0.0568
Mental summary score	45.46 ± 10.57	51.57 ± 9.04	2.49	0.0154*

SD standard deviation

*Statistically significant with $p < 0.05$

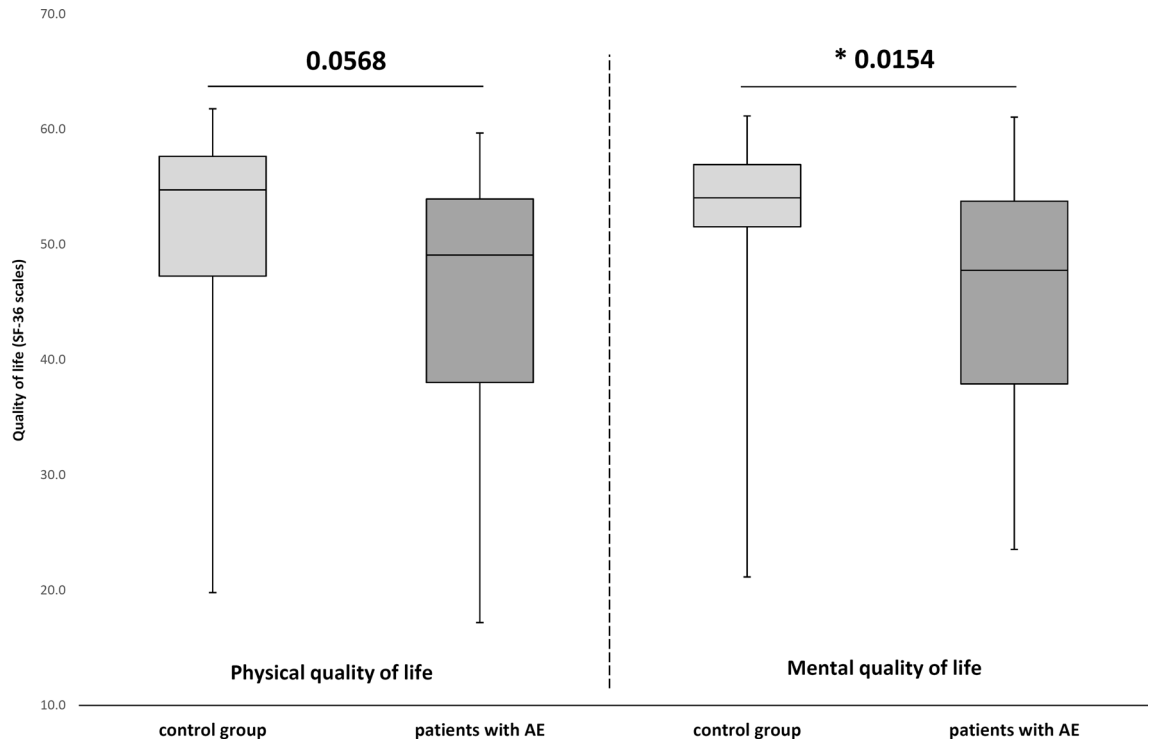

Fig. 2 Box plot of physical and mental summary scores for the study and control groups (*statistically significant with $p < 0.05$)

a significantly lower score (45.46 ± 10.57) than the control group (51.57 ± 9.04); $p = 0.0154$ (Table 3; Fig. 2). Figure 2 gives a graphical representation of the physical and mental quality of life in patients with AE and the control group, showing the location and scatter of the physical and mental summary score scales.

Multivariate analysis taking into consideration possible confounders such as gender ($p = 0.2541$), BMI ($p = 0.7525$), age ($p = 0.1398$) and duration of disease ($p = 0.9271$) showed no statistically significant differences and no influence of the variables on the physical quality of life ($F = 1.71$; $p = 0.1267$) (Table 4). With a probability of error of 5 percent, the multivariate model likewise did not show any significant effects of gender ($p = 0.3383$), BMI ($p = 0.3940$), age ($p = 0.2752$) or duration of disease ($p = 0.4925$) on the mental quality of life ($F = 1.22$; $p = 0.3095$) (Table 4).

Table 4 Results of analysis of variance and multivariate analysis of variance

Source	DF	Sum of squares	Mean square	*F*	Pr > *F*
Physical quality of life					
Model	7	1404.02	200.57	1.71	0.1267
Error	53	6217.18	117.30		
Corrected total	60	7621.21			
	Wilks' lambda	Numerator DF	Denominator DF	*F*	Pr > *F*
Age	0.95933418	1	53	2.25	0.1398
BMI	0.99810805	1	53	0.10	0.7525
Gender	0.97552958	1	53	1.33	0.2541
First diagnosis	0.99984046	1	53	0.01	0.9271
Age*BMI	0.97407298	1	53	1.41	0.2402
Age*BMI*gender	0.98007241	1	53	1.08	0.3039
Age*BMI*gender*first diagnosis	0.98593151	1	53	0.78	0.3884
Source	DF	Sum of squares	Mean square	*F*	Pr > *F*
Mental quality of life					
Model	7	864.75	123.53	1.22	0.3095
Error	53	5375.83	101.43		
Corrected total	60	6240.59			
	Wilks' lambda	Numerator DF	Denominator DF	*F*	Pr > *F*
Age	0.97757453	1	53	1.22	0.2752
BMI	0.98625851	1	53	0.74	0.3940
Gender	0.98268634	1	53	0.93	0.3383
First diagnosis	0.99106847	1	53	0.48	0.4925
Age*BMI	0.99940185	1	53	0.03	0.8593
Age*BMI*gender	0.97563608	1	53	1.32	0.2551
Age*BMI*gender*first diagnosis		1	53	1.09	0.3015

