

The Prevalence and Risk Factors of Hepatitis C Virus Infection in Adult Population in Romania: a Nationwide Survey 2006 - 2008

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Abstract

Aims: This study was aimed at determining the seroprevalence of hepatitis C virus (HCV) infection in Romania and the possible risk factors and modality of HCV transmission. **Methods:** A nationwide cross-sectional survey among the adult population was conducted between 2006-2008 in Romania through a population multicenter stratified random cluster sampling. Serum samples from 13,460 subjects were tested with a 3rd generation ELISA and a standardized questionnaire concerning the socio-demographic characteristics and potential risk factors was used. **Results:** The prevalence rate of HCV infection in Romanian adult population was 3.23% with significant differences between the main geographical regions (Moldavia 4.25%, Wallachia & Dobrogea 3.35% and Transylvania & Banat 2.63%), as well as between different counties (maximum 7.19%, minimum 0.56%). Overall participation rate to the survey of the selected subjects was 74.69%. Risk factors for HCV infection were: blood/blood products transfusions ($p=0.0001$), previous surgery (elective and emergency, $p=0.0001$ and $p=0.043$, respectively), frequent hospitalizations ($p=0.0001$), injections at home ($p=0.0001$), accidents/trauma ($p=0.0001$), occupational hazard related to blood exposure ($p=0.025$), intravenous drug administration ($p=0.002$), a partner chronically infected with HCV/hepatitis B virus (HBV) ($p=0.046$), first sexual intercourse <18 years ($p=0.019$), familial exposure to HCV/HBV infection ($p=0.001$) or to chronic HBV/HCV liver disease ($p=0.001$), personal history of chronic HBV infection ($p=0.001$). HCV RNA positivity was detected in 91% of the anti HCV positive subjects. **Conclusions:** Overall HCV prevalence in Romania is 3.23%. Both nosocomial and non-nosocomial routes are implicated as risk factors for HCV infection.

Key words

Hepatitis C virus (HCV) – infection – epidemiology – prevalence – risk factors.

Introduction

With a global prevalence of 2%, hepatitis C virus (HCV) infection represents a major public health problem worldwide with significant geographical and temporal heterogeneity [1, 2]. The epidemiology of HCV infection in Europe is continuously evolving and epidemiological parameters such as prevalence, incidence, genotype distribution and risk factors have changed substantially during the last decade as a result of improvement in healthcare conditions, an increasing number of intravenous drug users (IDU) and immigration from endemic areas [3]. However, there is a scarcity of epidemiological data from several former communist Eastern European countries that joined the European Union after 2000 [4]. With the actual globalization and large-scale migration, the lack of a vaccine and a 50% of non-responders to state-of-the-art combination therapy, a better knowledge of the prevalence and risk factors of HCV infection from all regions can help to create primary preventive strategies for dissemination as the single measure to control HCV infection.

Although HCV infection represents a major public health problem in Romania, its prevalence in the general population and risk factors are largely unknown. A study performed in 2001 on 1,668 subjects evidenced a 6.28% prevalence rate of anti-HCV in 11 counties from Transylvania [5], confirming the endemicity of HCV infection in our country. In addition, HCV infection has been identified as the leading cause of chronic hepatitis (64%) and liver cirrhosis (59%) in Romania [6]. Moreover, based on a Markov decision model, it was estimated that prevalence of HCV-related liver cirrhosis and hepatocellular carcinoma will continue to increase in Romania from 88,124 and 1,708 cases in 2009 to 146,209 and 2,686 cases, respectively, in 2030 [7].

The scarcity of data and the degree to which they are out of date were the main reasons behind a nationwide cross-sectional survey aimed to determine the prevalence and risk factors of HCV infection in the adult general population in Romania.

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Study design and method

Study design

A nationwide cross-sectional survey was conducted among the adult population between 2006-2008 through a multicentre, stratified, random cluster sampling method. This study was designed as part of a collaborative project between Romanian gastroenterological associations and Roche Romania aimed at assessing the impact of hepatitis B virus (HBV) and HCV infections in Romania (ML 21277/2006).

