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Epidemiological Indicators of the State of Cystic Echinococcosis in Republic of Bulgaria for the Period 2011-2020

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ABSTRACT

Objective: Cystic echinococcosis (CE) is one of the most severe parasitoses, which leads to prolonged disability, frequent recurrences, and even to death. In Bulgaria it is one of the most frequently registered and severe helminthic infection.
The aim of this study is to determine the epidemiological indicators as morbidity, mortality and lethality from CE in Bulgaria for the period 2011-2020, as well as a comparative analysis of morbidity in the country with that of other EU member states.
Materials and Methods: The study is a retrospective analysis of confirmed cases of CE, as well as of the deceased from this parasitic disease. Data from several sources were used - the annual analyzes of parasitic morbidity in the country, prepared by the NCIPD, as well as information from the National Center for Public Health and Analysis and the National Statistical Institute. Statistical methods were used to calculate morbidity and mortality rates.
Results: From 2011 to 2020, a total of 2626 cases of CE are registered in Bulgaria (95% Confidence Interval: 263 ± 3.16), with an average incidence for the period of 3.7‰ (95% CI: 3.65 ± 0.357). The registered primary cases are 2336 (95% CI: 233.6 ± 3.03) in total and 290 (95% CI: 29 ± 1.04) are recurrences. Cystic echinococcosis is comparatively more prevalent in women than in men, respectively 1397 (95% CI: 139.7 ± 2.39) and 1229 (95% CI: 122.9 ± 2.14) registered cases for the period and for morbidity values are 3,7‰ (95% CI: 3.71 ± 0.36) to 3,5‰ (95% CI: 3.53 ± 0.343). The most affected is the age group 20–59 years, i.e. people of active working age. The number of affected children aged 1 to 19 (509 cases) is relatively high, which indicates an active transmission of the parasite. During the studied period deceased patients due to echinococcosis are 65 of whom 38 men and 27 women. The average mortality and the lethality are respectively 0.09‰ (95% CI: 0.09 ± 0.103) and 2.49% (95% CI: 2.49 ± 0.405).
Conclusion: The results show a reduction in examined indicators regarding cystic echinococcosis compared to data for the 1990s and the studied from us period, but these values are still higher than the established EU averages.

Keywords: Cystic echinococcosis, morbidity, mortality, lethality

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INTRODUCTION

Zoonoses are diseases transmitted between animals and humans. They have a cosmopolitan distribution (1). About 150 infectious and parasitic diseases common to animals and humans are known. Their relevance and health significance have increased significantly in recent years worldwide (2). Among helminthic zoonoses the most significant are echinococcosis, trichinosis, toxocariasis, filariasis, fasciolosis (3). Cystic echinococcosis (CE) is a foodborne parasitic disease which may take a severe clinical course that often leads to prolonged disability. The disease tends to relapse frequently after treatment and sometimes can cause permanent disabilities and even death (4). In Bulgaria, studies on the prevalence of CE have been conducted since the beginning of the 20th century. Over the years, a significant number of large-scale studies have been conducted on the dynamics of morbidity, mortality and lethality in this parasitosis (5, 6). In addition CE in Bulgaria is subject to mandatory notification and registration, including both primary cases and recurrences. An investigation record form approved by the Ministry of Health is filled in for each registered case.

Surveillance of CE is important for health care due to the possibility of long-term disease, frequent recurrences, permanent disability and death. After the political and economic changes in 1989, the incidence of CE in Bulgaria increased significantly, and in 1998 and 2002 two peaks were registered - 8.47 per 100,000 and 8.32% per 100,000 (7).

Therefore between 2004 and 2008 a National program for the control of echinococcosis in humans and animals was conducted. After the end of the program and so far a tendency for gradual reduction of the incidence from CE was established in Bulgaria and in 2020 reached their lowest values - 95 primary cases and relapses, as well as an incidence of 1.37‰.

