

CLINICAL AND SOCIAL ASPECTS OF PATIENTS WITH VIRAL CHRONIC HEPATITIS C IN BIHOR COUNTY

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Abstract. The hepatitis C virus infection affects approximately 160 million people, i.e. approximately 2.35 % of the population of the world, according to a recent study in 2011 (Lavanchy, 2011). In Europe it is estimated that there are about 12 million people infected with C virus. Approximately 10% of them are located in Romania, therefore occupying 1st place in morbidity with HCV and 4th place at the rate of mortality due to liver disease. The study was conducted by prospective epidemiological investigation on clinical and laboratory data recorded on a selected sample of the general population. The study took place at the County Clinical Emergency Hospital Oradea, Department of Gastroenterology Clinic between January 2006 and June 2008, which is a section for adults. The study was conducted on a sample of 274 patients with clinical and laboratory examination, including histology, who were diagnosed with chronic hepatitis C. All were drafted in an evaluation sheet and a consent form. The people with HCV cirrhosis, those diagnosed with hepatocarcinoma C virus and the degree of fibrosis METAVIR F4 histology were excluded from the study. Social implications of infected persons should be given more attention, because every patient should receive counseling to avoid isolation, family problems and stigma.

Keywords: hepatitis C virus, chronic C hepatitis, risk factors, fibrosis.

Introduction

The infection with the hepatitis C virus (HCV) is a major health problem worldwide due to asymptomatic evolution towards cirrhosis and liver cancer, affecting about 160 million people, or approximately 2.3% of the global population

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(Lavanchy, 2011). WHO estimates that 3-4 million new cases occur each year (Soriano et al., 2009).

In Europe it is estimated that there are about 12 million people infected with virus C and about 10% of them are located in Romania, occupying the first place of HCV morbidity and 4th as liver disease mortality rate. It is estimated that in Romania the number of patients with liver cirrhosis with virus C and HCC, and also liver disease deaths will increase significantly by 2030, thus implying significant medical and social costs (Gheorghe et al., 2010).

I resorted to making this study given the very high risk of infection with virus C in Bihor County, which as noted is ranked first among counties in Romania in this regard. The objective of the study is to identify social factors and risk factors for chronic hepatitis C. A proper assessment of the factors that contribute to current and future HCV prevalence is needed to plan prevention and public health expenditure forecast. A sociological survey among patients diagnosed with HCV may reveal the main socio-demographic and clinical data in this regard.

The article is based on the presentation of certain theoretical aspects of the classification, the prevalence of C virus and its mode of transmission. Also, there are certain socio-demographic factors of importance that are identified based on literature, regarding the clinical course of HCV. Following a brief presentation of the methodology, the paper presents and discusses the results highlighted by the inquiry conducted. Conclusions from the final aim to complete the whole picture on clinic-social profile of patients with HCV identified in Bihor County.

Clinical and epidemiological aspects of virus C infection

History and classification of Virus C. Prevalence, transmission and clinical C virus infection

The post-transfusion hepatitis was named “hepatitis non-A, non-B” (HNANB) by Feinstone, 1975, and it indicated that an infectious agent was responsible for this disease (Alter et al., 1978). Two articles were the ones that made known the discovery of HCV in April 1989, in the Science magazine (Choo et al., 1989). HNANB virus has been referred to as Hepatitis C Virus (HCV).

HCV types and subtypes show *different geographical distribution* and are classified into three categories (Stumpf & Pybus, 2002): 1. **Epidemic Group**: subtypes 1a, 1b, 2a, 2b and 3a, which have a distribution across the globe. 2. **Endemic group** contains genotype 1 and 2 for West Africa, genotype 4 for Central Africa, genotype 3 for India and genotype 6 for Southeast Asia. 3. **Local epidemic group** prevailing in certain areas and for certain populations. For example, subtype 4a is present in approximately 10% of Egypt; it is rarely seen outside the Middle East. In Romania, in a study by Prof. M. Grigorescu and published in 2009 genotype 1b was found in 93.7% of cases, similar to Moldova (96%), Hungary (94.5%) and Bulgaria (77.5), and the presence of genotype 1: 99.1%.

