

## Review paper

# Epidemiology of HCV infection in the Central European region

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## Abstract

Opinion leaders in each of four countries in the Central European region summarize the available data on hepatitis C virus (HCV) epidemiology. The overall prevalence of anti-HCV antibody reactivity in this region varies between 0.2% and 2.1%, the most prevalent HCV genotype is GT 1. The commonest route of transmission is intravenous drug abuse at present.

**Key words:** hepatitis C virus, prevalence.

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## Introduction

Epidemiological characteristics of hepatitis C virus (HCV) infection differ significantly among different regions worldwide. This reflects many conditions including the historical context, social status, system of transfusion services and many others. On the other hand, the knowledge of epidemiological characteristics gives specialists the rational background for key decisions and recommendations, e.g. whether to perform the universal screening, how to perform such screening, which population or population subgroup is at risk and should be screened, which population should (or should not) be treated etc. This information is of particular relevance especially now, when many new highly effective but very expensive drug combinations are entering the market.

The purpose of this brief review is to provide such information and to compare epidemiological data in several Central European countries which recently established the Central European Hepatology Cooperative Group.

## Czech Republic

The prevalence of anti-HCV reactivity in the general population of the Czech Republic was published in 2001 by V. Němeček [1]. They evaluated more than 3500 serum samples and found anti-HCV reactivity in 0.2%. This is the only one serological survey which has been performed up today in the Czech Republic. Chlábek *et al.* performed a similar study in approximately 1500 samples collected between 2013 and 2015 and they found anti-HCV reactivity in 0.4% (personal communication, unpublished data). This study was not intended as a serological survey, therefore the method of sample collection was different.

It is obligatory for the physician who diagnoses the HCV infection as the first one to report this infection to the Czech EPIDAT system. This way the EPIDAT system registers approx. 800 cases of NEWLY reported HCV infection cases annually (Table 1). Approximately 200 cases out of all reported cases every year were reported as acute – the definition may vary, this is based on the reporting physician's decision.

**Table 1.** Reported cases of HCV infections (number of cases)

	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
HAV	322	132	128	1648	1104	862	264	284	348	673
HBV	361	307	307	306	247	244	192	154	133	105
HCV	844	1022	980	974	836	709	812	794	873	866
HEV	37	35	43	65	99	72	163	258	218	299

EPIDAT provides us also with the proportion of cases among intravenous drug users which is the only one risk factor to be reported in the system. The results are shown in Table 2.

EPIDAT does not register the HCV genotypes, so epidemiological data regarding HCV genotype are reported by investigators from large hepatological centers [2, 3]. Based on such reports we can conclude that the most prevalent HCV genotype in the Czech Republic is HCV GT 1b (80-85%) followed by HCV GT 3 (3a mostly, 10-15%).

## Slovak Republic

Information about the prevalence of HCV infection in the general population in Slovakia is based on results of two larger studies. In the first study 3,608 collected sera, within two serological surveys in the years 1997 and 2002, were tested for anti-HCV and HCV RNA. The antibody prevalence was 1.52% and HCV RNA positivity was confirmed in 0.67% [4]. More recent data are available from the EPID study, a prospective multicenter epidemiological study performed in 2010-2011. In total 4,598 adult patients were tested with 1.41% anti-HCV prevalence and 0.70% HCV RNA positivity [5]. Similar results of both studies suggest an estimated number of 35,000 HCV infected persons in Slovakia. On the other hand, according to the Slovak National Institute of Health, only less than 4,000 HCV positive cases were reported between 1990 and 2014 in Slovakia, so most of the infected patients remain undiagnosed. The HCV genotype 1b was identified as the most common, followed by genotype 3a, other genotypes (including 1a) are rare [6].

The EPID study showed a significant difference in anti-HCV prevalence according to ALT activity. Patients with elevated ALT had a 3.8 times higher prevalence than those with normal ALT ( $p < 0.001$ ), so ALT

seems to be an appropriate warning sign of HCV infection [4]. Also these results underline the problem that the examination of ALT is not included into routine checkups of general practitioners in Slovakia. An additional fact related to ALT contributing to a low diagnosis rate of HCV infection is a delay of the diagnostic process. An inadequately long time, reaching 6.5 years between first time documented ALT elevation and beginning of the antiviral treatment, was observed in a cohort of 178 patients. In most cases, the underestimation of relatively low ALT values ( $ALT < 2 \times UNL$ ) in asymptomatic patients was the main reason for this delay [6].

In order to estimate the future epidemiologic situation, a disease progression model was designed. According to this model, HCV prevalence in Slovakia reached the maximum in the year 2005 and will decrease in the future. But the number of decompensated cirrhosis cases will rise for the next 20 years (peak around 2037), the number of HCC cases will rise for the next 25 years (peak around 2039) and a 35% increase in liver-related deaths as a result of HCV is estimated from 2013-2030 [7]. There are several strategies how to face this problem, including an increased treatment success rate by introducing new therapies and increased annual treatment rate with accepting the rational indications, but first of all it is the task to increase the diagnosis rate.

Former population-based or risk groups-based screening programs helped to improve the situation partially, however other new effective screening programs are needed. The projects cooperating with general practitioners focused on patients with elevated ALT, seem to be most promising.

