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Original article ■

Seroincidence of Echinococcosis at the Territory of the City of Niš

Suzana Otašević^{1,2}, Nataša Miladinović Tasić^{1,2}, Aleksandar Tasić², Dragan Zdravković²,
Jovana Đorđević¹, Aleksandra Ignjatović¹, Roberta Marković², Dragana Cvetković¹

¹ *Universtiy of Niš, Faculty of Medicine, Serbia*

² *Public Health Institute Niš, Serbia*

SUMMARY

Cystic echinococcosis (CE) is caused by the larva of tapeworm *Echinococcus spp.* Echinococcosis may develop after accidental ingestion of tapeworm eggs.

The aim of this study was to examine the seroprevalence and seroincidence of echinococcosis at the territory of the City of Niš in the last 22 years.

From 1988 until the end of 1998, 1.303 patients suspected of having echinococcosis were screened serologically by indirect immunofluorescent test (IIFT-INEP-Zemun, Serbia). After this period for immunodiagnosis of this parasitosis in 938 patients indirect haemagglutination assay (IHA-Siemens, Germany) or/and indirect enzymimmunoassay (ELISA-R-Biopharm, Germany) were used besides IIFT. Statistical analysis was performed using the SPSS 14.0 for Windows 2003.

In the survey, 570 seropositive patients (25.%) were found. Statistically significantly higher seroprevalence ($p=0.037$) was obtained in the last eleven years (33.0%) when minimum two immunodiagnostic tests were used in regard to previous period of time (1988-1998=20.0%). CE seroincidence in the last 22 years was very high (10.79 per 10^5 inhabitants). However, in the study, the statistically significant increase of CE seroincidence ($p=0.237$) regarding the number of applied methods was not found.

The high seroprevalence and seroincidence of echinococcosis in inhabitants of the City of Niš suggested that clinicians and public health authorities should pay greater attention to this disease.

Key words: *Echinococcus granulosus*, seroincidence, seroprevalence

Corresponding author:

Suzana Otašević •

tel. 018/42 26 448 •

e-mail: otasevicsuzana@gmail.com •

INTRODUCTION

Echinococcosis, hydatidosis or cystic echinococcosis (CE) is a cosmopolitan parasitic infection. It is caused by *Echinococcus granulosus*, most popularly known as the dog tapeworm, but it can be caused by other species of this genus, too (1-3). Adult form of this helminth parasites in the digestive tract of dogs. The tapeworm eggs are excreted with the feces of these animals. Following accidental ingestion of these eggs, echinococcosis in larval stage may develop in intermediate hosts (usually sheep, cattle, goats, horses, pigs and rarely humans) (4). Hydatid cyst as a larval form of *Echinococcus spp.* in human body is usually located in the liver (60%), lung (20%), rarely in the spleen, brain, bones etc.

Hydatid cysts grow slowly so that the infection is initially asymptomatic. Later, the cyst reaches larger dimensions and starts to make pressure to the surrounding tissue and organs. That leads to disturbances of these organs' function. Pathological changes, clinical signs and symptoms depend on the localization of cyst in the human body (5).

Localization in the liver is followed by nausea, feeling of disgust at fat meals, pain below the right rib cage, icterus. Cyst in the liver rarely regresses. The most common clinical signs and symptoms of lung echinococcosis are chronic bronchitis, followed with cough, dyspnea, chest pain, pleurisy and immune hyperactivity. Brain and hearth echinococcoses are the most serious clinical forms of this parasitosis (2, 4).

General signs and symptoms of CE include weight loss, frequent occurrence of allergic manifestations and chronic intoxication. Complications are rupture of cysts and dissemination of parasite that are followed by the appearance of fever, urticaria, eosinophilia, or even fatal anaphylaxis (2, 4, 5).

The diagnosis of echinococcosis usually starts with radiological and ultrasound tests (5, 6). Detected cyst in the affected organ must not be punctured during diagnostic procedure. That procedure carries a risk of hyperreactivity in a host, and the possibility of echinococcosis dissemination. Only surgically extracted cyst can be used for histopathological and parasitological examinations.

Microscopic detection of proligera vesicles and protoscoleces inside the cyst is a reliable proof of echinococcosis and it represents the referent standard in diagnosis of this helminthosis.