Virus C is endemic in most of the world. Data on the prevalence of C viral infection are often incomplete because population studies do not include high infection risk groups: prisoners, drug or alcohol addicts, illegal immigrants and the homeless. In a recent study it is estimated that worldwide there are about 2.4%, more than 160 million people infected with virus C (Lavanchy, 2011). Virus C infection exhibits great variability in geographical distribution, with: **very low prevalence areas:** Switzerland, UK and Scandinavian countries (below 0.5%); **areas with low prevalence** (0.5-1%) Western Europe (Germany 0.6%, France 1.1%), North America, Canada (0.8%), Australia (1.1%); **areas with intermediate prevalence** (1.1-5%): 1.58% Morocco, Eastern Europe, India, China (3.2%), Japan (1.5-2.3%), the Mediterranean basin (southern Italy 2.2%) and **high prevalence areas:** Northern Italy 20%, Libya over 7%, Egypt 25%, Pakistan (10 million infected with HCV). In Egypt there are 4 million people infected with HCV, this means 45% of the population aged over 45 years). Nearly 10% of all HCV infectees are in two countries: Pakistan and Egypt. CDC notes that although the global number of new cases of acute viral hepatitis C decreases from 230000 cases/year to 19,000 cases/year, the HCV infection rate among young people is increasing (Wasly, Grytdal & Galagher, 2008). Romania ranks first in Europe in terms of the prevalence of viral hepatitis infections and the fourth in mortality rate hepatitis. Hepatitis B is 15.7% of total chronic viral hepatitis and the virus C is 64%, with 44.5 deaths per 100 000 inhabitants (Figure 1) (Negro & Alberti, 2011).

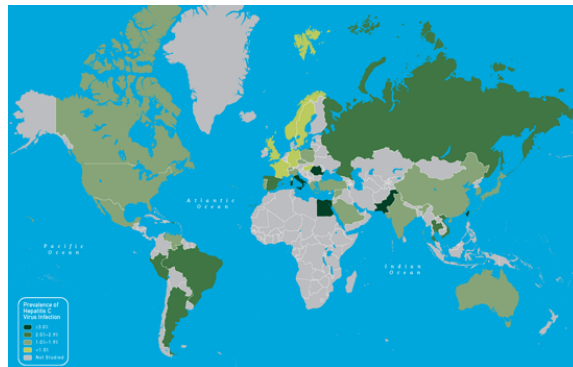


Figure 1. *The Prevalence of HCV worldwide 2011*

According to a study conducted in 2009, Romania was in an intermediate prevalence area, so in the general population aged 18-69 years, the prevalence was 3.23% (Gheorghe et al., 2010). After the testing campaign called “Hepatitis C does not hurt. Just kills” carried out in the first six months of 2013 by the Association of chronic patients from Romania, together with the National Institute for Infectious Diseases “Matei Balş” from Bucharest (INMB) of the 50.000 Romanian who were tested for free, **4.63%** tested positive for virus C infection. In the neighboring countries prevalence is 0.7% in Poland, 0.5% Czech Republic, 2% Hungary and 1% Bulgaria. A study by the Romanian Association for the Study of Liver in 22

counties of Romania in 2009 show a prevalence for virus C between 4.5% in Southeast regions of Romania and 7% in the West and North regions.