Study area and subjects' selection

To construct the national probability sample, first we had to take into account the administrative division of the country into 41 counties and the municipality of Bucharest (divided into six districts), because all national statistics are collected on this basis. A multistage random cluster sampling was used to select the study population. An important demographic characteristic considered for this study is that ~45% of the population is living in rural areas. Therefore, two centers representing a two family physician (FP) praxis, one from an urban area and one from a rural area were chosen at random. The metropolitan area of Bucharest was represented by six urban centers, one for each district. The FPs were selected at random from the FPs' list that was provided by the national MEDINET network. The sample consisted of 200 randomly selected subjects aged between 18 and 69 years (average life expectancy for males in Romania), registered on the list of each selected FP. The final result was a number of 17,600 subjects from 88 centers (46 urban, 42 rural).

To invite the selected subjects to participate in the survey a letter was sent with standardized information regarding the study. The subjects who were not found or declined to participate were not replaced. A written informed consent was obtained from all subjects prior to enrollment.

The study was approved by the National Ethics Committee (4154/26.10.2006) and conformed to the ethical guidelines of the 1975 Declaration of Helsinki.

Blood testing and epidemiologic questionnaire completion

Blood samples collected from the study subjects were tested for anti-HCV antibodies by using a third-generation enzyme-linked immune assay (Kit EIAgen antiHCV antibodies, ADALTIS Italy, S.p.A.). The seropositive samples were further assessed for HCV RNA by polymerase chain reaction (PCR, limit of detection 15IU/mL).

Information on socio-demographic characteristics and the potential risks for HCV transmission was obtained using a structured questionnaire. Interviews were conducted by the FPs. Socio-demographic information included gender, age, area of residence, marital status, ethnicity, education and employment. The following risk factors for HCV infection were investigated: familial exposure to HCV or HBV infection (infected person in the household) or to chronic B or C hepatitis, personal history of chronic hepatitis B, anti-hepatitis B vaccination, personal history of medical invasive procedures (dental treatment, elective and emergency surgery, frequent injections at a medical

facility or at home, blood/blood products transfusions prior to 1995, hemodialysis, solid organ transplantation etc), tattooing, body piercing, acupuncture, attending beauty salons (unsterile cutting instruments), sharing toothbrush or blades, sexually transmitted diseases, accidents/injuries with serious trauma, occupational hazard, history of IDU, age at the first sexual intercourse, sexual risk behavior (sex with prostitutes or unknown people, men who have sex with men, >10 lifetime sexual partners), prison and time spent within, alcohol abuse. To take into account the regional particularities we introduced a question on regional affiliation, because historically the territory of Romania was divided into three main geo-traditional regions: Transylvania & Banat (16 counties), Wallachia & Dobrogea (17 counties and Bucharest with 6 districts) and Moldavia (8 counties).

Statistical analysis

The crude prevalence of HCV infection of different age, gender, ethnic, residential, educational levels was calculated with a 95% confidence interval (CI) for the national sample. When estimating the HCV prevalence by geographical regions and by county level, the samples were weighted for gender and age structure according to national sample structure. Univariate comparisons were performed using chi-square test, Fisher's exact test, and Wilcoxon rank sum test, as appropriate. Using multiple logistic regression, adjusted odds ratio (OR) for gender, age structure (on 10-year group, excepting the first and the last group) and area of residence, together with the corresponding 95% CI was determined for the majority of investigated variables. All statistical tests were two-sided and a level of $p < 0.05$ was used to indicate statistical significance. Statistical analysis was performed using the Stata 7.0 software.

Results

Out of the 17,600 subjects randomly selected across the country, 13,460 subjects signed the informed consent and were consequently enrolled in the study. Out of them, 276 subjects (~2%) were removed because of compromised blood samples or incomplete data collection and 38 subjects (0.3%) for inconclusive anti-HCV tests. Finally, the prevalence of HCV infection was assessed on 13,146 subjects, with an overall participation rate of 74.69 %.