Despite successes in reducing reported cases and morbidity, cystic echinococcosis deaths have been reported each year, most commonly in cases of multiple echinococcosis, lung involvement, or cyst rupture with anaphylactic shock. As one of the most important helminthiasis in Bulgaria in this study, we tried to update the data on the main epidemiological indicators concerning CE. Objectives of this report are to determine the epidemiological indicators as morbidity, mortality (mortality is the number of deaths per hundred thousand citizens of a given community over a given period of time) and lethality (lethality, usually expressed as a percentage, is the ratio of the number of deaths to the total number of patients with certain disease over a period of time) from cystic echinococcosis (CE) in Bulgaria for the period 2011-2020, as well as a comparative analysis of morbidity in the country with that of other EU member states.

MATERIALS AND METHODS

Study design

The study is a retrospective analysis of confirmed cases of CE, as well as of the morbidity and lethality from this parasitic disease in Bulgaria for ten year period. Only aggregate data were used in the study and it was not necessary to obtain permission from the Institutional Ethics Committee.

Data collection

Currently, surveillance and control of echinococcosis is carried out in accordance with Regulation №5 of Ministry of Health for the diagnosis, prevention, and control of local parasitic diseases. All newly registered cases are subject to rapid notification and epidemiological investigation by the Regional Health Inspectorates, which send these data to the National Centre of Infectious and Parasitic Diseases for further processing and analysis. In addition to this data, we also used data from other sources such as the National Center for Public Health and Analysis and the National Statistical Institute regarding mortality rates and the number of Bulgarian population by year.

Patients

The current study includes all registered cases of CE for a ten-year period 2011-2020, with patients grouped by gender and age (children and adolescents up to 19 year, and adults).

Descriptive statistics were used to determine some statistical indicators such as mean, standard deviation and 95% confidence interval of the mean..

RESULTS

From 2011 to 2020, a total of 2626 cases of CE are registered in Bulgaria, with an average incidence for the period of 3.7‰(Table. 1).

The highest values of the incidence are reported in 2012 and 2014 - 4.75‰ and 4.6‰, but the general trend for the whole period is gradual decrease of the registered cases and morbidity, which in 2020 reached 1.37‰ and is the lowest of 40 years (5).

The registered primary cases of CE clearly shows the trend of gradual decline, while recurrences lack special dynamics and they vary from 20 to 40 per year. In total for the period the cases of recurrence represent 11.08% of all registered cases of CE. In 2020, there are only nine relapses, most likely due to missed diagnostics related to the pandemic of SARS-CoV-2.

The follow-up of the dynamics of the incidence of CE by

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Table 1: Cases of CE divided by type and sex

Year	Registered cases (n)	Primary cases (n)	Relapses (n)	Male sex	Female sex	Annual incidence per 100 000 population
2011	347	312	35	159	188	4.7
2012	346	312	34	162	184	4.75
2013	307	266	41	148	159	4.2
2014	332	296	36	156	176	4.6
2015	313	283	30	141	172	4.37
2016	269	238	32	120	149	3.78
2017	218	196	22	118	100	3.1
2018	207	178	28	90	117	2.93
2019	192	168	24	90	102	2.74
2020	95	86	9	45	50	1.37
Total	2626	2335	291	1229	1397	36.54
Mean	262.60	233.5	29.1	122.9	139.7	3.65
Standard deviation	26.16	74.75	9.06	38.22	45.55	1.10
95% CI of mean	263 ± 3.16	233.5 ± 3.03	29.1 ± 1.04	122.9 ± 2.14	139.7 ± 2.39	3.65 ± 0.357

gender for the studied period shows that both the cases and the incidence in women prevail over those in men - 1397 to 1229 registered cases and 3.8‰ to 3.5‰ established average incidence (Figure 1).

