ADDRESSING HCV INFECTION IN EUROPE: REPORTED, ESTIMATED AND UNDIAGNOSED CASES

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SUMMARY

The hepatitis C virus (HCV) is a major public health problem due to its high prevalence, high rate of onward transmission and health complications. As many as 85% of people infected with HCV may go on to become chronic carriers of the disease with the risk of developing liver cancer or cirrhosis. At present, it is the most common cause of chronic liver disease and liver transplantation in a number of countries, with an estimated 250,000 people dying annually from HCV-related causes.

Despite the magnitude of the problem, the virus does not receive adequate attention from either the general public or from health policy-makers. This study assesses HCV prevalence from both estimated totals and undiagnosed cases in selected European countries. Secondary sources were assessed and experts in 17 European countries were interviewed about HCV prevalence, reporting strategies and transmission.

Available data suggest that only between 10% and 40% of people with HCV in Europe are aware of their infection (up to 90% of the prevalent pool are undiagnosed in such countries as Germany or Poland). Though the virus affects people of all ages, races and backgrounds, in Europe, between 20% and 90% of new HCV cases have been identified among past or current injecting drug users (IDUs). It is of the utmost importance to improve both public awareness and access to early testing and counselling, with the goal of prevention of further infections, maintenance of health and provision of treatment to avoid cirrhosis and liver cancer.

Additionally, as previous studies in central and eastern Europe show, evidence-based measures to prevent and manage HCV among IDUs, where most current transmission is concentrated, remain limited. Therefore, there is a strong need for intensified advocacy to put HCV higher on both public health and harm reduction agendas.

Key words: health policy, hepatitis C – prevalence, drug use, central and eastern Europe, Europe

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INTRODUCTION

In recent years, the hepatitis C virus (HCV) has emerged as a major threat to public health worldwide. The global disease burden of HCV is staggering, with an estimated 180 million people infected with the virus (1). In contrast, it is estimated that 33.2 (30.6–36.1) million individuals are living with the human immunodeficiency virus (HIV) worldwide (2). The prevalence of HCV in the general population varies substantially, from 0.5% in northern Europe to 3% in Mediterranean countries (3), and reaching over 13% in Egypt, for example (4). However, the data on HCV prevalence in Europe are often very limited.

The epidemiology of HIV and hepatitis coinfection is also significant, as both viruses share common routes of transmission (sharing of unsterile injecting equipment). One crucial difference, however, is the greater infectivity of hepatitis. HCV is about 10 times more infectious than HIV (5) and, consequently, exposure carries greater risk of infection. Public awareness is also low, in part because HCV often presents no symptoms. The combination of these factors contributes to the fact that the vast majority of infected people are unaware of their status.

However, HCV presents an important public health problem globally. Without diagnosis and treatment HCV causes chronic infection in up to 85% of those infected, and among those chronically infected, cirrhosis may develop in 5 to 20% of cases (6). The scale and urgency of the HCV problem is made alarmingly clear in mortality statistics, with an estimated 250,000 people dying annually of HCV-related causes (7). It is already the most common cause of chronic liver disease and the most common reason for liver transplantation in US and western Europe. Furthermore, morbidity and mortality rates from HCV infection are rising and are expected to continue to rise in the coming decades (6).

This study analyses the available data on HCV prevalence in selected European countries and estimates the proportion of undiagnosed people with HCV.

MATERIALS AND METHODS

Information on reported HCV cases, the estimated prevalence both in the general population and in different risk groups, and the estimated number of undiagnosed cases was collected in three stages:

1. Assessment of existing secondary data from international agencies and organizations: Centers for Disease Prevention and Control (CDC), European Association for the Study of the Liver (EASL), European Centre for Disease Prevention and Control (ECDC), European Liver Patients Association (ELPA), European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), Viral Hepatitis Prevention Board (VHPB) and WHO Europe were contacted and/or information available online was assessed.
2. Literature review: A search was conducted through the online versions of *Journal of Hepatology*, *Journal of Gastroenterology & Hepatology*, *European Journal of Gastroenterology & Hepatology*, *Hepatology International*, *Gut – An International Journal of Gastroenterology & Hepatology* and *Comparative Hepatology*. Additionally, a more general search on hepatitis in Europe was carried out through PubMed, and official reports of national healthcare agencies available in English or Russian were searched.
3. Questionnaire: A standardized questionnaire was developed and sent to experts in 25 European region countries: WHO country offices, national health protection agencies, hepatology and patient associations/organizations, NGOs and harm reduction programmes, with the goal of collecting data on HCV prevalence in the selected countries.