Direct diagnosis of CE may include the detection of antigen of this tapeworm in the blood and other fluids. Recently, genetic tests for detection of the parasites DNA have been used in laboratory examination. Direct serological and genetic tests are very sensitive and specific, however, very expensive so that are usually available for referent laboratories (5, 6).

Indirect serological tests are commonly used in routine diagnosis of echinococcosis. In serological

diagnosis, it is recommended to apply two or more immunodiagnostic tests to avoid false negative results. Indirect immunoenzyme method (ELISA), passive hemagglutination test (IHA) and indirect immunofluorescence test (IIFT) is the most common tests for the detection of specific antibodies in the serum of the patient. For confirmation and differentiation of Echinococcus species infection, patients sera has to be retested by Western-blot (6-9).

Until recently, surgical intervention was the only option for the treatment of echinococcosis. The beginnings of chemotherapy started with using of mebendazole at high dose (50 mg/kg) and they had diverse effect. Successful usage of albendazole and praziquantel in the treatment of inoperable hydatid cysts were reported. Besides this, larvicide may be preoperatively administered with the purpose to destroy parasites and prevent their possible dissemination (4, 7).

All people are equally sensitive to echinococcosis regardless of age, gender or other epidemiological characteristics. Endemic areas have been mostly confirmed in developing countries. Prophylaxis involves veterinary control and regular treatment of dogs as well as personal hygiene, primarily for individuals who are professionally in contact with dogs (2, 3, 8, 9).

The aim of the paper was to investigate the sero-incidence and seroprevalence of echinococcosis at the territory of the City of Niš in the period from January 1988 until the end of 2009.

MATERIAL AND METHODS

Between January 1, 1988 and the end of 2009, 2.241 patients suspected of having CE (because their ultrasound or computerized tomography scans showed round or oval lesions of different size in the liver or lung) were serologically examined for this disease at the Department of Parasitology, Institute of Microbiology, Faculty of Medicine in Niš.

The sera were obtained from patients of both genera and different ages and all patients were inhabitants from the territory of the City of Niš.

In the period from 1988 until the end of 1998, the sera from 1.303 patients were screened by an indirect immunofluorescence test (IIFT-INEP-(Zemun, Serbia). After this period, in the last 11 years, the sera of 938 were analyzed for specific antibodies detection by IIFT and using indirect haemagglutination (IHA-Siemens-Cellognost-Echinococcosis-Marburg, Germany) and / or indirect enzymelinkedimmunoassay (ELISA Ridascreen-Echinococcus IgG, R-Biopharm, Darmstadt, Germany).

All immunodiagnostic methods were carried out according to manufacturer's instructions. Detection of specific antibodies in diagnostically significant titers was treated as seropositive results.

The results were elaborated with the statistical method of descriptive and quantitative analysis (SPSS 14.0 for Windows 2003). A chi-square test for trend

was used to compare the proportions over time using each year as a different exposure level. $P < 0.01$ was considered as statistical significance.

RESULTS

During the study period of 22 years, the specific antibodies were found in 570 patients (25.4%). Comparing the results of serological tests for CE significant difference in seroprevalence of echinococcosis ($p = 0.037$) was observed regarding the number of applied immunodiagnostic tests. Using only the IIFT method in the time period from 1988 to 1998, echinococcosis seroprevalence was 20.0%, while with the parallel use of IIFT with IHA and/or ELISA, the CE seroprevalence was approved in 33.0% of patients (Table 1).

Seroprevalence of echinococcosis in the investigation period regarding the years when analysis was performed is shown in Table 2. During the period in which only one test was applied, the seroprevalence ranged from 9.7% in 1989 to the maximum value of 36.8% in 1993. In the following years, when we used

two or three immunodiagnostic methods, CE seroprevalence ranged from 20.0% to even 49.2% in 2000.

Cumulative CE seroincidence (population in the City of Nis = 239.50 inhabitants) in the twenty-two year period was $10.79/10^5$ inhabitants.

Although the comparison of used methods in immunodiagnostics of echinococcosis showed a higher cumulative seroincidence ($11.74/10^5$ inhabitants) in the period 1999-2009 as compared to the previous period (1988-1998: $9.85/10^5$ inhabitants.), there was no statistically significant difference in cumulative seroincidence of CE ($p = 0.237$) (Table 3).

Regarding the sex, statistically significantly higher seroprevalence of echinococcosis was more proved in women than in men ($p < 0.001$), because out of 570 seropositive patients in total, 380 (66.7%) were females (Table 4).