Cystic echinococcosis (CE) affects all age groups. According to age and gender, the highest number of patients in males is in the groups 30-39 years (212) and 20-29 years (209), and in females - in the groups 30-39 years (212) and 60-69 years (210) (Figure 2, Figure 3). Also in the groups between 40 and 60, women (616) are significantly more affected than men (421). Our data show that affected by this helminth infection are mainly people of working age, 58% of registered patients are in the age group of 20 to 59. The incidence in the age groups of 20-29 (4.85‰), 30-39 (4.2‰), 40-49 (3.48‰) and 50-59 (3.39‰) shows decreasing values and only in the group of 60-69 (3.6‰) this indicator is higher, probably due to the higher number of registered women with cystic echinococcosis (Figure4).

In children, the registered cases of cystic echinococcosis in boys aged 0 to 19 are 281, and in girls - 228. In the age groups from 0 to 9, and 10 to 19 the number of affected boys is more than girls - 112 to 70, and 169 to 158. Although reported cases of cystic echinococcosis are higher in the age groups between 20 and 40 years in both men and women, the highest incidence is found in the age group between 10 and 19 years. (5.06‰) (Figure 4).

During the studied period, both the number of cases and the incidence rate vary in different regions of the country (Fig. 5). Most patients with CE are from the districts of Plovdiv (276), Sliven (249), Burgas (199), Varna (192) and Kardzhali (161), although the morbidity is highest in the districts of Sliven (13.09‰), Kardzhali (10.5‰), Shumen (7.75‰) and Dobrich (7.36‰).

During the studied period by reason of echinococcosis there were 65 deceased patients, the largest number - 23, is in the age group 70-79 year followed by the groups 60-69 year with 13 patients and 50-59 year with 9. Among the group of children and adolescents, two cases with fatal outcome were registered in two boys aged 4 and 15.

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Depending on gender, 38 of the deceased are men and 27 are women. Forty-two of the deceased lived in rural areas, and they are more than those from the urban areas, where they are 23. Both from the villages and from the cities the number of deaths among men were higher - 24 males vs 18 females among the rural and 14 vs 9 among the urban residents.

The average rate of mortality and lethality from CE for the period from 2011 to 2020 were 0.09‰ and 2.49% (Figure 6, Figure 7). The annual values of this indicators were the highest in 2012, respectively 0.19‰ and 4%, and in 2016 - 0.15‰ and 4%.

Data on the organ location of echinococcal cysts show that 70% of them are in the liver, 20% in the lungs and in 6.5% of patients cysts are with extra hepatopulmonary localization.