The countries were selected on the basis of geographical location, with the goal of representing the different subregions of Europe (western, central and eastern Europe) while also taking into account the varying levels of economic and social development. As a result, information was obtained from 17 countries: Armenia, Belarus, Bulgaria, the Czech Republic, France, Georgia, Germany, Hungary, Italy, the Netherlands, Lithuania, Poland, Romania, Russia, Spain, Ukraine and the United Kingdom.

RESULTS

Available data for HCV confirms that HCV prevalence varies substantially among countries and suggests a higher prevalence in the countries of central and eastern Europe (Table 1), reaching 4.9% in Romania and 6.7% in Georgia. In western Europe, the highest estimated prevalence is in Spain (2%) and Italy (3.07%).

However, current HCV prevalence data in most European countries is unrepresentative and thereby uncertain. In order to determine the number of people undiagnosed we calculated the difference between reported cases and estimated cases, if not indicated otherwise in the footnotes for Table 2.

The availability and quality of national HCV reporting, resources and screening varies dramatically from country to country, but overall there are significant inconsistencies that exist in HCV awareness and diagnosis across Europe. Only between 10% to 40% of people with HCV know about their infection in such diverse countries as the Czech Republic, Germany, the Netherlands, Poland and the United Kingdom (for more details see Table

Table 1. *HCV prevalence in selected European region countries*

Country	Population (millions) [1]	Estimated number of cases in general population [2]	% of total population
Bulgaria	7.8	84,240	1.08 [3]
Czech Republic	10.2	20,400	0.2 [4]
France	61.0	500,000 – 650,000	0.08 – 1.07% [5]
Georgia	4.4	295,000	6.7 [6]
Germany	82.4	400,000 – 500,000 [7]	0.48-0.6
Hungary	10.1	60,600	0.6 [8]
Italy	58.6	1.800,000 [9]	3.07
Lithuania	3.4	50,000 – 70,000 [10]	1.5
The Netherlands	16.4	13,120 – 65,600	0.08 - 0.4 [11]
Poland	38.1	750,000 [12]	2.0
Romania	21.5	1.058,000 [13]	4.9
Russian Federation	142.4	6.000,000 [14]	4.2
Spain	43.5	800,000 – 1.000,000	2 [15]
Ukraine	46.6	310,000 – 700,000	0.7 – 1.5 [16]
United Kingdom	60.4 (England, Wales and Scotland)	231,000 (144,000 – 381,000) [17] 466,000 – 900,000 chronic infections in England and Wales [18] 50,000 in Scotland [19]	0.52% - 1.49% [20]

[1] The latest information is taken from the World Bank, World Development Indicators database, 2008.
[2] The number of estimated cases is calculated based on the % of HCV prevalence in general population if not indicated otherwise in the footnotes to particular countries.
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[6] Personal correspondence with D. Otiashvili, "Alternative Georgia", August 2007.
[7] The number of estimated cases is provided by Robert Koch Institute (National Public Health Institute, Germany) and is included here, since corresponds to more updated information. According to other estimates, HCV prevalence in general population is 0.4 – 0.7%, for example as published in Thierfelder W, Hellenbrand W, Meisel H et al.: Prevalence of markers for hepatitis A, B, and C in the German population. Results of the German National Health Interview and Examination Survey 1998. Eur J Epidemiol, 2001; 17: 429-35.
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[10] The estimation is made on the projection of estimated HCV cases in the country – 400,000–500,000. Personal correspondence with A. Ambrozaitis, Department of Infectious Diseases and Microbiology, Vilnius University, August 2007.
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[12] Personal correspondence with J. Cianciara, Department Hepatology and AIDS, Institute of Infectious and Parasitic Diseases. Warsaw Medical University, August 2007.
[13] The % is based on the number of estimated cases – 1,058,000 as reported in the First National Campaign for Hepatitis C. http://www.afladec.ro (in Romanian).
[14] The estimation of people living with HCV in Russia was never done but by comparing with other viral infections experts estimate that the official number of reported cases should be multiplied by *at least* 3, therefore according to the number of reported cases – 2,000,000, the estimated HCV cases in country can be as high as around 6.000,000.
[15] The % corresponds to 800,000 – 1,000,000 people. VHPB. Hepatitis C epidemiology in Spain, including molecular diagnosis and prevalence in dialysis units. Viral Hepatitis, 15–2, Viral Hepatitis Prevention Board (VHPB), 2007.
[16] Shaginian VP. The role of perinatal transmission in hepatitis B and C prevalence in Ukraine and the improvement of epidemiological surveillance. Kiev, 2007 (in Russian).
[17] HPA (2006) Hepatitis C in England: An update 2006. London: Health Protection Agency Centre for Infections (HPA), December 2006. The number corresponds to prevalence in people aged 15–59, additionally estimated 30,000–40,000 under 15 and over 60 can be anti-HCV positive.
[18] The UK vs. Europe: Ready to Fight Back a joint report by Hepatitis C Trust and University of Southampton, May 2005.
[19] This number can be different now, since the estimation done for 2004, with total 16,500 reported cases at that time (making about 67% of all cases undiagnosed in 2004 with about 75% of chronic hepatitis C carriers, in Hutchinson SJ, Roy KM, Wadd S, Bird SM, Taylor A, Anderson E, et al. Hepatitis C virus infection in Scotland: epidemiological review and public health challenges. Scottish Medical Journal. 2006;51:8-15.
[20] The % also includes the average (35,000) of estimated people under 15 and over 60 living with HCV.