Prevalence of HCV infection

Positive anti-HCV antibodies were detected in 425 subjects, 388 of them being replicative when further tested by PCR (91%). The prevalence of anti-HCV in the Romanian population was 3.23%, corresponding to approximately 489,000 individuals aged 18-69 years (95% CI, 445,000 to 538,000) chronically infected with HCV.

The lowest HCV prevalence of 2.63% was found in Transylvania & Banat region. Wallachia & Dobrogea showed a significantly higher value of 3.35% for HCV prevalence, presenting an increased risk for HCV infection, while Moldavia had the highest prevalence ratio of 4.25% as compared to Transylvania & Banat (Table I). The prevalence of HCV infection varied significantly, ranging from 0.56% in Covasna county (Transylvania) to 7.19% observed in Tulcea county (Dobrogea).

Socio-demographic characteristics of HCV-infected population

The study population consisted of 7,630 female and 5,516 male subjects. The HCV prevalence was higher among females (3.51% vs. 2.85%, $p=0.033$). The HCV prevalence for inhabitants of rural areas was 3.80% compared to 2.68% for subjects living in urban and metropolitan areas ($p=0.0003$). The mean age of participants was 45.3 ± 13.8 years. The prevalence of HCV infection increased markedly with age (Table I, Fig. 1). Among people aged 40-49 years, the OR for HCV infection was 1.87 (95% CI 1.22-2.86, $p=0.004$), while among those aged 50-59 years, the risk increased to OR=2.77 (95% CI 1.87-4.12, $p=0.0001$) and for those 60-69 years, the infection risk reached the value of OR=4.46 (95% CI 3.01-6.60, $p=0.0001$).

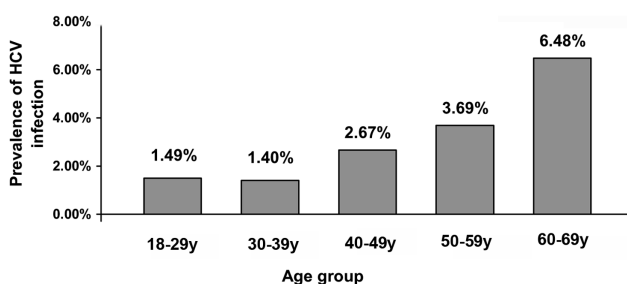


Fig 1. Evolution of prevalence of HCV infection with age group.

It is worth noting that Hungarian subjects living in their vast majority in Transylvania & Banat showed a low anti-HCV prevalence of 1.79% as compared to Romanian subjects. A higher HCV prevalence was observed among divorced or widowed subjects (5.53% and 6.46%, respectively). A negative association of HCV infection with years of education was found with OR=0.75 (95% CI 0.59-0.96, $p=0.023$) for people who had completed 12-13 years of education and OR=0.69 (95% CI 0.52-0.91, $p=0.009$) for those who had studied >13 years. The prevalence of HCV infection was not associated with employment reflecting the social status.

Risk factors of HCV infection

Table II shows the OR adjusted for gender, age and area of residence resulted from multiple logistic regression for potential risk factors of HCV infection (only statistically significant variables shown).

No association between HCV seropositivity and organ transplantation, hemodialysis, imprisonment, dental therapy, tattooing, body piercing, acupuncture, attending beauty saloons, sharing tooth brush or blades, history of sexually transmitted diseases, having multiple sexual partners and alcohol abuse was observed in the multiple regression analysis.

None of the possible risk factors was associated with the presence of positive HCV RNA in study subjects.

Among subjects infected with HCV, 4.47% of subjects were detected with concomitant HBV infection (HBsAg positive) and 36.94 % of subjects had previous exposure to HBV infection (HBcAb positive).