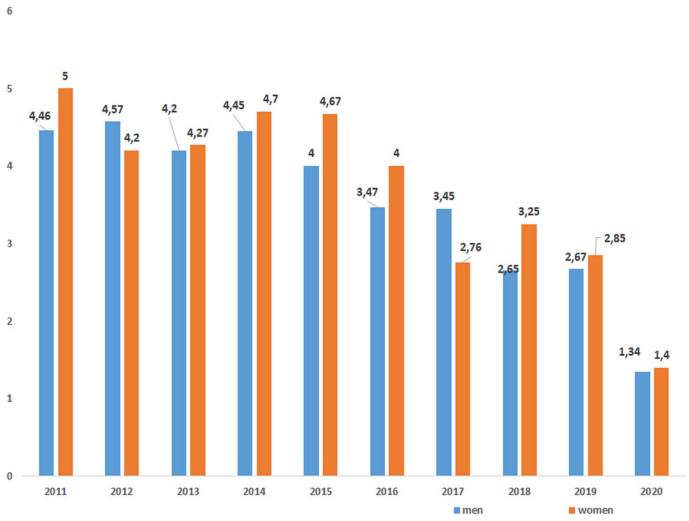

Figure 1. Incidence by years distributed by gender per 100 000 population

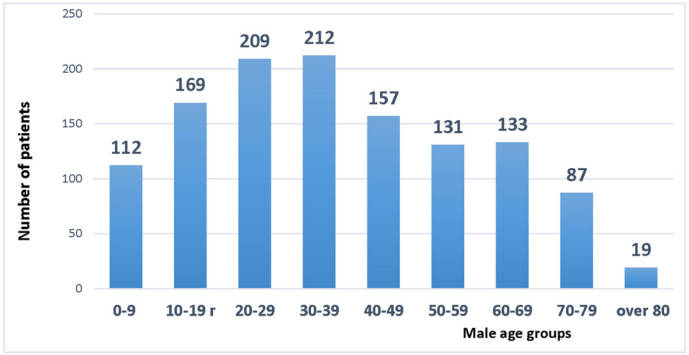

Figure 2. Registered cases of cystic echinococcosis by age groups in males

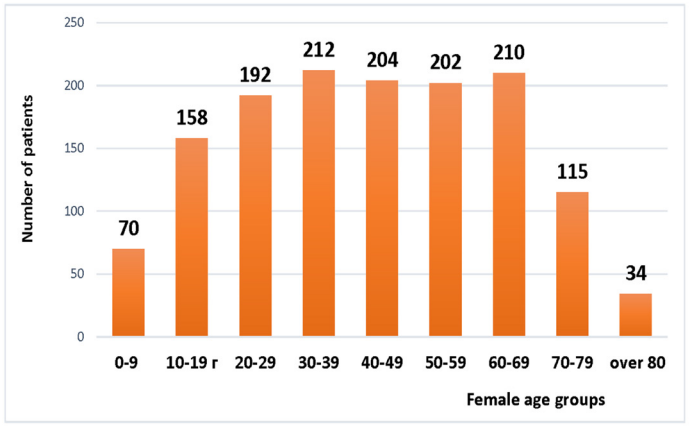

Figure 3. Registered cases of cystic echinococcosis by age groups in females

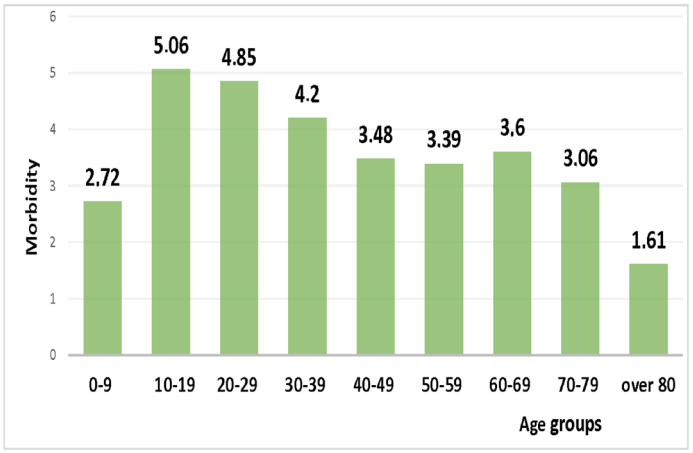

Figure 4. Morbidity by age groups for the studied period 2011-2020 per 100 000 population

Figure 5. Registered cases of cystic echinococcosis by regions of the country

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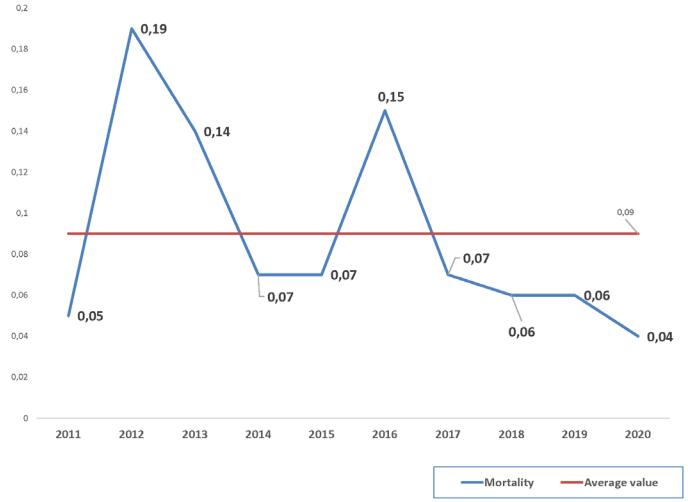

