**Research Article** 

# Investigation of the prevalence of cystic echinococcosis in Gaziantep-Türkiye by ELI.H.A Echinococcus ELITech between 2015-2022

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Cystic echinococcosis Indirect hemagglutination test

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**Abstract:** In this study, 1811 serum samples of 1764 patients who applied to the parasitology laboratory of Gaziantep Dr. Ersin Arslan Training and Research Hospital between 1 January 2015 and 31 December 2022 with preliminary diagnosis of cystic echinococcosis (CE) were investigated, in order to evaluate the demographic data of the patients and CE seropositivity on an annual base. 1811 serum samples were analyzed by ELI.H.A Echinococcus ELITech (MICROBIO, France) test which is based on the indirect haemagglutination principle. Seropositivity was detected in a total of 519 patients. Of the patients who were found to be positive, 341 were women and 178 were men.

The highest positivity rate was found in patients over 50 years of age (29.3%), followed by the 20-30 age group (23.1%) and the 30-40 age group (22.9%), respectively.

While 232 of the admitted patients with preliminary diagnosis of CE were Syrians, 1532 patients were Turkish citizens. The positivity rate in Syrian patients was determined to be 41.8%, (n=100) while this rate was 26.7% (n=419) in Turkish patients. Despite the developments in the socioeconomic field, the investments of local governments in sanitation and the establishment of single health awareness, CE continues to exist as an important public health problem in Gaziantep due to both the effect of migration and the inability to reach the desired levels of personal hygiene.

Özet: Bu çalışmada 1 Ocak 2015 - 31 Aralık 2022 tarihleri arasında Gaziantep Dr. Ersin Aslan Eğitim ve Araştırma Hastanesi parazitoloji laboratuvarına kistik ekinokokkoz ön tanısıyla başvuran 1764 hastanın 1811 serum örnekleri araştırıldı. Hastaların demografik verilerinin yanı sıra kistik ekinokokkoz seropozitifliğinin yıllara göre değerlendirilmesi amaçlandı. 1811 serum örneği indirekt hemaglütinasyon prensibine dayanan ELI.H.A Echinococcus ELITech (MICROBIO, Fransa) testi ile retrospektif olarak analiz edildi. Toplam 519 hastada seropozitiflik tespit edildi. Pozitif olduğu tespit edilen hastaların 341'i kadın, 178'i erkekti.

En yüksek pozitiflik oranı 50 yaş üstü hastalarda (%29,3) görüldü, bunu sırasıyla 20-30 yaş grubu (%23,1) ve 30-40 yaş grubu (%22,9) izledi.

KE ön tanısı ile başvuru yapan hastaların 232'si Suriyeli, 1532'si ise Türk vatandaşıydı. Suriyeli hastalarda pozitiflik oranı %41,8 (n=100), Türk hastalarda ise bu oran %26,7 (n=419) olarak belirlendi. Sosyoekonomik alanda yaşanan gelişmelere, yerel yönetimlerin sanitasyona yönelik yatırımlarına ve tek sağlık bilincinin yerleşmesine rağmen, gerek göçün etkisi gerekse kişisel hijyen düzeyinde istenilen seviyelere ulaşılamaması nedeniyle Gaziantep'te kistik ekinokokkozis önemli bir halk sağlığı sorunu olarak varlığını sürdürmektedir.

Introduction

Cystic echinococcosis (CE) is a complex disease caused by infection by tiny tapeworms of the genus *Echinococcus* Rudolphi and requires well-equipped health care systems, well-trained health personnel and adequate resources for its treatment. CE is usually in an asymptomatic state, which can last for several years, if no complication occurs (Agudelo Higuita *et al.* 2016) CE causes slowly enlarging masses (cysts) in various parts of the body, mostly in the liver or lungs, and symptoms appear as pain or discomfort in the upper



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abdominal region or chest, nausea and cough, depending on the affected organ. The infection is transmitted via fecal-oral route, mostly to intermediate hosts such as sheep, cattle, goats and pigs from the feces of canid animals, especially dogs. Humans are incidental intermediate hosts and do not transmit the infection further (WHO 2023, CDC 2023).