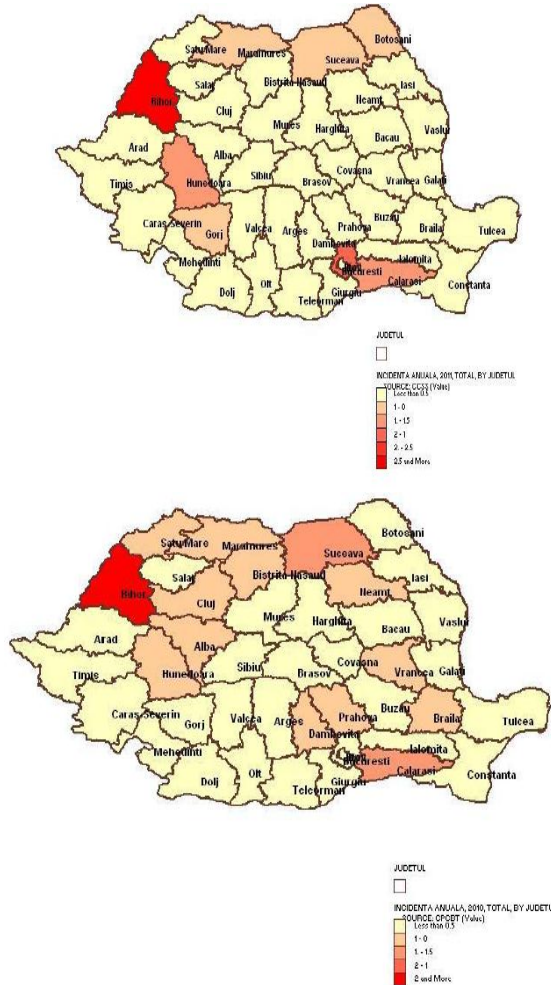


Figure 2. Counties incidence of acute viral hepatitis C in 2011 and 2010

(Source: National Institute for Public Health)

In 2011, in Romania the highest values were recorded in the counties of Bihor (2.53%^{0/000}), Ilfov (1.79%^{0/000}), Călărași (1.29%^{0/000}), Hunedoara (1.09%^{0/000}) Suceava (0.99%^{0/000}) and in 2010 in the counties of Bihor (2.0%^{0/000}), Călărași (1%^{0/000}), Suceava (1%^{0/000}) (Figure 2).

Main ways of transmission of the virus C are:

- **Iatrogenic transmission** through the reuse of needles, droppers, syringes and instruments used in invasive procedures were before the 90s an important means of transmission of HCV. Unfortunately, diagnostic and therapeutic procedures may still be responsible for transmitting HCV in Romania and in

developing countries. It has been shown that 34.5% of patients on dialysis programs are infected with HCV (Diaconescu & Olteanu, 2011).

- **Blood transfusions** were a major risk factor for transmission of HCV infection before 1990. It is estimated that the residual risk of transmitting the virus C due to donors who are in the immunologic window ranges from 1 to 100,000, the total risk is less than 1 in 1 million units transfused (Seed et al., 2005).
- **Intravenous drug use** is the main way of transmission of the virus C in developed countries. By 2011, 12 countries are known with high prevalence > 80% of HCV among drug users including: Mexico, Netherlands, Denmark, southern Italy, Pakistan (90%), Thailand, Estonia, and so on; 25 countries with a prevalence of 60-80%, including Romania, USA, most of European countries, Asia, Australia; 24 countries with prevalence of 40-60% and 16 countries with prevalence of <40% (including Hungary and Bulgaria) (Nelson et al., 2011). Transmission of HCV can be done by the use of a drug mixing tanks, filters, buffers, as well as those using intranasal cocaine. It emphasizes the role of direct contact with infected blood (Sutton et al., 2008).
- **Sexual transmission.** The risk of sexual transmission of HCV infection in heterosexual monogamous couples is low, but increases with homosexuals, those with multiple partners, i.v. drug users or certain favorable conditions (syphilis, gonorrhoea, chlamydia trachomatis, Trichomonas vaginalis, herpes simplex II, HIV).
- **Vertical transmission.** Perinatal transmission occurs in 4.3 to 5.3% of children born to mothers infected with HCV and HCV RNA positive. The risk increases from 8.3 to 22.1% in the case of co-infected with HIV. Cesarean delivery is recommended if there are high levels of viremia.
- **Organ transplantation** is an important factor for the transmission of HCV infection. It is believed that between 30 and 80% of patients who received a transplant were infected with HCV, with poor outcome.
- **Other routes of transmission** are tattooing, piercing maneuvers applied in traditional medicine (acupuncture, scraping, putting suction cups, circumcision), cosmetic maneuvers (manicure, pedicure, brushing teeth, cosmetics and hairdressing). Non-sexual transmission within the family when a family member has a C liver disease with high viral load by direct mechanism or unapparent percutaneous or permucos. There are times when you cannot identify any risk factor.