Discussion

HCV infection represents a serious problem worldwide, with 2% of the world's population chronically infected [1]. The burden of HCV infection in Romania is an area of great concern for at least three main reasons: 1) based on scarce and outdated information, Romania is considered the European country with the highest prevalence rate; 2) it represents one of the most important sources of migrant population towards Western Europe, altering the decreasing trend of HCV prevalence in this area; 3) there is an urgent need for national strategies for active detection and control of the silent epidemic of the HCV-infected population.

The prevalence and potential risk factors of HCV infection were examined for the first time by using representative national data. The sample population in this study represents the general population in Romania age-, gender-, education-, occupation-specific, residing in different geographical areas throughout the country. It is to note that most of the studies aiming at evaluating HCV epidemiology, even the recent ones, are usually cross-sectional in design and performed in selected populations (e.g. female patients, blood donors, patients with chronic liver disease, haemodialysed patients, IDU), which are not representative for the community or region in which they reside [8-10]. The multicenter, stratified, random cluster sampling method used in our study was preferred with the following argumentation: it ensures a higher participation rate, lower costs, easier logistics, a smaller operative team, and it might be finalized in a shorter period of time (1-3 years) [11]. 13,146 out of 17,400 contacted subjects agreed to be interviewed and sampled, giving a participation rate of 74.69%, which is in the range of previous studies (55-85.5%) [12-16]. The adopted sampling method, the sample size and the relatively high participation rates minimize selection bias, ensuring an accurate assessment of HCV prevalence in our study.

Considering the overall prevalence of 3.23% emerged from this study, HCV infection in adult population does not confirm the results of previous Romanian studies [5, 17-19]. Most of these studies are regional, out of date, whose major criticism consists of methodological biases (sample population, tests accuracy, data extrapolation). The present figure fits within the ranges of 2.5 - 3.5% reported for Southern Europe, one of the major area of recent migration of Romanian population [3].

There are significant differences of HCV infection between geographical regions, with the highest rate for Moldavia and the lowest one for Transylvania & Banat. The major factors influencing the geographical distribution of prevalence were hygiene, access to medical services vs. empirical treatments/treatments at home, and the proportion of population below the national poverty threshold. These figures from our country are consistent with differences in prevalence previously reported between Northern and Southern Italy (from 2.6% in north up to 16.2% in south) [20, 21].

The increasing rate of HCV infection by age in the present study is consistent with previous data in the literature [12, 20-

Table I. Prevalence of HCV infection by demographic characteristic and adjusted OR for the presence of anti-HCV antibodies. The OR value is adjusted for gender, age (on 10-year group, except the first and last group) and area of residence