On the basis of available data in the last 11 years, in relation to the age of the patients, 21 (6.8%) patients were younger than 14 years.

Table 1. Seroprevalence of echinococcosis in relation to the number of used immunodiagnostic tests

Time period	Seroprevalence of echinococcosis
1988-2009	25.4%
1988-1998 (using IIFT*)	20.0%
1999-2009 (using IIFT and ELISA** or/and IHA***)	33.0%****

*IIFT, indirect immunofluorescence test

**ELISA, enzyme-linked immunoassay

***IHA, indirect haemagglutination

****Statistically significant difference $p = 0.037$

Table 2. Seroprevalence of echinococcosis in relation to the time period

Year	Seroprevalence of echinococcosis using IIFT	Year	Seroprevalence of echinococcosis using IIFT and ELISA or/and IHA
1988	29.5	1999	27.6
1989	12.8	2000	49.2
1990	16.5	2001	23.1
1991	25.8	2002	36.4
1992	18.8	2003	26.3
1993	36.8	2004	20.0
1994	25.4	2005	21.9
1995	18.7	2006	37.1
1996	9.7	2007	36.5
1997	17.7	2008	35.8
1998	13.9	2009	32.9

Table 3. Cumulative seroincidence of echinococcosis regarding the number of immunodiagnostic tests

Time period	Cumulative seroincidence of echinococcosis per 100.000 inhabitants
1988-2009	10.79
1988-1998 (using IIFT)	9.85
1999-2009 (using IIFT and ELISA or/and IHA)	11.74

Table 4. Seroprevalence of echinococcosis with respect to gender

Patients	Seroprevalence of echinococcosis (%)
Women	380 (66.7%)*
Men	190 (33.3%)
Total	570 (100%)

*statistically significant difference $p < 0.001$

DISCUSSION

Echinococcosis-hydatidosis is „an old disease“, that was described by Hippocrates and Aristotle as the emergence of water cyst in the body of the patient (8, 10).

This "old disease" is still a current health problem in many countries despite the established and implemented preventive measures to control the spread of infectious diseases.

Globally, people and animals that live on all continents can be infected by this parasite. Based on data from the referent literature, authors from more than 100 countries have discussed this issue. After systematic research and evaluation studies, with the aim of monitoring the effectiveness of the preventive measures against echinococcosis, to date, it has been found that the prevalence of infected people has significantly decreased only in the island countries such as Cyprus, Tansmania and New Zealand (11, 12).

On the contrary, significantly higher prevalence of echinococcosis has been observed in China, northern and eastern Africa, Australia and South America. Also, a significant percentage of this parasitic disease has been found in the former Soviet countries such as Kazakhstan and Kyrgyzstan (11, 12).

In Europe, echinococcosis affects people in all countries of this continent. The incidence ranges from 1-8 per 100.000 inhabitants with the exception of Ireland, Denmark and Iceland. Endemic zones have been established in some parts of Spain, southern Italy

and Sardinia (7, 8, 10).

In our environment, echinococcosis is still a significant problem for public health despite campaigns with the goals to control this disease. For example, after the prevention programme in Bulgaria, a decline of echinococcosis incidence, both in humans and animals, was detected. However, in the following years, despite preventive measures, the prevalence of this parasitic disease increased, and in Bulgaria there are still hyperendemic areas of human and animal echinococcosis (13).

During the seventies of the 20th century in Greece (10), the incidence of echinococcosis was even 12.9% per 100.000 inhabitants. A multidisciplinary approach to the problem brought about the implementation of education and prevention campaigns, which resulted in the decrease of echinococcosis incidence. However, in some recent studies, a very high seroprevalence of echinococcosis has been established (29%) in residents of the north part of this country.

In the former Yugoslav republics, echinococcosis is reported as one of the dominant infectious diseases. The incidence of this parasitoses in Bosnia and Herzegovina ranges from 0.56-1.64%/10⁵ inhabitants, while in Herzegovina the incidence is extremely high and ranges from 4.1 up to 20.8/10⁵ inhabitants (11). In the eastern Slovenia, for the clinical and public health authorities, hydatidosis still represents a problem. Although we should emphasize the fact that the incidence of this parasitosis has declined recently (from 4.8 to 1.7%/10⁵ inhabitants) (7).

From the economic and social aspects, in a very difficult period since 1988 to 2000, the seroincidence of echinococcosis at the territory of Niš district (based on 1991 census there were 396.043 inhabitants) was significantly high and ranged from 2.02 to 10.86/10⁵ inhabitants (14).