Figure 6. Mortality of cystic echinococcosis for the period 2011-2020 per 100 000 population

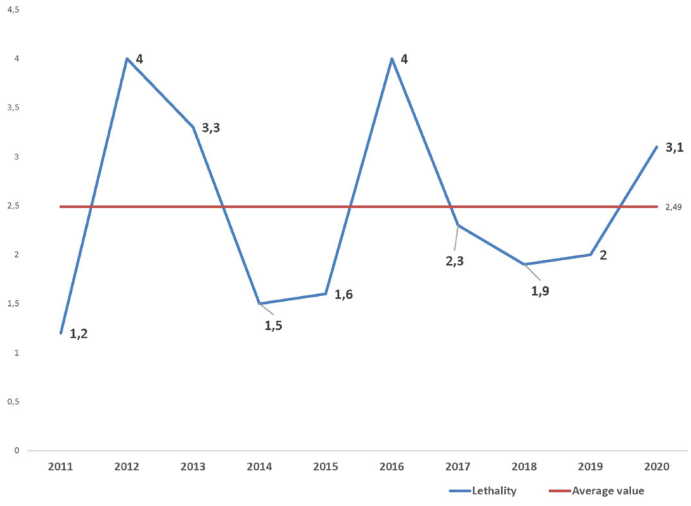

Figure 7. Lethality of cystic echinococcosis for the period 2011-2020 in %

DISCUSSION

CE is one of the parasitic diseases of greatest medical importance in Bulgaria (7). For the studied ten-year period the average incidence is 3.7 per 100,000. A comparison of the data obtained with those of a previous study conducted in the period 2001-2010 with an established average incidence of 6.77 per 100,000 shows that an almost twofold reduction in the incidence of CE has been achieved (8). Probably the decrease in the annual incidence rates of CE is largely due to

implementation of the National Program for the Control of Echinococcosis among Humans and Animals conducted between 2004 and 2008. Within the framework of this program, a mass serological screening of at-risk contingents of 9 390 individuals was carried out throughout the country, as a result of which 66 new undiagnosed cases of CE were detected. A diagnostic-therapeutic algorithm was prepared to be applied by medical specialists, as well as measures for health information for the population on measures to prevent infection. The veterinary part was mainly related to the implementation of preventive measures for deworming, mainly of stray dogs. However, both registered cases and morbidity in Bulgaria remain higher than in other EU countries. During the 2004 - 2008, a total of 4 306 cases of CE were reported in the EU countries, and these data show that 61% of those registered with this parasitic disease are from Bulgaria (9). The recent cross-sectional ultrasound-based survey that recruited volunteers from 50 villages in four districts of Bulgaria was with data for 31 persons with abdominal CE of 8602 people screened in Bulgaria (10).

In total for the period the cases of recurrence represent 11.08% of all registered cases of CE. Previous study by Harizanov et al. covering the period 2006 - 2017 presents data for 9.9% recurrences for the period (11). This shows that the relative part of recurrences remains at relatively constant levels in the country, despite the fact that according to Bulgarian legislation, all cases of CE treated surgically or with PAIR technique are subject to subsequent anti-relapse treatment with albendazole, which is reimbursed 100% by the National Health Insurance Fund. This gives us reason to believe that not all cases subject to anti-relapse treatment are covered by the health system in the country. Our data for the cases of recurrence are similar with these of other authors. According to a study by Velasco-Tirado et al. cases of recurrence are 11.5% in the contingent of CE patients studied by them (12).

The registration of CE to a large extent in the active, working age can be explained by the chronic course of the disease, progressing over time and often diagnosed years after infection. And the higher incidence among females compared to males is probably due to more frequent contact of women with pets and the work done to grow low-stem vegetables and fruits on the private farm.