Clinic C virus infection. It is considered that 20% of people infected with virus C, are progressing to acute form of spontaneous healing, 50-80% by persistent chronic hepatitis C virus; of these, 4-20% progressing to cirrhosis in about 20 years. Among patients with chronic hepatitis C, 1-5% presents the risk of progression to HCC (Brass, Moradpour & Blum, 2007).

Acute viral hepatitis C. The symptomatic forms (20-15%) are generally oligosymptomatics and nonspecific: asthenic syndrome, indigestion, muscle and joint pain, loss of appetite. The icterus occurs in 10-20% of cases of symptomatic acute hepatitis C and is associated more frequently with a self-limiting evolution. In terms of socio-demographic criteria, self-limited development would be favored by: **young age:** there are studies showing that infected patients under 20 years, 70% were cured; over 20 years the cure rate drops to 24% (Alter, 1999); and 40-45% of children born to mothers infected with HCV heal spontaneously; **race:** Caucasians healing is 32% and the black race is 14%;

Viral chronic hepatitis C. The persistence of detectable HCV RNA 6 months after the onset of acute hepatitis C is defined as chronic hepatitis C. The clinical picture is dominated mostly by fatigue. Less common symptoms are nausea, apathy, myalgia, arthralgia, hepatalgia, drowsiness. The socio-demographic factors that influence the evolution of HCV infection are related to the host or external factors:

- **Age:** only 2% of infected patients under age 20 will develop cirrhosis compared with 6% between 35-40 years and 37% of those infected over 50 years (Poynard et al., 2003);
- **Gender:** Women seem to have a slower progression, especially young women; this is demonstrated by similar chronicity rate of 55% in the 2 studies involving 704 Irish women, and 917 German women who were infected with contaminated immunoglobulins (Wiese et al., 2000)
- **Race:** Afro-Americans have a higher rate of chronic infection, a lower response to interferon and ribavirin, and twice increased risk of developing hepatocellular carcinoma (Nguyen et al., 2004)
- **Co-morbidity:** co-infections with HIV, HBV, non-alcoholic hepatic steatosis, overweight, schistosomiasis increase progression of the illness;
- **Development of disease:** about 31% of HCV-positive patients and with elevated transaminases are developing, in time, HCC, compared to 4% of patients with normal or intermittent transaminases (Grigorescu, 2009).
- **Alcohol** accelerates the progression of the illness; **smoking and toxic environmental factors** have been associated in some studies with accelerated evolution of chronic hepatitis C.

Considerations on psychosocial changes in patients diagnosed with virus C.

Most patients with chronic HCV infection are asymptomatic and are unaware of the virus. The first problems of the patients are related to fear of infection, although if proper personal hygiene is maintained, there is no reason why HCV carriers cannot work under normal conditions in any field. Insufficient knowledge and fear of contamination can lead to isolation of individuals who are HCV carriers.

Another category of problems are related to life within the family. Many of infected patients do not always inform their partners. The difference from B virus infection is that there is a vaccine against the virus C that could solve psychological problems in life couple.

