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**Human Echinococcosis in Armenia: an Old and Neglected Challenge**

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**Introduction**

Human echinococcosis is a parasitic disease caused by the larval stages of cestodes belonging to the genus *Echinococcus*. The World Health Organization (WHO) classifies echinococcosis as one of 20 neglected tropical diseases and includes *Echinococcus granulosus sensu lato* (*E. granulosus*) and *Echinococcus multilocularis* (*E. multilocularis*) among food-borne parasites with global public health importance. The two most common clinical types of echinococcosis, cystic echinococcosis (CE) and alveolar echinococcosis (AE), impose a significant health and financial burden, particularly in low-income countries [15]. *E. granulosus* is well known as a parasite of concern in domestic animals, while *E. multilocularis* is a wildlife parasite. The life-cycle of the echinococcosis parasites involves carnivores (canids or felids) as definitive hosts, which hold the adult egg-producing stage in the intestine, and intermediate host animals (herbivores, e.g., sheep, goats, cattle) in which the infective metacestode stage develops after peroral infection with eggs. Humans are accidental (aberrant) intermediate hosts and the dead-end of the life cycle. Except Antarctica continent, *E. granulosus* can be found all over the world (especially in certain rural settings). The causative agent of AE, *E. multilocularis*, is widely distributed in the northern hemisphere and central regions of Asia [3, 4, 15]. Human CE and AE are both chronic diseases: CE is a disabling disease with a low fatality rate, on the other hand, AE is often a life-threatening disease due to tumor-like progression. CE and AE do not cause symptoms in the early stages, and CE cysts and AE lesions can remain

asymptomatic for 10 to 15 years [15]. The most reliable diagnosis is generally obtained by parallel testing using diagnostic imaging methods (ultrasonography (US), computed tomography, and magnetic resonance imaging) and immunodiagnosis (ELISA-based serological tests). One of the most serious issues with human CE and AE is the frequent occurrence of relapses [3, 4, 15].

CE is common among ruminants and nearly the whole territory of Armenia is affected, however, the proportion of livestock species and infection rates vary by area. The most common mode of parasite transmission is the feeding of shepherd dogs with infected offal [8]. The Molecular Parasitology research group of the Scientific Center for Zoology and Hydroecology NAS RA investigated the epidemiological status of *Echinococcus spp.* in free-ranging dogs and wild animals in target regions of Armenia. The following parasite species were identified based on the results of egg DNA sequencing: in dogs, *E. multilocularis*; in lynx, *Echinococcus canadensis* [12]. The aim of this study was to analyze the epidemiological features, high-risk areas and mortality data of human echinococcosis in Armenia from 2014 to 2022.

## Material and Methods

A retrospective study was designed. The database at the National Center for Disease Control and Prevention (passive surveillance system) includes CE surgical cases from hospital discharge records. The database containing human CE and AE cases identified during active epidemiological observation was analyzed with a descriptive analysis, according to region, age, gender of patients and cyst localization. The annual incidence and mortality rates of CE and AE were calculated using population denominators given by the National Institute of Statistics. The Healthcare Information and Analysis Center of the National Institute of Health named after academician S. Avdalbekyan provided population-based mortality data for *Echinococcus spp.* Echinococcosis-related deaths are classified in the system using the International Classification of Diseases (ICD-10) codes: B67.0-B67.9. Cases were mapped using ArcGIS 10.7 software.

## Results and Discussion

Over the study period, 752 CE surgical cases were reported. CE surgical incidence increased between 2012 and 2019 (Fig. 1).

