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EPIDEMIOLOGY OF HCV INFECTION IN CENTRAL AND EASTERN EUROPE

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ABSTRACT

AIM OF STUDY is the estimation of prevalence of HCV infection in fourteen Central and Eastern European countries (CEEC).

MATERIAL AND METHODS. This review describes the comparative data of persons possessing anti-HCV antibodies and persons with HCV viremia (% of population and number) in fourteen Central and Eastern European countries (CEEC). The study was performed according to data on the ≥15 years of age populations obtained from the Statistical Offices of the countries.

RESULTS. The prevalence of anti-HCV in populations varied between 0.27 and 3.5%. The lowest values were reported from Kosovo, Hungary, Germany and the Czech Republic; 0.3-0.6%. The highest values of anti-HCV antibodies were noted in Latvia, Lithuania and Romania; 2.4, 2.85 and 3.5%, respectively. From eight countries the percentages of persons with HCV viremia were available (0.2-3.5%).

CONCLUSIONS. The paper gives an estimate of the number of people infected with HCV in the general population of 8 countries from the CSEEC region. This number is approximately ~1.16 million.

Key words: *Hepatitis C, anti-HCV antibodies, HCV-RNA, prevalence in general population and first-time blood donors; countries of Central and Eastern Europe*

INTRODUCTION

Hepatitis C infection is an important problem of public health, recognized by the WHO (1). Due to the long-term asymptomatic HCV breakthrough, the disease is very dangerous. The consequences of unrecognized infection, in most cases, are liver cirrhosis and hepatocellular carcinoma. It is estimated that 10-40% of Europeans are not aware of their disease, and they are a potential source of infection for other persons (2). The prevalence of anti–HCV antibodies in Europe is uneven and fluctuates between 0.4% and 6%, but in some regions of Italy they reach up to 20% (3).

An estimation of the number of people infected with HCV in the population is very important for the health policy of the given country. This allows planning of preventive and therapeutic interventions, and also allows determination of the need for treatment of infected persons. According to recent exact determinations, there are 115 mln persons with anti-HCV, a number which is lower than that quoted by the WHO (130–150 million people with hepatitis C); and 80 mln HCV viremic individuals in the world; this number has not been reported before (4). Several papers have appeared recently, with the aim of comparing the prevalence of anti-HCV antibodies between different countries, but they do not deal specifically with CEEC region (4-7). According to Wikipedia and data from the World Bank this region is composed of 18 countries (8-9). The countries are: Estonia, Lithuania, Latvia, Germany, Poland, Czech Republic, Slovakia, Hungary, Romania, Bulgaria, Slovenia, Croatia, Albania, Bosnia and Herzegovina, Kosovo, Macedonia, Montenegro, Serbia and Belarus, in some descriptions. (Fig. 1.)

The purpose of this review was to estimate: 1) the number of adults who had contact with the virus (anti-HCV positive), and 2) the number of persons actually infected with HCV (presence of HCV RNA) in 14 European countries of the Central and Eastern European region, for which the data were available, but which had not been studied systematically yet. Central and Eastern Europe includes countries which share common

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Figure 1. Map of Central and Eastern Europe

cultural and historical roots, especially sharing a past as a buffer to socialist republics of the Soviet Union, or as a component part of the Soviet Union.

METHODS

The following terms were used for the PubMed search: **hepatitis** C AND (**name of the country**) AND **prevalence** AND **viremia**. The papers selected represented unique data for the particular countries. Full original papers were obtained for 11 countries. However, in the Table I letter to the editor containing original results was also included, as well as conference material with the original data (Romania and Slovakia respectively). No original data were found for Belarus and Czech Republic, thus review papers were the source of data. Papers rejected did not contain data on the prevalence of HCV, but concerned only HCV genotypes in the country (Macedonia).

In the present study, the prevalences of anti-HCV and/or HCV RNA were estimated on the basis of published data, compared with the number of the adult population. The population of each country was taken from Statistical Office: the Main Statistical Office of Poland, the Czech Statistical Office, the Statistical Office of the Slovak Republic, the Hungarian Central Statistical Office, the National Institute of Statistics of Romania, the National Statistical Institute of the Republic of Bulgaria, the Croatian Bureau of Statistics, the Statistical Office of the Republic of Serbia, the Federal Office of Statistics of Bosnia and Herzegovina, the Kosovo Agency of Statistics, the Department of Statistics of Lithuania, the Central Statistical Bureau of Latvia, the Federal Statistical Office of Germany and the Ministry of Statistics and Analysis of Belarus. The number of the adult population (≥18 years) were not available for all the countries analyzed in this study, and therefore we adjusted the obtained values to give the population from 15+ years. Therefore, the data on the prevalence of anti-HCV and / or HCV RNA was related to a population of persons ≥15 years of age. Adolescents between 15 and 17 years of age, as the population of adults under take actions and social behavior, which may contribute to an increased risk of HCV infection. In Kosovo the total population was taken, because a value for the population from 15+ years was not found in Kosovo Agency of Statistics for 2003.