Characteristic	Participants tested, N	Crude prevalence of anti-HCV (95% CI), %	*Wilcoxon test or **Chi-Square test P value	Adjusted OR (95% CI)	P value
Geographical region			0.001**		
Transylvania & Banat	4,902	2.63 (2.2 - 3.12)	-	1.0	-
Wallachia & Dobrogea	6,032	3.35 (2.91 - 3.83)	0.0295*	1.3 (1.04 - 1.63)	0.023
Moldavia	2,212	4.25 (3.45 - 5.18)	0.0003*	1.6 (1.22 - 2.11)	0.001
Gender			0.033**		
Male	5,516	2.85 (2.42 - 3.32)	-	1.0	-
Female	7,630	3.51 (3.11 - 3.95)	0.0331*	1.26 (1.03 - 1.55)	0.022
Area of residence			0.0001**		
Urban	6,642	2.68 (2.3 - 3.1)	-	1.0	-
Rural	6,504	3.8 (3.35 - 4.29)	0.0003*	1.35 (1.1 - 1.64)	0.003
Age			0.0001**		
18 -29 y	2,071	1.49 (0.97 - 2.02)	-	1.0	-
30 - 39 y	2,774	1.4 (0.97 - 1.84)	0.7930*	0.94 (0.58 - 1.51)	0.789
40 - 49 y	2,623	2.67 (2.005 - 3.28)	0.0060*	1.87 (1.22 - 2.86)	0.004
50 - 59 y	3,304	3.96 (3.3 - 4.63)	0.00001*	2.77 (1.87 - 4.12)	0.0001
60 - 69 y	2,374	6.48 (5.49 - 7.48)	0.00001*	4.46 (3.01 - 6.6)	0.0001
Ethnicity			0.051**		
Romanian	11,542	3.34 (3 - 3.66)	-	1.0	-
Hungarian	1,115	1.79 (1.01 - 2.57)	0.0052*	0.51 (0.32 - 0.8)	0.003
Rroma	228	3.51 (1.1 - 5.91)	0.8854*	1.4 (0.68 - 2.87)	0.362
Other	60	5 (0 - 10.68)	0.4745*	1.45 (0.45 - 4.7)	0.531
Unreported	201	4.48 (1.59 - 7.36)	0.3728*	1.28 (0.65 - 2.54)	0.472
Marital status			0.0001**		
Unmarried	1,805	2.22 (1.53 - 2.89)	0.0453	1.54 (1.07 - 2.21)	0.020
Married/Consensual union	9,960	3.08 (2.74 - 3.42)	-	1.0	-
Divorced	488	5.53 (3.49 - 7.57)	0.0027*	1.79 (1.19 - 2.7)	0.005
Widowed	774	6.46 (4.72 - 8.19)	0.00001*	1.28 (0.92 - 1.77)	0.135
Unreported	119	0.84 (0 - 2.5)	0.1578*	0.23 (0.03 - 1.65)	0.142
Educational Level			0.0001**		
No elementary school	142	4.23 (8.77 - 7.57)	0.9119*	1.09 (0.48 - 2.51)	0.835
Elementary school (4-8 yrs)	5,477	4.42 (3.88 - 4.96)	-	1.0	-
High school (12-13 yrs)	4,547	2.38 (1.93 - 2.81)	0.00001*	0.75 (0.59 - 0.96)	0.023
College & University (>13 yrs)	2,980	2.32 (1.77 - 2.86)	0.00001*	0.69 (0.52 - 0.91)	0.009
Social status			0.0001**		
Employer/Self-employed person	480	2.92 (1.4 - 4.43)	-	1.0	-
Employee	6,170	1.93 (1.58 - 2.27)	0.1364*	0.68 (0.38 - 1.19)	0.180
Unemployed	295	3.05 (1.08 - 5.02)	0.9149*	1.05 (0.45 - 2.46)	0.913
Retired	3,893	5.8 (5.07 - 6.54)	0.0088*	1.2 (0.67 - 2.15)	0.531
Housewife	1,578	2.79 (1.97 - 3.6)	0.8818*	0.86 (0.46 - 1.61)	0.650
Others	730	1.78 (0.82 - 2.74)	0.1908*	0.75 (0.34 - 1.65)	0.475

26]. This trend indicates a cumulative risk of HCV infection over time, suggesting at the same time a cohort phenomenon with reduced transmission in recent years due to continuous improvement in healthcare conditions. Since the middle of 1990s, disposable syringes, materials, and instruments were broadly introduced, blood was systematically tested for HCV infection, access to medical services has improved, and,

as a consequence, the rate of nosocomial transmission of HCV infection has declined. The significant decline in HCV prevalence (overall 2.6%) is underlined in a recent Italian study, which emphasizes, at the same time, the increasing trend with age, from 1% in adult subjects aged <30 years to 7.7% in persons >70 years) [22].