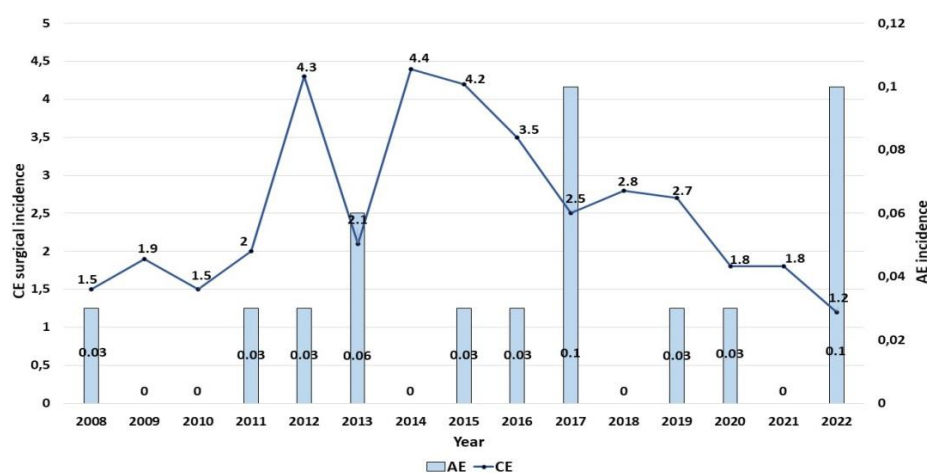


Fig. 1. Incidence of *Echinococcus spp.* per 100 000 population, Armenia 2008-2022

A majority of CE patients were females (55%), from rural communities (58%). Age ranged from 4 to 90 years, with a median of 37 years, mean age was  $38.8 \pm 18.6$  years. Higher annual incidence was observed among younger and older age groups (Fig. 2).

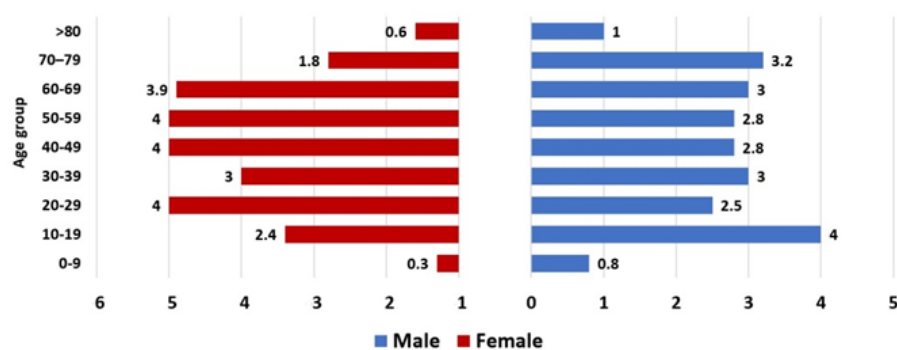


Fig. 2. Age- and sex-specific annual average incidence of *Echinococcus spp.* per 100 000 population, Armenia, 2014-2022

The highest average incidence was found in Aragatsotn, Ararat, Armavir, Gegharkunik regions (Fig. 3). Cysts were identified in the liver (81%), lungs (11%), unusual locations (6%) and involvement of two organs simultaneously (2%).