Effective diagnosis, from disease confirmation to mapping, screening, surveillance, monitoring and evaluation, is a prerequisite for Neglected Tropical Diseases (NTD) programs to achieve the targets related with the disease for 2030. It can also contribute progress towards elimination of the disease by ensuring that cases are identified and treated so that they do not become potential sources of infection. Access to diagnostic services can reduce morbidity by reducing progression and disability by providing early diagnosis and management, thereby minimizing NTD program costs (WHO 2023).

Ultrasonography (US) is the most accurate imaging method that should be preferred in determining the stages of the cyst, when compared to other imaging techniques such as Magnetic Resonance Imaging (MRI) and Computed Tomography (CT). Because CE can be featured with a seronegative appearance in most cases, the diagnosis of CE based on seronegativity will be unreliable, but positive serology after imaging of a CE-compatible lesion is a useful method to confirm the diagnosis, despite the heterogeneity of serological tests (Siles-Lucas *et al.* 2023).

According to the road map for neglected tropical diseases 2021–2030 report, effective diagnostics are critical to accelerating progress towards elimination, reducing morbidity and reducing programme costs (WHO 2020).

It is estimated that more than 1 million individuals worldwide may be living with CE during the same time period. Most of these people will suffer from serious clinical conditions that can be life-threatening if they cannot access treatment. Even if these patients are treated, they continue their lives with a significant decrease in their quality of life. The annual cost for treating CErelated cases and losses to the livestock industry is estimated to be US\$3 billion (WHO 2023). CE is estimated to cause 19,300 deaths worldwide each year, according to the 2015 WHO Foodborne Disease Burden Epidemiology Reference Group (FERG) report (WHO 2015). A cross-sectional study covering three countries, including Türkiye, in 2014-2015 revealed that the prevalence of CE in the rural population is not fully understood and many cases remain asymptomatic despite not being able to reach appropriate medical diagnosis and treatment (Tamarozzi et al. 2018).

According to the Current Situation Report on Cystic Echinococcosis in Turkey, studies on the epidemiology of the parasite have been limited to the provinces of Erzurum, Adıyaman, Çorum, Manisa, Adana, Malatya, Aydın, Kars, Hatay, Mersin, Istanbul and Kocaeli. During the preparation of the action plan, determining the distribution of the parasite by region and conducting epidemiological screening are important in determining the current situation in our country (Altintas *et al.* 2020).

Currently, the gold standard in serological diagnosis is based on the detection of IgG antibodies against cyst fluidderived antigens in ELISA or immunoblots (Mandal & Mandal 2012).

In this study, 1811 serum samples of 1764 patients, who applied to the parasitology laboratory of Gaziantep Dr. Ersin Arslan Training and Research Hospital between 1 January 2015 and 31 December 2022 with preliminary diagnosis of CE, were investigated in order to evaluate the demographic data of the patients and the CE seropositivity based on the annual scale.

## **Materials and Methods**

Gaziantep is located at the southeast part of Türkiye near Syrian border with a population of 2.154.051. Republic of Türkiye Ministry of Interior, Presidency of Migration Management latest report includes a data that the country currently hosts around 434,563 registered Syrian patients. The rate of the registered Syrians to the total number of people living in the city is 16.83% (<u>Göç</u> <u>İdaresi Başkanlığı 2024</u>).

In the study, 1811 serum samples of 1764 patients with a preliminary CE diagnosis were analyzed retrospectively. For this purpose, samples were exposed to a process to determine agglutination, if any using the ELI.H.A Echinococcus IFU 8000140 FR-EN -2012 kit (ELITech Microbio, France). According to the kit prospectus, the presence of anti-Echinococcus granulosus Batsch serum antibodies results in agglutination of sensitized red blood cells consisting of sheep red blood cells coated with E. granulosus antigen, resulting in a cloudy red/brown residue lining the well in the U-bottom microplate where the test is performed. In the absence of specific antibodies, the absence of hemagglutination of red blood cells forms a ring-like accumulation at the bottom of the well, indicating a negative reaction. Non-sensitized red blood cells ensure the specificity of the reaction and make it possible to eliminate any interference from natural antisheep agglutinins, such as Forssman heteroantibodies, ELI.H.A Echinococcus, E. granulosus infectious mononucleosis antibodies.

A titer of less than 1:160 indicates the possible absence of hydatid cyst, a titer of 1:160 indicates a suspicious reaction, and a titer of 1:320 and above indicates a significant reaction in favor of progressive hydatidosis.