In conclusion, Slovakia is a country with a relatively low prevalence of HCV infection, but the number of cases with advanced liver disease as a result of the HCV infection will increase in the next 20 years. The

**Table 2.** Reported cases of HCV infection among IVDU (number of cases)

	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
HCV	131	261	362	365	499	512	546	534	526	711	686	658

estimated number of HCV-infected people in Slovakia exceeds by far the number of patients diagnosed until now, therefore efforts should be made in particular to improve screening of the infection.

## Hungary

### Risk factors

Only few studies examined possible risk factors. Previous surgery, having more than three pregnancies, blood transfusion and tattooing were associated with a HCV infection [8, 9]. High rates of HCV infection in the IDU population also indicate IDU as a risk factor [10], although the rates of IDU in Hungary are reportedly lower than that in other European countries [11]. A recent study showed 2.1% anti-HCV positivity among healthcare workers.

### Prevalence

Limited national data are available from the National Centre for Epidemiology in Hungary.

Based on a national seroepidemiological study in 2000 by the National Centre for Epidemiology in Hungary, there were estimated 60 000-70 000 HCV cases in Hungary, which represented 0.6-0.7% of the population [10]. In 2001, a study of 477 hospital workers found a prevalence of 2.7%, indicating that occupation could be a potential risk of infection [12]. A large blood donor study in south Hungary in 2001 indicated that the prevalence of HCV in 45 719 blood donors was 0.4% [8]. Earlier blood donor studies reported slightly higher prevalence rates. One reported a prevalence of 0.73% in 15 864 blood donors [9]; another screened 9707 blood donors and found a prevalence of 0.53% [13]. Studying 120 children who received one or more blood transfusions before implementation of anti-HCV screening, a rate of 1.7% was observed [8]. Barna *et al.* [9] found that prevalence increased with age. Mihaly *et al.* [12] also reported an increased prevalence with age, from 0% in those < 21 to 9.5% in those older than 50 years. According to the Drug-Focus Point reporting system, the prevalence of HCV is increasing among people who inject drugs (PWID) [14]. This is also reflected during the screenings done in the prisons (unpublished personal data of the author).

### Diagnosed incidence

The number of acute cases per 100 000 inhabitants decreased slightly from 0.4 in 2001 to 0.2 in 2005 [10, 15]. Mainly symptomatic acute HCV cases are report-

ed via the national communicable disease reporting system [10].

## Genotype

Genotypes are quite different according to the mode and time of acquiring the infection. Among the people infected before 1993 via blood and blood products, the genotype is almost exclusively 1b. In turn, the most prevalent recently infected PWIDs genotype is 1a and the remaining is about equally distributed between 3 and 1b [14].

## Poland

Broad access to modern therapies has raised the need for proper assessment of HCV distribution in the population of each country. Seroprevalence of HCV in Poland was assessed in a number of studies. Results of the largest Polish study were published in 2011 by Flisiak *et al.* Approximately 26 000 persons were screened and anti-HCV antibodies were identified in 1.9% of individuals [16]. Next year Godzik *et al.* published results of screening of 4822 persons and found seropositivity in 0.95% [17]. The difference was mainly a consequence of using single step ELISA versus double step test. However, the most important findings were exactly the same: 0.6% of examined population were viremic (HCV-RNA-positive). In Flisiak study, groups of higher anti-HCV prevalence were identified. Males (2×), urban citizens (2×), people with a history of more than 3 hospital admission (2×), with blood transfusion before 1992 (3×) and intravenous drug users (7×) had been considered at higher risk of HCV infection.

These observations are in accordance with data and a general opinion that majority of chronic HCV cases are a result of blood-borne transmission, which means they were acquired in health care settings. Improvement of hygienic standards in hospitals, a low risk of vertical transmission and changes in narcotic use habits (dominance of orally administered drugs) cause a very low number of infections in infants and children. Analysis of HCV infections distribution according to age and sex shows the highest prevalence in younger males (between 30 and 60 years old) and older females (45-80 years old). These trends are similar to England and Sweden and differ from the situation in France and Spain.

In 2012 data about HCV distribution in most Polish regions were collected [18]. Genotype 1 is predominant in all regions, however the highest numbers are observed in the Western part of Poland. In North-Eastern regions, genotype 3 is present in more than 20%

of patients, whereas in central and western parts this genotype is less frequent. According to recent IFN-free therapies, this may be of great importance.

In 2014 the number of yearly registered new HCV infections exceeded 3500. It is almost 1000 more compared to previous years. In part it is a consequence of active screening campaigns, better health care providers and patients education, but also of a new case definition modified in 2014 and based on the definition accepted by the European Commission in 2012. The most important criterion is the presence of HCV-RNA or core antigen. This information shows how important methodology is for future screening strategies [19]. An increasing diagnostic rate together with broad access to modern efficient and safe therapies may only allow to control or even eradicate HCV infection.

## Conclusions

Our brief review summarizes the currently available information on HCV epidemiology in four countries of the Central European region. It also illustrates nicely that there are significant differences not only in HCV epidemiology itself but also, and maybe more importantly, in the way of data collection which seems to be rather heterogeneous. Nevertheless, we can conclude that the overall HCV prevalence in our region is low, the most prevalent genotype is HCV 1 but the number of HCV GT 3 cases is increasing, the main route of transmission nowadays is intravenous drug abuse. Data modeling in all countries also show that HCV infection will cause significant morbidity and mortality in our countries within upcoming decades. All these facts strongly force the authors as the opinion leaders in their countries to immediately act in order to diagnose and treat more HCV infected patients.

## Disclosure

Authors report no conflict of interest.

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