Table 2. *Undiagnosed cases of HCV in selected European countries*

Country	Reported number of cases	Estimated number of cases in general population	Estimated number of undiagnosed cases
Czech Republic	7,372 [21] (cumulative, 1993–2006)	20,440	13,068
France		365,055	Around 56% of cases are identi ed, corresponding to about 44% undiagnosed in 2005 [22]
Germany	47,235 [23]	400,000–500,000	352,765–452,765
Italy	Not available	1.800,000	500,000–700,000 [24]
Lithuania	3,000–3,500 [25]	50,000–70,000	47,000–67,000
Poland	20,000 [26]	750,000	730,000
United Kingdom			
England and Wales	66,264 [27]	231,000 (144,000–381,000) 466,000–900,000 chronic infections	164,736 (194,736–204,736) 399,736–833,736
Scotland	22,073 [28]	50,000	27,927

[21] A cumulative reported cases 1993–2006, personal correspondence with V. Řehák, August 2007
[22] Estimated percentage of people knowing their status in 2005. The UK vs. Europe: Losing the fight against hepatitis interim report by Hepatitis C Trust and University of Southampton, 2005.
[23] Robert Koch Institute (National Public Health Institute, Germany) data, based on Epidemiological Bulletin 46/2006, cumulative for 2001–2006, http://www.rki.de.
[24] Estimation of undiagnosed HCV cases is based on the projection of undiagnosed cases of HCV in health care workers, see Proietti L, Origlio A, Sandona PB, Duscio D, Malaguarnera M. Prevalence of HCV in health care workers in Southern Italy, Clin Ter. 2003 May-Jun;154(3):159-62.
[25] Data corresponds to the number of cases reported in health care centers providing hepatitis C treatment in Lithuania (5 centers) up until September 2006, personal correspondence with A. Ambrozaitis (Department of Infectious Diseases and Microbiology, Vilnius University), August 2007.
[26] Personal correspondence with J. Cianciara (Department Hepatology and AIDS, Institute of Infectious and Parasitic Diseases Warsaw Medical University), August 2007.
[27] A number of cumulative reported cases between 1992–2006 by Health Protection Agency.
[28] Health Protection Scotland. Weekly Report, 41-2007/22, June 2007, Health Protection Scotland (Scotland); 2007.

2). For example, data from the United Kingdom illustrates that almost two-thirds of estimated HCV cases are undiagnosed (official figures show 88,337 diagnosed and 199,736 undiagnosed, while other sources have estimated the number of undiagnosed cases between 399,736 and 833,736). In some European countries, it is estimated that more than 90% of people who are infected with HCV have not been diagnosed; for example, in Poland the estimated number of cases in the general population is 750,000, while only 20,000, or barely 3%, of cases have been diagnosed; in Germany there are an estimated 400,000–500,000 HCV cases with around 35,000–450,000 people can still be unreported. According to the National Hepatitis Centre in the Netherlands, there are about 60,000 people with chronic hepatitis C (0.37% of total population), with around 5,000 to 10,000 aware of their status (8).

In most of the countries assessed, the infection primarily affects men and is concentrated in individuals under the age of 45. An increasing number of cases have been identified in young adults

(aged 15–30), as reported from Belarus, the Czech Republic, Germany, Poland, the Russian Federation, Spain and the United Kingdom.

In countries with a high prevalence in older age groups, such as Italy – where 60% of estimated HCV cases are in people older than 65 years – therapeutic injections 30–50 years ago probably had a substantial role in HCV transmission (9). A review of data for 1997 also showed that diagnostic or treatment procedures in hospitals were among the key transmission routes of HCV in the countries of central and eastern Europe in the late 1990s (e.g. approximately 59−65% of cases in Poland, 59% in Latvia and 46% in Lithuania) (10).