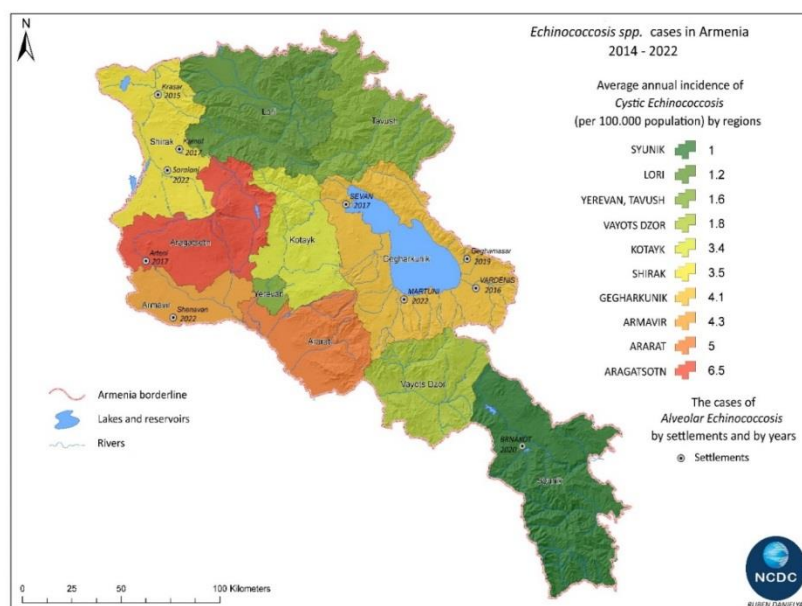


Fig. 3. Geographical distribution of CE average annual incidence per 100 000 population and AE cases, Armenia, 2014-2022

As for AE, 10 cases were identified. AE incidence per 100,000 population varied between 0.032 in 2008, and 0.1 in 2017 and 2022, the years with the highest AE annual incidence. Age ranged from 21 to 52 years with a median of 41 years, mean age was  $38 \pm 12$  years. Patients were mostly females (62.5%) and from Gegharkunik region ( $n=4$ , 50%). All patients had liver involvement.

During 2014-2022, 108 deaths of human echinococcosis were registered. After 2015 mortality rate of *Echinococcus spp.* in Armenia dropped considerably (Fig. 4).

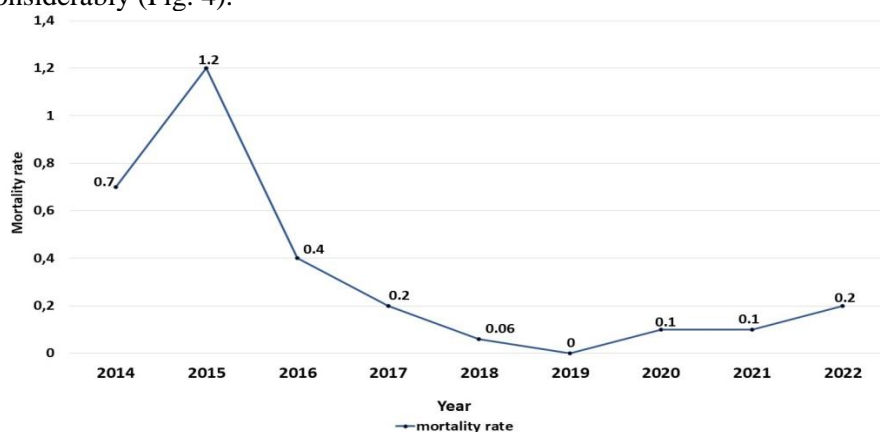


Fig. 4. Mortality rate of *Echinococcus spp.* per 100 000 population, Armenia, 2014-2022

More than half (55%) were female, and during the period 2014-2022, the male/female ratio of the deaths occurring was 0.83. Most deaths were registered among  $\geq 80$  age group (54%), following by 70-79 age group (20%) (Fig. 5).