The following methods were used to detect anti-HCV antibodies: immunochemical (ELISA, EIA, CMIA), immunochromatography tests or Western Blot. The genetic material of the virus (HCV RNA) determination was performed by PCR Cobas Amplicor ver 2.0 and Real Time PCR.

RESULTS

The results of this study are presented in the Table 1.

The prevalence of anti-HCV in the populations of countries within CSEEC varied from 0.27 to 3.5%, the range expected for Europe. The percentages of persons with HCV viremia amounted to 0.2-3.5%. The following studies were performed on the adult general population: Germany, Czech Republic, Croatia, Romania, Belarus, Lithuania and Latvia. The exceptional country which estimated values obtained from blood donors in the general population was Bosnia and Herzegovina. Two countries reported the prevalence of anti-HCV antibodies in voluntary blood donors: Kosovo and Hungary. Two countries performed their studies on patients who were admitted to hospital because of diseases other than viral hepatitis: Slovakia and Bulgaria. The results obtained in the study of patients from emergency wards in Poland, were standardized to general population 18+ years old.

DISCUSSION

The original HCV prevalence in the general population was not available for two countries: the Czech Republic and Belarus. In the Czech Republic there were no population studies, nor a national screening programme for hepatitis C. However, an expert panel defined the prevalence of anti-HCV in the population as 0.6% and the percentage of persons with viremia as 0.4% (5-6). The next difficult country is Belarus, for which we did not have original data, but values taken from the review paper (4).

Data described for the seroepidemiology of HCV in Germany showed the prevalence of antibodies in 0.3% and HCV-RNA in 0.2% of the big group of ~7000 persons tested (13). However, there are also two review papers available with show higher percentages of anti-HCV: 0.4% and 0.5% among studied individuals (5-6); and HCV RNA in 0.3% (6). As a source of data for the Table 1 the original paper from Robert Koch Institute in Berlin was chosen (13).

As a comment to Table 1, we have to add that there are two papers from Poland (3,23); one was included in the Table 1. The first study was undertaken on 4822 subjects from orthopedic and traumatic wards which were chosen at random (3). Study was performed with double-step ELISA for anti-HCV, i.e. positive sample was repeated twice to obtain the second positive result (3). The second study investigated 26057 patients (suffering from diseases other than viral hepatitis) and health care workers; the study group was not randomized. Single-step EIA was used in this study and gave

Table I. Demographic data and hepatitis C infection indices in Central and Eastern European countries

	Country and year(s) of study	Population studied	Presence of anti-HCV antibodies [%]	Presence of HCV RNA [%]	References	Number of persons with anti-HCV	Number of persons with viremia
1	Belarus (2013)	general adult population	1,3	0,9	(4)	104046	72032
2	Bosnia and Herzegovina (2009)	voluntary first time blood donors (general adult population - estimated)	0,27 (0,29-0,89)	nd	(10)	5230 (5618-17240)	nd
3	Bulgaria (2010-2011)	patients (for causes other than viral hepatitis)	0,7	0,35	(11)	45307	22653
4	Croatian (2010-2011)	general adult population	0,9	nd	(12)	33731	nd
5	Czech Republic (2012)	general adult population - estimated	0,6	0,4	(6)	53735	35823
6	Germany (2008-2011)	general adult population	0,3	0,2	(13)	212431	141621
7	Hungary (2007-2009)	prison`s staff	0,5	nd	(14)	42692	nd
8	Kosovo (2000-2003), part of Serbia; independent 2008	voluntary first time blood donors	0,3	nd	(15)	6048*	nd
9	Latvia (2010)	general adult population	2,4	1,7	(16)	46541	32967
10	Lithuania (2010)	general population; cross-sectional survey of random anonymous volunteers	2,85	nd	(17)	73821	nd
11	Poland (2010)	patients hospitalized in emergency wards, for causes other than viral hepatitis (standardized to general adult population)	0,91 (0,86)	0,6 (0,59)	(3,18)	278998	191405
12	Romania (2006-2008)	healthy adults	3,5	3,5	(19)	638364	638364
13	Serbia (2005)	patients, blood donors and healthcare staff of a hospital	0,5	nd	(20)	40600	nd
14	Slovakia (2010-2011)	patients >=15y.old (cause other than viral hepatitis)	1,41	0,7	(21)	64426	31984

* population, total; nd - not done

a relatively higher level of anti-HCV antibodies in the studied group – 1.9%; while HCV RNA was found in 0.6% of 18233 subjects who completed a questionnaire (23).