Since the introduction in 1989, or shortly thereafter, of blood- and blood-product-screening in most European countries, the predominant source of new HCV infections has now become injecting drug use. This is particularly the case in countries where most newly identified cases occur in young adults. The percentage of newly diagnosed cases that can be attributed to either active injecting drug users (IDUs) or people with a history of injecting in European countries varies from 20% to 89% (11–14).

The data from countries also showed that HCV prevalence varies substantially within countries. For example, in Italy prevalence in different regions varies from 3% to over 20% (9); in different parts of Poland it varies from 1.2% to over 15% (15).

DISCUSSION

Due to the diverse surveillance and reporting systems existing in countries and the fact that HCV is not a notifiable disease in some countries, the number of reported cases does not always correspond to the number of diagnosed cases. This should be taken into account when interpreting the number of undiagnosed cases.

Determining the prevalence of HCV infection is difficult because most acute infections are asymptomatic. Even in countries where HCV is notifiable by law, the number of newly diagnosed cases remains underreported. Furthermore, some countries (Hungary, Italy, Lithuania and Ukraine) do not report chronic hepatitis C cases, which means that there is lack of information about how many people are at risk of developing chronic liver diseases and how many people will eventually need hepatitis C treatment.

More data on the estimated prevalence of HCV infection is available from population-based studies performed in western Europe than for central and eastern Europe.

Awareness of HCV in the general population and among risk groups is low. This is demonstrated not only by the dramatically low proportion of people aware of their infection status, but also by the fact that most newly reported cases of HCV are of chronic hepatitis C infection, indicating a lack of timely diagnosis. For example, data from Belarus showed that half of the reported cases in 2006 were for chronic hepatitis C (16); in Georgia this number rises to 80%. Low awareness about the infection not only puts many people at risk of long-term liver damage, it also means that they may unknowingly transmit the virus to others.

Greater commitment from policy-makers, health care officials and health care providers is needed to raise awareness about HCV and to facilitate and improve early diagnosis. France is a clear example of the positive impact that public awareness campaigns can have. Currently, an estimated 56% of those infected know that they have the infection, compared with 24% in 1994 (17).

It is equally important to improve diagnostic services for HCV and to make testing and counselling accessible and affordable. Though testing availability, access to health care and diagnostics policies were not considered in the framework of this study, a recent study on HCV in central and eastern Europe suggests that such services are not readily available, especially for risk groups such as IDUs (18).

Current transmission routes also suggest that HCV has become an increasingly important health issue among IDUs. Due to the particular efficacy of transmission of HCV through the sharing of infected injecting equipment, it is estimated that after 5 years of exposure, the majority of IDUs may acquire HCV (19). Therefore, the prevalence of HCV among IDUs is extremely high, reaching up to 80 to 90% in some European countries (18). Despite being the group with the highest risks of HCV transmission, there is inadequate prevention, treatment and care for IDUs – especially across the new European Union member states, Russia and other eastern European countries. An assessment focusing on HCV among IDUs showed that in most of the countries in central and eastern Europe, IDUs do not have access to testing and counselling. HCV services are poorly linked to established health services for IDUs and there is a generally low level of HCV research within IDU communities and into ongoing risk behaviours (18). IDUs are also systematically denied the HCV treatment, care and support that they need.

International guidelines clearly state that active drug use cannot be an exclusion criterion (1, 20), yet in at least 9 out of 13 countries of the region drug use is identified as a contraindication to HCV treatment. One of the few exceptions is Slovenia, where drug users with health insurance can access treatment and be treated by multidisciplinary teams of specialists in infectious diseases and addiction treatment (18). Therefore, effective management of HCV in Europe is not possible without a greater commitment to address the needs of IDUs, including a scale-up of harm reduction services and the linking of HCV testing and counselling to existing harm reduction services.

HCV coinfection with HIV is also common among active and former IDUs, who may acquire both viruses from injecting drugs. Such coinfection reduces the chance of recovery from acute HCV, compromises the effectiveness of existing HCV treatment and accelerates the progression of HCV infection to cirrhosis and liver failure (21). Liver disease is also becoming one of the leading causes of death in people living with HIV and AIDS (1). In European countries high HCV prevalence among IDUs living with HIV has been reported from Russia (93% among HIV-positive IDUs in Togliatty) and Poland (90% among HIV positive IDUs in Bialystok); in Spain, three estimates ranged from 48% to 95% (18–22).

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