The data on the established highest morbidity in the age group 10-19 years (5.17 per 100,000) is quite alarming and shows that there is an active transmission of the disease (13). The number of affected children and adolescents up to 19 years of age in our study is relatively high (509 cases) but is more than twice lower than the number of affected persons in the same age group for the period 2000 - 2010 (1193 cases, incidence 6.4 per 100.000) (13). The established high values of the incidence in the age group 10-19 years are possible due to insufficient hygiene habits in children and their more frequent contact with dogs for play. Also since 1990, the country's population of stray dogs has increased significantly that are not regularly dewormed, particularly in areas with developed livestock

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breeding and especially sheep breeding (13). Sheep are the most important intermediate host of *E. granulosus*. Their role in the spread of the cystic echinococcosis is determined by their constant contact with dogs and the high percentage of fertile echinococcal cysts. This explains the widespread prevalence of echinococcosis in countries with developed sheep breeding (14). The highest average incidence rate of CE was recorded mainly in four regions:

Sliven (13.09 per 100,000), Kardzhali (10.5 per 100,000), Shumen (7.75 per 100,000) and Dobrich (7.36 per 100,000). Sheep farming is well developed in all four areas. Sliven District is located in the Southeastern region of the country where 21.5% of the sheep are raised, Kardzhali is in the South Central region, and 23.2% of the sheep are raised there, and Shumen and Dobrich are located in the Northeast region of the country, where more than 15% of sheep are bred (15).

In terms of mortality and lethality, the data obtained can be explained by the relatively large number of cases of cystic echinococcosis registered in the country and unfortunately delayed diagnosis due to lack of clinical symptoms, creating preconditions for spontaneous or traumatic rupture of echinococcal cysts and/or cysts, which almost always leads to anaphylactic shock with lethal outcome. Of course, this can include complications arising after surgery for the disease, especially in multiple and multi-organ involvement, as well as rare localizations affecting vital organs and systems (heart, CNS). However, it should be noted that compared to a previous study covering the period from 1991 to 2002, the mortality rate from cystic echinococcosis in Bulgaria decreased 2 times and the lethality 1.6 times (6).

The data on the organ localization of echinococcal cysts are not surprising, because according Eckert et al., the relative percentages of liver and lung localizations together account for at least 90% of the hydatid cysts in humans (16). Data from previous study in Bulgaria presents data for location the first place in the liver (65.47%) and in the second in the lungs (23.48%) (6). In the Timis County, Romania, of the 182 individuals studied between 2004 and 2010 with CE, localization in the liver was found in 81.9% of them (17). However, the relative part of cases with extrahepatopulmonary localization of 6.5% shows that they are also quite common and mainly affected are the spleen, abdominal cavity, kidneys and muscles/ subcutaneous tissue. Similar data were presented from Harizanov et al, according which for the period 2010–2019, the cases with extra-hepatopulmonary localization were 5.17% (18).

Analyzing the data, the logical question arises: Why are there so many cases of echinococcosis in Bulgaria? In our opinion, the answer is multifaceted and the reasons for this are different. In the first place are the measures against the main reservoir source of the disease in synanthropic foci - the dog. The control over the number of the stray dog population is weak or absent, and the measures for their regular deworming are fragmentary and only in some settlements. This also applies to domestic and shepherd dogs, especially in small settlements, where animal husbandry and basic sheep breeding are practiced, because sheep are the most important intermediate host of *E. granulosus* (14). We believe that in the field of human medicine, with the exception of prevention, there are no particular problems, both in terms of diagnosis and in terms of treatment, surveillance and control of the disease. However, serious veterinary control is required with regard to the final host (dog) and the main intermediate (sheep).

CONCLUSION

In conclusion, it can be said that despite the successes achieved in the surveillance and control of CE in Bulgaria, the disease is still of great health and public impact. Measures to reduce the incidence, mortality and lethality include enforcement of the preventive actions by the public health authorities with media collaboration and involvement.

Competing interests: The authors declare that they have no competing interest.

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Ethical approval: Only aggregate data were used in the study and it was not necessary to obtain permission from the Institutional Ethics Committee.