Some socio-demographic correlations in our study were

Table II. Prevalence of anti-HCV antibodies and adjusted OR according to different risk factors. The OR value is adjusted for gender, age (on 10-year group, except the first and last group) and area of residence

	Participants tested, N	Ac anti HCV positive, N (%)	*Wilcoxon test or **Chi-Square test P value	Adjusted OR (95% CI)	P value
Occupation with risk to exposure to blood products			0.172**		
No	12251	389 (3.18%)	-	1.0	-
Yes	619	28 (4.52%)	0.0646*	1.58 (1.06 - 2.34)	0.025
Unreported	276	8 (2.9%)	0.7953*	0.9 (0.44 - 1.83)	0.764
HCV/HBV infections in the family			0.016**		
No	10107	312 (3.09%)	-	1.0	
Yes	1222	58 (4.75%)	0.0021*	1.62 (1.21 - 2.16)	0.001
Not Known	1693	50 (2.95%)	0.7679*	0.97 (0.71 - 1.31)	0.855
Unreported	124	5 (4.03%)	0.5460*	1.28 (0.52 - 3.18)	0.589
Diagnosed with HCV/HBV infection			0.0001**		
No	11969	322 (2.69%)	-	1.0	
Yes	521	80 (15.36%)	0.00001*	6.37 (4.88 - 8.33)	0.0001
Not known	555	20 (3.6%)	0.1969*	1.4 (0.88 - 2.23)	0.159
Unreported	101	3 (2.97%)	0.8626*	1.08 (0.34 - 3.44)	0.895
Chronic B/C hepatitis in the family			0.001**		
No	10637	322 (3.03%)	-	1.0	
Yes	790	44 (5.57%)	0.0001*	1.99 (1.43 - 2.76)	0.0001
Not known	1623	56 (3.45%)	0.3582*	1.15 (0.86 - 1.54)	0.344
Unreported	96	3 (3.13%)	0.9556*	1.02 (0.32 - 3.28)	0.961
Diagnosed with B hepatitis			0.0001**		
No	12324	381 (3.09%)	-	1.0	
Yes	209	18 (8.61%)	0.00001*	2.86 (1.74 - 4.71)	0.0001
Not known	514	21 (4.09%)	0.2049*	1.29 (0.82 - 2.03)	0.271
Unreported	99	5 (5.05%)	0.2632*	1.58 (0.64 - 3.93)	0.324
Diagnosed with C hepatitis			0.0001**		
No	12314	320 (2.6%)	-	1.0	
Yes	105	71 (67.6%)	0.00001*	69.59 (45.05 - 107.5)	0.001
Not known	472	22 (4.66%)	0.0064*	1.77 (1.13 - 2.77)	0.012
Unreported	255	12 (4.71%)	0.0378*	1.86 (1.02 - 3.36)	0.041
Blood transfusion			0.0001**		
No	11708	304 (2.6%)	-	1.0	
Yes	1119	106 (9.47%)	0.00001*	3.13 (2.48 - 3.96)	0.0001
Not known	148	10 (6.76%)	0.0017*	2.35 (1.21 - 4.53)	0.011
Unreported	171	5 (2.92%)	0.7894*	1.06 (0.43 - 2.61)	0.895
Surgery			0.0001**		
No	6933	164 (2.37%)	-	1.0	
Yes	6093	259 (4.25%)	0.00001*	1.52 (1.24 - 1.86)	0.0001
Not known	14	0 (0%)	-	-	-
Unreported	106	2 (1.89%)	0.7472*	0.71 (0.17 - 2.94)	0.645
Emergency surgery			0.097**		
No	2950	108 (3.66%)	-	1.0	
Yes	2538	118 (4.56%)	0.0662*	1.32 (1.01 - 1.73)	0.043
Not known	64	4 (6.4%)	0.2933*	1.8 (0.64 - 5.1)	0.266
Unreported	521	29 (5.57%)	0.0395*	1.61 (1.05 - 2.48)	0.029
Frequent hospitalization			0.0001**		
No	11892	338 (2.84%)	-	1.0	
Yes	1050	75 (7.14%)	0.00001*	2.06 (1.58 - 2.68)	0.0001
Not known	18	4 (22.22%)	0.00001*	12.59 (3.94 - 40.24)	0.0001
Unreported	186	8 (4.3%)	0.2366*	1.5 (0.73 - 3.09)	0.267
Injections at home			0.0001**		
No	8294	221 (2.66%)	-	1.0	
Yes	4631	195 (4.21%)	0.00001*	1.49 (1.22 - 1.82)	0.0001
Not known	76	3 (3.95%)	0.4904*	1.97 (0.61 - 6.38)	0.255
Unreported	145	6 (4.14%)	0.2770*	1.48 (0.64 - 3.41)	0.355