In this survey, we found that the territory of our city represents the area with extremely high seroprevalence and seroincidence of echinococcosis. Cumulative seroincidence of CE in defined period was 10.79 /10⁵ inhabitants. But there was no statistically significant difference in seroincidence of this parasitosis in relation to the number of the applied diagnostic methods ($p=0.237$). Statistically significant difference (0.037) was found in the seroprevalence of CE in the last 11 years compared with the period in which the immunodiagnosics included only one serologic test.

In the recent years, the major problem regarding echinococcosis is the fact that the incidence of this parasitic infection in children younger than 14 years is very high. In our study, based on the available data, the seroprevalence of echinococcosis in children was 6.8%. Unlike other countries, at the territory of the City of Niš, the seroprevalence of echinococcosis is still not significantly high in the population group of people below the age of 14 (7, 10, 13). According to sex, in this investigation, we found higher rate in seroprevalence of

CE in women, as has been confirmed in the researches carried out in other counties (9, 11).

Echinococcosis is one of the health problems that require a multidisciplinary approach and cooperation between clinicians and parasitologists, as well as veterinary services. Thus established cooperative work could cause a reduction in the number of infected people and animals. A constantly reduced number of the infected with this parasite can make eradication of echinococcosis possible. Maintaining and enforcement of control programs for CE in the long run is the only way to reduce the number of patients. Also, the most important thing in the prevention of this disease is health education. It is the basis for achieving the "control of disease" and the most significant link in the campaign for eradication of echinococcosis (3, 9, 10, 13).

CONCLUSION

The high seroprevalence and seroincidence of echinococcosis in inhabitants of the City of Niš suggest that this territory needs immediate constitution and implementation of control programs for CE and greater attention, primarily of public health authorities.

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SEROINCIDENCIJA EHINOKOKE NA TERITORIJI GRADA NIŠA

Suzana Otašević^{1,2}, Nataša Miladinović Tasić^{1,2}, Aleksandar Tasić², Dragan Zdravković²,
Jovana Đorđević¹, Aleksandra Ignjatović¹, Roberta Marković², Dragana Cvetković¹

¹ Univerzitet u Nišu, Medicinski fakultet, Srbija

² Institut za javno zdravlje Niš, Srbija

Sažetak

Cističnu ehinokoku (CE) prouzrokuje larva cestode roda *Echinococcus*. Ehinokokoza kod čoveka nastaje slučajnom ingestijom jaja ovog parazita.

Cilj ovog rada bio je utvrditi seroprevalenciju i seroincidenciju ehinokokoze na području grada Niša u poslednje 22 godine.

Od 1988. do kraja 1998. godine, kod 1303 bolesnika kod kojih postoji sumnja da boluju od CE, urađen je serološki skrining primenom samo indirektno imunofluorescentne metode (IIFT-INEP-Zemun, Srbija). Nakon ovog perioda, imunodijagnostika ove parazitoze kod 938 bolesnika, obuhvatila je pored IIFT korišćenje i indirektnog hemaglutinacionog testa (IHA-Siemens, Germany) i/ili indirektnog imunoezimskog testa (ELISA-R-Biopharm, Germany). Statistička analiza dobijenih rezultata sprovedena je metodom deskriptivne i kvantitativne analize (SPSS 14.0 for Windows 2003).

U istraživanju je utvrđeno 570 seropozitivnih bolesnika (25.4%). Statistički značajno viša ($p=0.037$) seroprevalencija (33.0%) ehinokokoze utvrđena je u poslednjih 11 godina, kada su za imunodijagnostiku primenjena minimum dva serološka testa u odnosu na raniji period (20.0%). U studiji je utvrđena značajno visoka seroincidencija ehinokokoze (10.79 na 10^5 stanovnika) u poslednje 22 godine, međutim, ne postoji statistički značajna razlika ($p=0.237$) u seroincidenciji ove parazitoze u odnosu na broj primenjenih metoda.

Visoka seroprevalencija i seroincidencija ehinokokoze kod stanovnika grada Niša ukazuje na neophodnost da se ovoj parazitozi posveti više pažnje od strane kliničara, dijagnostičara i autoriteta odgovornih za javno zdravlje.

Ključne reči: *Echinococcus granulosus*, seroincidencija, seroprevalencija