It is known that there is depression pathology in these patients. The infectivity of HCV, inadequate knowledge on the mode of transmission of the virus can lead to the isolation of these people, and social isolation may be one of the causes of elevated occurrence of mental disorders. Stigma has been associated with increased anxiety and depression, decreased quality of life and the difficulty of dealing with them. The high rate of psychiatric disorders may be related to fear and potential stigmatizing chronic HCV infection, with negative consequences on social, familial and occupational levels. The problems are more pronounced in the first 3-6 months after diagnosis, it can be said that this is a period of acceptance and adaptation.

Methodology

The study was conducted by prospective epidemiological investigation on clinical and laboratory data recorded on a selected sample of the general population. The study took place at the County Clinical Emergency Hospital Oradea, the Department of Clinic Gastroenterology which is a section for adults, between January 2006 and June 2008.

The study was conducted on a sample of 274 patients with clinical and laboratory examination, including histology, patients who were diagnosed with chronic hepatitis C. For all there were drafted evaluation sheets and consent forms. People with HCV cirrhosis were excluded from the study, also those diagnosed with hepatocarcinoma C virus and the ones with a degree of fibrosis F4 METAVIR at their histological examination.

The results of the research

Socio-medical characteristics of patients with viral chronic hepatitis C

Gender

In terms of gender balance is slightly inclined towards the female gender, suggesting a higher risk of women becoming infected with hepatitis C, compared with the male population (Figure 3).

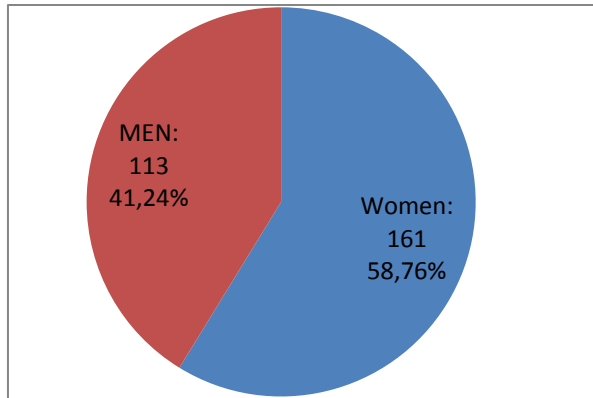


Figure 3. *Distribution of subjects by gender*

Age

By performing statistical parameters of average age of subjects in the study it is observed that chronic hepatitis C is a disease of adults aged 46 years old (Table 1).

Table 1. *Statistical parameters of age*

Statistical Parameter	Total
<i>MINIMUM AGE</i>	19
<i>AVR AGE - STDEV</i>	36.01
<i>AVR AGE</i>	46.03
<i>MEDIAN AGE</i>	44
<i>AVR AGE + STDEV</i>	56,05
<i>MAXIMUM AGE</i>	69
<i>STDEV</i>	10.02

Virus C prevalence records an upward trend until the age of 55. After this age there is a decrease to the maximum age of 69 years (Figure 4).