Table II (continuation)

			0.0001**		
Serious accidents					
No	12428	386 (3.11%)	-	1.0	
Yes	574	37 (6.45%)	0.00001*	2.02 (1.42 - 2.88)	0.0001
Not known	3	0 (0%)	0.7565*		
Unreported	141	2 (1.42%)	0.2494*	0.43 (0.1 - 1.73)	0.234
Injecting drug use					
No	12984	414 (3.19%)	-	1.0	
Yes	23	4 (17.39%)	0.0001*	5.89 (1.94 - 17.92)	0.002
Not known	17	1 (5.88%)	0.5278*	2.62 (0.34 - 20.31)	0.356
Unreported	122	6 (4.92%)	0.2804*	1.37 (0.6 - 3.15)	0.455
Age of first sexual intercourse					
≥ 18 y	8890	268 (3.01%)	-	1.0	
< 18 y	3917	142 (3.63%)	0.0705*	1.29 (1.04 - 1.60)	0.019
Unreported	320	15 (4.69%)	0.0885*	2.17 (1.26 - 3.72)	0.005
Chronic HCV/HBV infection in sexual partner					
No	11352	353 (3.11%)	-	1.0	
Yes	144	9 (6.25%)	0.0320*	2.01 (1.01 - 4.01)	0.046
Not known	1487	56 (3.77%)	0.1754*	1.34 (0.99 - 1.79)	0.051
Unreported	163	7 (4.29%)	0.3881*	1.57 (0.72 - 3.4)	0.249

strongly inconsistent with data published in the literature, for example the higher rate of HCV infection in females and rural-residing subjects. They can be attributed to the excessive nosocomial risk for the female gender due to illegal abortion during the communist period. Although the majority of published studies showed no difference between genders [22, 27-29] or higher prevalence in males [30-32], Guadagnino et al. [32] demonstrated also more anti-HCV positive tests among females (14.1% vs 10.5%, $p < 0.05$). A striking difference was noticed in this study performed in southern Italy in 1996 for females aged 50-59 years compared to males (26% vs 5.3%) and ≥ 60 years (34.4% vs 3.1%), suggesting probably a similar route of HCV infection as in the Romanian female population. The higher rural prevalence of HCV infection can be explained by the aging population in rural communities and a cohort effect, as well as by their hygiene conditions, lifestyle and mentalities which limit the access to medical facilities. The extensive use of non-disposable syringes for parenteral anti-microbial treatment before 2000 was also suggested as a possible cause of higher rural prevalence of HCV infection in other studies [13, 33]. Nosocomial transmission of HCV is well documented and seems to be the major route of infection in many developing countries [13, 28-29, 33]. It was largely present in our country in the communist era due to the lack of awareness of infection-control practices, such as sterilization of medical and surgical equipment. One notable fact is that the strongest association with anti-HCV seropositivity was observed with parenteral treatments, surgical interventions and frequent hospitalizations, but not with dental treatment, as in similar studies [22, 24, 28, 33]. However, the association of HCV infection with familial exposure to viral hepatitis and iatrogenic maneuvers certify the major routes of HCV transmission in Romania.

The strength of this study resides in the accurate sampling of the adult general population in Romania obtained through random cluster sampling from all geographical regions,

urban/rural communities, age groups and gender, educational and socio-economic level and the high quality laboratory tests.

Conclusion

The results of this first nationwide survey realized in Romania, contribute to the actual epidemiology of HCV infection in Europe. These data are critical to a better understanding of the burden of the disease and developing appropriate preventive strategies/programs to control the spread and consequences of HCV infection in Romania.

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Potential competing interests

None.

Appendix

The Medinet Epidemiological Study Team

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