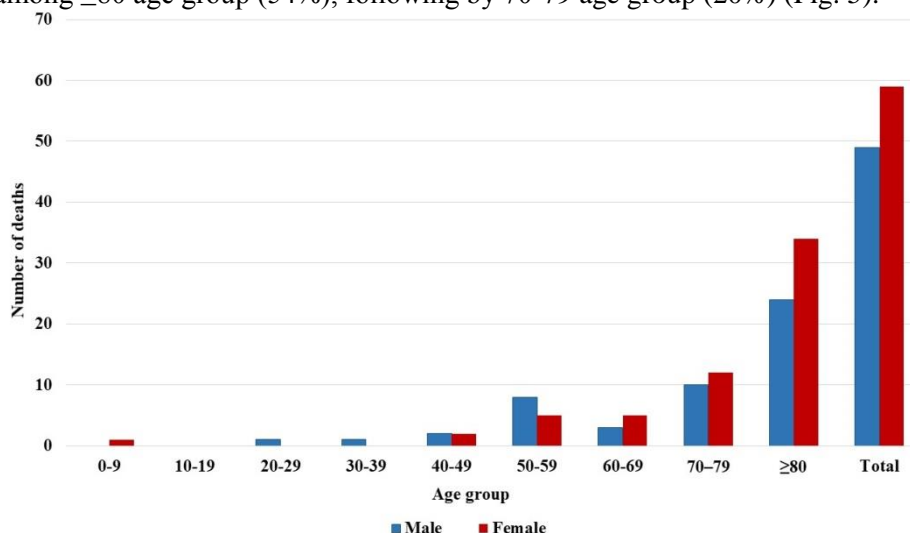


Fig. 5. Echinococcosis-related deaths by age group, Armenia, 2014-2022

The highest number of echinococcosis-related deaths was in Yerevan (44%), Ararat (17%) and Kotayk (13%) regions. The liver was the most often affected organ and 2 deaths were AE-related (Table).

Table

*Echinococcosis-related deaths by ICD-10 codes, Armenia, 2014-2022*

ICD-10	n
B67.0	43
B67.1	1
B67.2	1
B67.3	1
B67.5	2
B67.8	55
B67.9	5
<b>Total</b>	<b>108</b>

The current study shows the trend of *Echinococcus* spp. incidence in Armenia. In endemic areas, the annual CE incidence varies from 1 to 200 per 100,000 population [15]. The presence of *E. granulosus* tapeworm has been widely recorded throughout the Mediterranean basin, including France, Spain, Italy, Greece and all Middle Eastern countries. The annual average incidence of surgically treated CE cases was 2,7/100 000 population which is higher than in

Iran (0,74/100 000 population) and in Lebanon (1,23/100 000 population) [5, 10]. Kyrgyzstan remains one of the highly endemic foci of echinococcosis. From 2004 to 2015, the incidence rate increased from 9,2 to 19,2 per 100 000 population [1]. The highest annual surgical incidence of AE was in Kyrgyzstan (3,02/ 100 000 population) [14]. The surgical incidence of CE in Uzbekistan was 4,4 per 100,000 population in 2011 and 2,3 per 100 000 population in 2018 [7]. For the years 2017–2021, the incidence rate of CE in the Russian Federation ranged from 0,16 in 2020 to 0.33 per 100 000 population in 2018, and the incidence rate of AE in the Russian Federation was an average 0.03 per 100 000 population. During 2020–2021, there was a significant decrease in incidence rates of CE due to the limited availability of routine medical care to patients during the COVID-19 pandemic [2].

Echinococcosis mainly affected the female population, which is consistent with findings from other countries [2, 5, 10, 14]. Paediatric cases were also reported, indicating an active transmission of the parasite in the environment [13]. There is an increase in the incidence of echinococcosis among children, and recently severe forms and cases were recorded more frequently [1]. Regarding cyst localization, the results showed that the liver was the most frequently affected organ, followed by the lungs, which is similar to findings from other countries (Russia, Kyrgyzstan, Iran, Lebanon) [2, 10, 11, 14]. The annual average AE incidence in Europe is quite low, with 0.03 to <1 case per 100,000 population, with a few endemic areas reaching slightly more cases (France, southern Germany, Switzerland, western Austria). *E. multilocularis* is found across northern Asia, with China accounting for around 90% of all reported human AE cases [9].

During the 17-year period (1990-2007), 41 people died from echinococcosis in the United States [6]. According to this official data, the lethality among patients with AE in the Russian Federation ranges from 2.08 to 6.25% [2].