Ethics committee approval for the study was received from Gaziantep University Clinical Research Ethics Committee Committee (Decision No: 2023/24).

## Statistical analysis

The data collected in the research were analyzed on a computer using the Statistical Package for the Social Sciences (SPSS) version 15 program.

# Results

Seropositivity was detected in a total of 519 patients. Of the patients who were found to be positive, 341 (65.7%) were women and 178 (34.3%) were men.

The highest positivity rate was found in patients over 50 years of age (29.3%), followed by the 20-30 age group (23.1%) and the 30-40 age group (22.9%), respectively.

While 232 of the admitted patients were Syrians, 1532 patients were Turkish citizens. The positivity rate in

**Table 1.** The distribution of seropositivity by age and gender.

Syrian patients was determined to be 41.8% (n=100), while this rate was determined to be 26.7% (n=419) in Turkish patients.

The distribution of seropositivity by age and gender is shown in Table 1.

In cases where seropositivity was detected, the average age of women was found to be 42.56, and 39.42 for men. The seropositivity rates by years are shown in Table 2.

Age	Gender	Positive	%	Negative	%	Borderline (1/160)	%	Total	
0.10	Female	0	0.0%	3	0.3%	0	0.0%	3	0.2%
0-10	Male	1	0.2%	4	0.3%	0	0.0%	5	0.3%
10-20	Female	17	3.3%	17	1.5%	4	2.9%	38	2.1%
	Male	14	2.7%	22	1.9%	4	2.9%	40	2.2%
<b>2</b> 0 <b>2</b> 0	Female	75	14.5%	65	5.6%	13	9.5%	153	8.4%
20-30	Male	45	8.7%	36	3.1%	9	6.6%	90	5.0%
30-40	Female	71	13.7%	146	12.6%	21	15.3%	238	13.1%
	Male	48	9.2%	67	5.8%	10	7.3%	125	6.9%
40-50	Female	71	13.7%	169	14.6%	29	21.2%	269	14.9%
	Male	25	4.8%	64	5.5%	13	9.5%	102	5.6%
50+	Female	107	20.6%	356	30.8%	24	17.5%	487	26.9%
	Male	45	8.7%	206	17.8%	10	7.3%	261	14.4%
Total		519	100%	1.155	100%	137	100%	1.811	100%

Table 2. The seropositivity rates by year.

Year	Positive	%	Negative	%	Borderline (1/160)	%	Total
2015	41	19.9	151	73.3	14	6.8	206
2016	69	34	124	61.1	10	4.9	203
2017	53	27	126	64.3	17	8.7	196
2018	66	23.8	187	67.5	24	8.7	277
2019	76	30.2	147	58.3	29	11.5	252
2020	47	35.9	72	55	12	9.1	131
2021	57	35.8	95	59.8	7	4.4	159
2022	110	28.4	253	65.3	24	6.2	387
Total	519	28.6	1155	63.8	137	7.6	1811

Researcher (Reference)	Interval	Province	Positive Results (%)	Number	Methods
Yılmaz <i>et al.</i> (2016)	2009-2013	Erzurum	9.5	2009	IHA (Hydatidose, Fumouze Laboratoires, France)
Kara <i>et al.</i> (2020)	2011-2018	Erzincan	22.5	1102	IHA (Siemens, Germany))
Çelik et al. 2022	2013-2020	Adıyaman	15.18	1607	IHA (Fumouze Laboratories, France)
Ertabaklar <i>et al</i> . 2019	2005-2017	Aydın	32	3446	ELISA
Samancı Aktar <i>et al.</i> 2020	2014-2017	Diyarbakır	26.7	829	IFA (Euroimmun AG, Lübeck, Germany)
Eryıldız et al. 2022	2011-2020	Edirne	15.5	2426	IHA (Fumouze Diagnostics, France)
Başer et al. 2021	2015-2020	Konya	21.6	1543	IHA (Fumouze Laboratoires, France)
Arslan et al. 2022	2018-2020	Kars	14.9	498	IHA (Fumouze Laboratoires, France)
Alver et al. 2021	2017-2018	Bursa	19.9	1072	IHA (Siemens Healthcare Diagnostics, Marburg, Germany)
Yürük <i>et al.</i> 2022	2013-2018	Kayseri	19.36	2283	IFAT (EuroimmunGmbH, Lübeck, Germany), IHA (Hydatidose, FumozeLaboratories, Signes, France) ve WB (EuroimmunGmbH, Lübeck, Germany)
Ulusan Bağcı 2023	10 Sep. 2017- 10 March 2020	İzmir	18.49	1444	IHA (Hydatidose, Fumouze laboratoires,
C	11 March 2020- 11 Sep. 2022		14.6	877	- France)
Beyhan et al. 2015	2009-2013	Ankara	15.03	2921	WB, ELISA, IHA
Current study	2015-2022	Gaziantep	28.6	1811	IHA (ELITech Microbio Signes France)