The lowest values of anti-HCV prevalence were reported from Germany, Kosovo, Hungary, Serbia and the Czech Republic, i.e. 0.3-0.6%. Bosnia and Herzegovina had a low value of anti-HCV in voluntary blood donors (0.27%), but the estimate for the adult population ranges from 0.29-0.89%. However, the study of Kosovo was performed on voluntary first time blood donors, which is not representative of the general population (15). There is another study from Kosovo, performed on a sample of the general population and health care workers, which reported 0.5% of anti-HCV in the studied group (20). In Hungary, unique studied group, the members of prison staff were investigated (value for anti-HCV equaled 0.5%); this value, according to the authors, reflects the situation in the general population (14,24). Earlier, another study was performed on voluntary first time blood donors - anti-HCV was found in 0.4% of them (25).

A serological survey performed in 2001 in the Czech Republic showed a low prevalence of anti-HCV antibodies (0.2%), but the data were published 11 years ago (26). The data for the Czech Republic: prevalence of anti-HCV antibodies and HCV RNA in the population were taken from two review papers (5-6). In our study, we have obtained for the Czech Republic the absolute numbers of adult persons with anti-HCV: ~53,700 and persons with HCV RNA: ~35,800; while the respective numbers in the Bruggmann paper were: 60,000 and 42,000 (6). This example shows the importance of adjustment of the national prevalence of HCV indices obtained in the 'adult population' into those for the real adult population as registered in the Statistics Office. At this point, the other difficulty appeared, that age groups which suited our demographic data, start from 15 years in the Statistics Offices, but not from 18 years (considered as the beginning of adulthood). The lower numbers obtained by us in comparison to the Bruggmann study originate from adjusting the HCV prevalence for the national population aged 15+.

In some countries the prevalence of anti-HCV in the general population was converted from values in blood donors, but no mathematical formula was introduced for counting; that is why these data should be treated with caution (7,10,11). Data from Bosnia and Herzegovina are examples of such estimations of values from blood donors to the general adult population (10).

The highest values of anti-HCV antibodies in the population, noted in this review, were in Latvia, Lithuania and Romania (2.4-3.5%). This last country is one of these for which we have two values, although not very different. The study quoted in the paper of Gower

et al., gives two values: 3.2% for anti-HCV in the adult population, and 2.9% as the adult viremic population (4). However, the original Romanian study quoted in the Table 1 determined the presence of anti-HCV in 3.5% of adult population, while the presence of HCV RNA also in 3.5% of adults, which was rather unexpected, because all the individuals with anti-HCV appeared as viremic (19). Such a situation was not observed in other countries studied so far. Romania has a relatively high emigration rate; thus, Romanian authors express the view that emigration from this country may cause HCV disease to be a burden in the immigrants' destination (19). Certainly, there are many known factors which may influence the increased prevalence of the anti-HCV/viremic state in a population, including hygiene of medical units (nosocomial causes of infection), intravenous drug use, frequency of tattooing, acupuncture and piercing, etc.

In contrast, while discussing the Kosovo results the authors concluded that there are few people living in a high-risk environment for HCV infection in this country (15).

Moreover, only the adult layer of the society was evaluated here in terms on hepatitis C antibody positivity and infection. Pediatric studies should be reviewed separately.

We are aware that the proper diagnosis of HCV should include serological anti-HCV testing, followed by HCV RNA determination (1), with a sensitivity of 25 IU/ml (27). The presence of HCV RNA indicates that the person with anti-HCV antibodies is currently infected with hepatitis C virus. The second step of diagnosis (detection of HCV RNA) was performed only in 8 countries.

The estimation of the number of infected persons determines the treatment policy of the country. As can be approximated from Table 1, the number of adult people infected with HCV from 8 countries (which performed HCV RNA determination) amounts to 1.16 mln. The range of HCV infected persons to persons possessing anti-HCV is usually between 31 to 67%. This is a broad range which does not allow counting the number of persons who should be treated in countries where the HCV RNA determination was not done.

The difficulty of this kind of review originates from the fact that data from different countries concerned various groups of the population. Also, a different epidemiological approach and diagnostic methods were used by authors (2), but standardization of methods is constantly conducted by WHO. To this end, WHO undertook efforts and created guidelines to unify the methodology of HCV determination screening and treatment (28). The report gives examples of countries, like Scotland, where HCV diagnostics is very effective and penetrates groups with a high risk of infection (28).

In the present review we summarized data of the prevalence of HCV in 14 counties of CEEC. However, data from Albania, Estonia, Macedonia, Montenegro and Slovenia were not available.

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