BMI body mass index, *F F* value, *Sig p* value, *DF* Degree of freedom
~statistically significant with $p < 0.05$

Discussion

The study presented here is the first to evaluate the health-related quality of life in people with alveolar echinococcosis and compare them with general population norms. Our results show that these patients have a reduced quality of life. In particular, there is a significant difference in the mental quality of life between patients with AE and a healthy population. Although no significant difference was found in the overall physical quality of life, scores were generally worse than in the controls. At present, there are no comparative studies on alveolar echinococcosis. However, it is well known from other rare or chronic diseases—including coronary artery disease, primary cutaneous amyloidosis, children with congenital heart disease, patients with post-kala-azar dermal leishmaniasis, and various types of cancer—that the quality of life in affected patients is considerably reduced [28, 29, 33–35]. The results of our study therefore seem plausible.

Physical summary score

The physical summary score did not show a significant difference between patients with AE and the general population norms. Since AE is seldom associated with signs and symptoms and is often diagnosed in the course of a screening examination, this result seems self-evident [12, 20–22]. The scales making up the physical summary score showed significant differences between the patients with AE and general population norms in physical functioning and general health, although there were no significant differences in bodily pain and role limitations due to physical health. Given the fact that patients rarely complain of symptoms, our results with respect to bodily pain seem plausible [12, 20–22]. Even so, we cannot rule out that appropriate therapy or the response to treatment explains the scores for bodily pain in these patients.

Mental summary score

The overall mental summary score showed a significant difference between the patients with AE and the general population norms. In the scales making up the mental summary score, the differences in energy/fatigue, social functioning, and role limitations due to emotional problems were significant, although there was no significant difference in emotional well-being. The psychological burden on patients with AE makes the reduced quality of life in the previously mentioned scales completely understandable. Many patients experience anxiety and panic related to the fox tape worm disease, which they did not feel before the diagnosis was made. Likewise, having to take benzimidazoles with fat-rich meals to improve absorption constitutes a restrictive and increasingly stressful factor. These factors may possibly explain the worse mental quality of life compared with general population norms. Patients also frequently report feelings of shame associated with their disease and the way in which they are stigmatised. Reduced social functioning, energy/fatigue, and participation associated with social withdrawal seem conceivable.

In the present study, we ruled out possible confounders of age, gender, BMI, and duration of disease, as well as their interactions and between-subject effects on the physical and mental quality of life. The outcome and estimation of the physical and mental quality of life in patients with AE allows us to make a patient-centred assessment of the individual health situation. Possible health-promoting somatic and preventative measures may help to improve the quality of life in patients with alveolar echinococcosis. The clearly reduced mental quality of life of these patients poses the question of possible psychotherapy. Patients with AE may benefit from appropriate psychotherapeutic guidance and care. A study on the impact of psychotherapeutic interventions on the quality of life in people with cancer showed that these patients benefitted from psychotherapeutic intervention, leading in turn to greater empowerment [36]. That study found a significantly better quality of life as well as improved emotional and social functioning [36]. Patients with rare or other chronic diseases also often initiate self-help groups. It has been shown that dialysis patients with end-stage kidney disease have a significantly better mental quality of life when they join self-help groups than controls who do not [37].

Finally, it should be noted that the SF-36 questionnaire for measuring the physical and mental quality of life is a suitable tool for evaluating the quality of life in patients with alveolar echinococcosis. Future research should aim to develop a disease-specific instrument for these patients.

Health metrics such as Disability-Adjusted Life Year (DALY) and Quality-Adjusted Life Year (QALY) are techniques which are used consistently to assess the healthy situation. These health metrics are often used in cost-benefit analysis in national and global health policy discussions on the allocation of health resources but cannot be used to evaluate the individual situation of patients [26, 27]. But the measurement of health-related quality of life provides an opportunity to evaluate the individual patient situation [26, 27]. However, each of these health metrics has its strengths and weaknesses and should be used and applied in the appropriate country-specific context, depending on needs, issues and levels of development.

The small sample size of patients with AE must be regarded as one of the limitations of the present study. Even so, our study provides an important preliminary outline of the situation regarding patients with alveolar echinococcosis. As a further limitation, it should be noted that there was no information available for the use of antidepressants in the studies and control group. We did not, however, look at socioeconomic or family-related factors. These possible confounders must be included in future research work. To date, the quality of life related to different forms of treatment (pharmacotherapy vs surgical treatment) has not been evaluated and should also be a key aspect of further research.

Conclusions

The results of the present study are the first to show that the health-related quality of life in people with alveolar echinococcosis is reduced in comparison with a control population. There is a reduced HRQoL in both physical and mental summary scores. Assessment of the physical and mental quality of life in patients with alveolar echinococcosis may help to evaluate the outcome. Changes in the physical or mental quality of life during treatment can be detected promptly. Personalised health-promoting or preventative measures and coping strategies can then be introduced swiftly to improve the individual patient's state of health. Large-scale studies are now required to evaluate the health-related quality of life with respect to the various forms of therapy and response to treatment in patients with alveolar echinococcosis.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical approval The study was approved by the local Ethics Committee approval and the Declaration of Helsinki (ref. No. 63/18).

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