Table 3. CE studies from Türkiye published after 2015.

# Discussion

CE is on the World Health Organization's list of neglected tropical diseases and is one of the most common public health problems around the world today, especially in endemic regions such as South America, the Mediterranean region, Central Asia, Western China and East Africa (Agudelo Higuita *et al.* 2016).

In a systematic review of human and domestic animal hosts in European Mediterranean and Balkan countries, Tamarozzi *et al.* (2020) found that the average annual incidence rates of CE in humans ranged from 0.10 to 7.74 per 100,000. They also found that Southern Italy, central Spain, Romania and Bulgaria reported the highest values. When studies conducted in Türkiye were evaluated, it was found that the seropositivity rate was between 9% and 32.5% (Table 3). In CE studies conducted in Türkiye, seropositivity rates ranged between 52.7% and 71.6% in women (Table 3), and similarly in our study, the seropositivity rate in women (65.7%) was higher than in men.

The highest positivity rate was found in patients over the age of 50 with 29.3% in our study, these results may be associated with factors such as the elderly population staying in rural areas during rural-urban migration or regional characteristics. The highest positivity rates were observed in the 16-30 age group in Kars, in the 20-40 age group in Bursa, Izmir and Konya, and in the 31-45 age group in Erzurum (Yılmaz *et al.* 2016, Alver *et al.* 2021, Başer *et al.* 2021, Arslan *et al.* 2022, Ulusan Bağcı 2023).

Acoording to Ulusan Bağcı (2023) the prepandemic, that is, 2019 and before, was compared with the Covid-19 pandemic period covering the years 2020-2022, it was determined that seropositivity increased during the pandemic period. While the IHA positivity rate, which was determined as 18.49% in the pre-pandemic period in Izmir decreased to 14.6% during the pandemic period, in our study, on the contrary, the seropositivity rate, which was 26.8% before the pandemic increased to 31.6% during the pandemic period (Ulusan Bağcı 2023).

It was stated in the According to ECDC's 2020 Annual Epidemiological Report that the notification rate of confirmed human echinococcosis cases to the EU countries decreased in 2020 compared to the previous four years, and it was observed that the COVID-19 epidemic did not have a significant impact on the number of cases reported in 2020 (ECDC 2022).

# Conclusion

Despite the ongoing developments in socioeconomic areas within the region on which the data of the present study depends, the decrease in the rural population in the region and in the investments of local governments in sanitation areas, parasitic diseases remain an important public health problem. The most important factors are the high number of Syrian immigrants in Gaziantep noncompliance with the rules in animal slaughter, open sale of meat products and the fact that the desired levels of personal hygiene and health education have not been reached.

Despite some advances in the control of echinococcosis, CE remains a life-threatening disease, a major public health problem in many countries, and an emerging and re-emerging disease in some others (Bhutani & Kajal 2018). When the distribution of cases by province is considered, the disease incidence rate in Van, where CE has the highest incidence rate, was 4.12 per 100,000 between 2010-2014 and increased to 8.70 per 100,000 between 2015-2019. Van was followed by the neighboring provinces Ağrı and Iğdır. When the Ministry of Health data was examined, it was observed that the number of cases increased over the years, and the number

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of cases, which was 408 in 2008, reached 1,867 at the end of 2019. In countries where CE is endemic, successful results have been achieved in eliminating the disease as a result of the implementation of control programs such as public health control and sheep slaughter in slaughterhouses (Altintaş *et al.* 2020).

More detailed studies are needed within the one health concept in order to better understand the epidemiology of CE in Türkiye.

**Ethics Committee Approval:** Since the article does not contain any studies with human or animal subject, its approval to the ethics committee was not required.

**Data Sharing Statement:** All data are available within the study.

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