However, the true incidence and prevalence of the disease in humans and animals remain unknown, there is likely an underreporting of cases. Since CE is asymptomatic in up to 70% of patients, many cases were probably excluded from the database [5, 7]. Human echinococcosis is a neglected but essential public health problem in Armenia that requires an adaptation of the “One Health” approach into the national control program, which should improve disease surveillance system in the country and involve prevention and control measures for both human and animal sectors. Priority should be given to regular dog deworming, a strict policy for stray dogs, an improved slaughter surveillance system, strong veterinary control to avoid home slaughtering of sheep and other livestock, awareness campaigns among health care providers, health education and a systematic search for asymptomatic carriers through community-based screenings. It is required to address knowledge gaps and conduct research on various aspects of the disease, including identifying the key

sources of infection and habits that may raise the risk of exposure. An international classification of US images for CE and for AE a PNM classification system (P=parasitic mass in the liver, N=involvement of neighbouring organs, and M=metastasis) is not utilized in Armenia in order to classify each patient according to clinical status [4]. Echinococcosis should be considered in the differential diagnosis of a liver or lung cyst.

#### Conflict of Interest

The authors declare no conflict of interest. This research received no funding.

#### Ethical approval

Approval was not required.

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### **Эхинококкоз человека в Армении: старая и забытая проблема**

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Два наиболее распространенных клинических типа эхинококкоза – кистозный эхинококкоз (КЭ) и альвеолярный эхинококкоз, вызывают значительное медицинское и финансовое бремя. Целью данного исследования было проанализировать эпидемиологическую характеристику, зоны повышенного риска и данные о смертности от эхинококкоза человека в Армении за 2014-2022 годы. Среднегодовая хирургическая заболеваемость диагностированных случаев КЭ составила 2, 7/100 000 населения, что выше, чем в Иране (0, 74/100 000 населения) и Ливане (1, 23/100 000 населения). Зарегистрированные детские случаи свидетельствуют о широком распространении паразита в окружающей среде. Однако истинная распространенность заболеваемости у людей и животных остается неизвестной и, вероятно, имеются неполные сообщения о подтвержденных случаях. Эхинококкоз человека является забытой, но серьезной проблемой общественного здравоохранения в Армении, которая требует адаптации подхода к национальной программе «Единое здоровье» по профилактике и контролю эхинококкоза, включая соответствующие меры как для людей, так и для животных.

### **Մարդու էխինակոկոզը Հայաստանում. հին և մոռացված խնդիր**

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Էխինակոկոզի երկու ամենատարածված կլինիկական տեսակները՝ բշտային էխինակոկոզը (ԲԷ) և ալվեոլյար էխինակոկոզը, առաջացնում են զգալի առողջապահական և ֆինանսական բեռ: Այս հետազոտության նպատակն է անալիզ անել Հայաստանում 2014-2022 թվականներին օպերատիվորեն բացահայտված և բուժված քիստային էխինակոկոզի (ԿԷ) դեպքերի էպիդեմիոլոգիական, ռիսկային գոտիների և մահացության դրուժնականությանը:

տակն էր վերլուծել Հայաստանում մարդու էխինակոկոզի՝ 2014-2022 թվականների ընթացքում համաճարակաբանական առանձնահատկությունները, բարձր ռիսկային գոտիները և մահացության տվյալները: ԲԷ-ի ախտորոշված դեպքերի տարեկան միջին վիրահատական հիվանդությունը կազմել է 2, 7/100 000 բնակչի հաշվով, ինչն ավելի բարձր է, քան Իրանում (0, 74/100 000 բնակչի հաշվով) և Լիբանանում (1, 23/100 000 բնակչի հաշվով): Արձանագրվել են նաև մանկական դեպքեր, որը վկայում է շրջակա միջավայրում մակաբույծի լայն տարածվածության մասին: Այնուամենայնիվ, մարդկանց և կենդանիների մոտ հիվանդության իրական դեպքերն ու տարածվածությունը մնում են անհայտ, և հավանաբար կա հաստատված դեպքերի թերի հաշորդում: Մարդու էխինակոկոզը Հայաստանում մոռացված, բայց էական հանրային առողջության խնդիր է, որը պահանջում է ազգային կանխարգելման և վերահսկողության ծրագրում «Մեկ առողջություն» մոտեցման ադապտացումը՝ ներառելով համապատասխան միջոցառումներ ինչպես մարդկանց, այնպես էլ կենդանիների շրջանում:

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