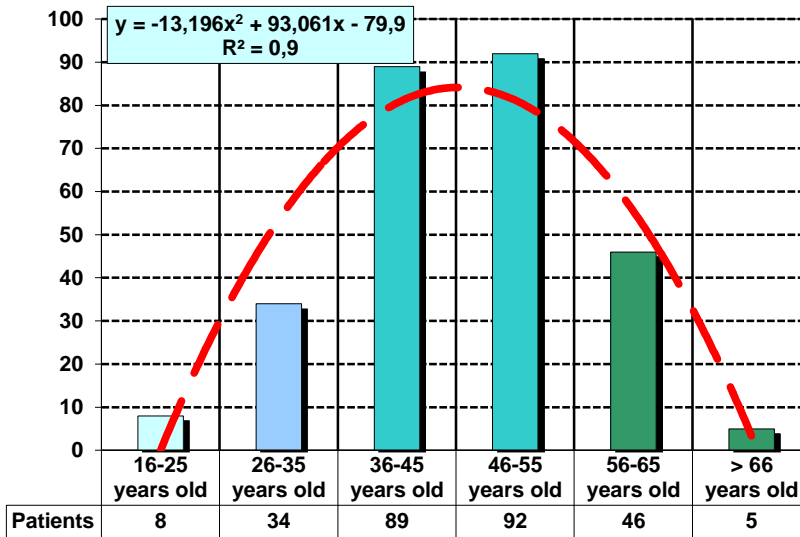


Figure 4. Distribution of subjects by age

The two age groups (36-45 years old and 46-55 years old) include patients who before the 90s were young and young adults with an increased risk of transmission of virus C infection due to socio-economic factors that were present in the Romanian context at that time.

The relation between gender and age

Average age that was recorded for males was lower than the average age recorded for females, men are infected with virus C earlier (Table 2).

Table 2. Statistical parameters of age by gender

Statistical Parameter	Men	Women
<i>MINIMUM AGE</i>	19	21
<i>AVR AGE - STDEV</i>	34,23	36,44
<i>AVR AGE</i>	44,93	45,88
<i>MEDIAN AGE</i>	43	45
<i>AVR AGE + STDEV</i>	55,63	55,32
<i>MAXIMUM AGE</i>	67	69
<i>STDEV</i>	10,7	9,44

By the age of 40 years old there are no significant differences of prevalence for virus C between genders, the values were close, with a slight difference in favor of

the male gender. After this age, about 2/3 of the patients are women. There is an increase of prevalence for virus C in female gender over 40 years old. These data show women were exposed to additional risk factors, before the 90s, related to birth, abortion or gynecological surgery (Figure 5).

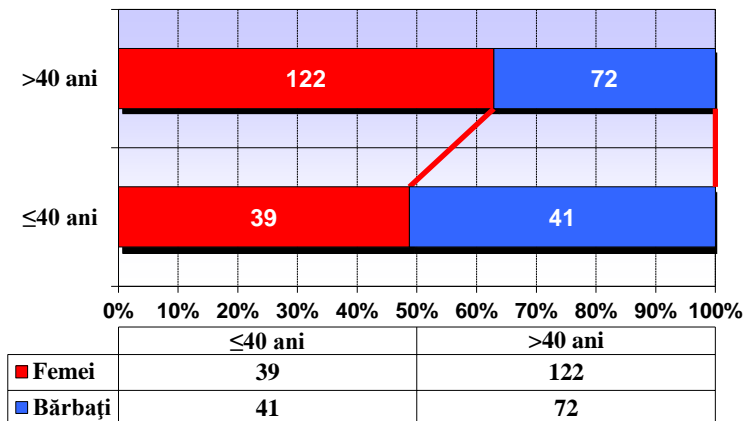


Figure 5. *Batch distribution by age and gender*

Area of residence

Over two thirds of the subjects have urban origin. More than half of patients with chronic hepatitis C (57.6%) have reported living in Oradea (Figure 6). Accessibility for patients to medical act before the 90s may be a contributing factor of this majority.

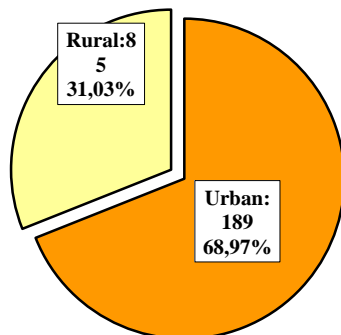


Figure 6. *Subject distribution by area of residence*

Risk factors for HCV transmission

Out of the total of the sample (274 subjects) there were identified approximately 13.1% possible risk factors of HCV infection. Parenteral transmission versus sexual transmission was 35:1. Approximately 10% of patients were identified as a possible surgery-way transmission of HCV (Table 3).