REFERENCES

1. WHO. The Control of Neglected Zoonotic Diseases: Community-based interventions for pre-vention and control. Report, 2011, WHO, Geneva.
2. Graczyk TK. Zoonotic infections and conservation. In: Conservation Medicine: Ecologi-cal Health in Practice. (Eds. A.A. Aguirre, R.S. Ostfeld, G.M. Tabor, C.A. House, M.C.Pearl), Oxford University Press, New York. 2002, pp. 220–8.
3. Robinson MW and Dalton JP. Zoonotic helminth infections with particular emphasis on fasci-olosis and other trematodiases. Philos Trans R Soc Lond B Biol Sci. 2009;364:2763–76.
4. European Food Safety Authority & European Centre for

International Journal of Echinococcoses 2022;1(2):26-32
DOI: 10.5455/IJE.2022.03.05

Disease Prevention and Control. The European Union summary report on trends and sourcesof zoonoses, zoonotic agents and food-borne outbreaks in 2016. EFSA Journal. 2017;15:5077

5. Boeva V, Genov G, Nikiforov S. Echinococcosis. Medicine and Physical Education Press, Sofia, 1983, 234.
6. Kurdova R, Yordanova D. Status of echinococcosis in humans in Bulgaria (1991-2002). Bulgarian Surgery 2003;3:6-12.
7. Harizanov R, Rainova I, Kaftandjiev I. Human Cystic echinococcosis, Trichinellosis and Toxocariasis in Bulgaria: an update of data for 2015-2017. International Medicine. 2019;1:43-50.
8. Marinova I, Kurdova R, Jordanova D, et al. Current status and trends of the major human parasitic zoonoses Echinococcosis and Trichinellosis in Bulgaria. Conference in veterinary parasitology, 21 June 2011. Zagreb, Croatia.
9. European Food Safety Authority & European Centre for Disease Prevention and Control. The European Union One Health 2020 Zoonoses Report. EFSA Journal 2021;19:6971.
10. Tamarozzi F, Akhan O, Cretu CM, et al. Prevalence of abdominal cystic echinococcosis in rural Bulgaria, Romania, and Turkey: a cross-sectional, ultrasound-based, population study from the HERACLES project. Lancet Infect Dis. 2018l;18:769-78.
11. Harizanov R, Rainova I, Kaftandjiev I, et al. Cystic echinococcosis in Bulgaria 2006 – 2017. 14th Workshop of the National Reference Laboratories for Parasites, 23-24 May 2019, Rome, Italy.
12. Velasco-Tirado V, Romero-Alegría Á, Belhassen-García M, et al. Recurrence of cystic echinococcosis in an endemic area: a retrospective study. BMC Infect Dis. 2017;17:455.
13. Jordanova DP, Harizanov RN, Kaftandjiev IT, et al. Cystic echinococcosis in Bulgaria 1996-2013, with emphasis on childhood infections. Eur J Clin Microbiol Infect Dis. 2015;34:1423-8.
14. Tzolov B. Canine Tapeworm - echinococcosis in animals and humans. Znanie Publishing House Sofia, 1988.
15. Harizanov R, Raynova I, Kaftandjiev I, et al. Geographical distribution and dynamics of cystic echinococcosis in Bulgaria for the period 2006 – 2016. 16th National Congress of Clinical Microbiology and Infection, 12-16 May 2018. Sofia, Bulgaria, 38.
16. Eckert, J, Gemmell, MA, Meslin, F-X and Pawlowski, ZS and World Health Organization. WHO/OIE Manual on Echinococcosis in Humans and Animals: A Public Health Problem of Global Concern. 2000, Paris, France: World Organisation for Animal Health.
17. Calma CL, Neghina AM, Vlaicu B, Neghina R. Cystic echinococcosis in the human population of a western Romanian county, 2004–2010, Clin Microbiol Infect 2011;17:1731–34.
18. Harizanov R, Rainova I, Kaftandjiev I. Extra-hepatopulmonary cystic echinococcosis in Bulgaria: Frequency, management and outcome of the disease. Parasitology. 2021;148:562-5.