Table 3. Risk factors for HCV transmission

Risk factors for transmission of virus C				Patients		
				%		No.
Parenteral	Surgical Interventions	Abdominal	Cholecystectomy	12.40	9.48	26
			Splenectomy		0.36	1
			Polypectomy		0.73	2
			Others		1.82	5
		Genital	Hysterectomy	3.64		10
		Renal	Nephrectomy	1.82		5
		Thoracic	Intrathoracic foreign body	0.72	0.36	1
			Coarctation of the aorta operated		0.36	1
		Others	2.19		6	
		Blood Transfusions			1.82	
	Hemodialysis			0.36		1
	Occupational exposure: medical personnel			2.92		8
	Total			25.91		71
Sexual	HCV infected partner		0.73		2	
Total			26.64		73	

Antecedents with pathological significance for HCV

Medical history

Endocrine and renal manifestations have been more than half of extrahepatic manifestations of virus C infection (Table 4). The percentage of extrahepatic manifestations is low compared to data reported in the literature (38-74%), but statistically significant since disease diagnosis preceded the diagnosis of chronic hepatitis C.

Table 4. Extrahepatic manifestations of HCV

Extrahepatic manifestations	Associated diagnoses	Patients		
		%		Nr.
Endocrine	Diabetes Type I	3.64	0.73	2
	Diabetes Type II		2.19	6
	Thyroiditis		0.36	1
	Hypothyroidism		0.36	1
Renal	Surgical Unique Kidney	2.55	1.82	5
	Chronic glomerulonephritis		0.73	2
Hematologic	Sdr. lymphoproliferative	1.46		4

Autoimmune	Mixed cryoglobulinemia	0.73	2
Cutaneous	Disseminated Lupus Erythematosus	0.36	1
Articular	Rheumatoid positive factor	0.73	2
Cardiac	Coarctation of the aorta	0.36	1
	Total	10.14	27

Conclusions

Infection with hepatitis C is at alarming rates worldwide, this situation is still kept under observation by the World Health Organization. In Europe, Romania ranks first regarding HCV morbidity and 4th in terms of mortality due to liver disease (Gheorghe et al., 2010). Nationally, the incidence of patients diagnosed with HCV in 2011 recorded the highest rates in Bihor county (2.53%₀₀₀) (Center for Disease Control and Prevention, 2011).

Statistical values related to the studied sample indicate a higher prevalence of hepatitis C virus among female subjects (58.8%), especially among adult women aged 36-56 years. Curettages, gynecological appointments, births are high risk on HCV infection. One of the contributory factors on the situation of women is the socio-cultural and economic conditions in Romania, especially before 1990. In that context, parenteral maneuvers listed above were held in poor hygienic conditions than those currently existing, causing an increased risk of infection.

In the present sample, 68.9% of subjects are from urban areas, especially in Oradea. In this regard, access to medical act favoring increased prevalence and exposure to risk factors.

In Romania, the main way of transmission of HCV is parenteral. The main risk factor associated with transmission of the virus C is found in the context of surgeries, regardless of their nature (9.8%), followed by the risk from blood transfusions (1.8%). In subsequent years, this hierarchy of routes of transmission and risk factors associated with HCV infection can know significant changes. Changes can be generated at a social level through extending deviant behaviors especially among young people in our country, namely intravenous drug use. It is estimated that by 2030 this practice will be identified as another major route of exposure and risk to virus C.

At least 1 of the 10 subjects included in this sample C virus infection has been associated with other pathologies that can accelerate progression to cirrhosis or hepatocarcinoma. By 2030 in Romania the number of patients with cirrhosis with virus C and hepatocarcinoma will significantly increase, and also the number of deaths from liver disease. This upward trend of cases of HCV prevalence and associated pathologies may involve significant social and medical costs for contemporary society. The infection with hepatitis C virus is and remains a major public health problem worldwide, and both national and county, as the evolution to cirrhosis and liver cancer is asymptomatic in most patients.

Social implications of infected people should be given more attention, because every patient should receive counseling to avoid isolation, family problems and stigma.

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