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Risk factors for hepatitis C virus infection

Egidia MIFTODE¹, Daniela LECA², Mihaela RADU³, Răzvan MIFTODE⁴

Abstract

Hepatitis C virus (HCV) infection in adults is the leading cause of chronic disease and cirrhosis. Globally, an estimated 200 million persons are chronically infected with HCV and 3 to 4 million persons are newly infected each year. Improved sanitary and socioeconomic conditions over time have greatly affected the frequency of HCV infection causing a decreased risk of infection along generation. However, the younger population is particularly at risk due to certain practices (use of intravenous drugs, tattooing, piercing) known to favor HCV transmission. Such practices often begin during adolescence when awareness of hepatitis C is low. We have conducted a prospective study in which have been included 286 patients with chronic hepatitis C hospitalized in the Clinic Hospital of Infectious Diseases Iasi between 2004 and 2007. The aim of this study was to investigate the risk factors for the acquisition of hepatitis C virus in patients with chronic hepatitis. The study confirms that the most relevant risk factors for the acquisition of HCV are transfusions of blood before 1993 (32%) followed by dental procedures (25,5%) and health care related procedures (20%). Accidental needstick, was reported by 16 patients (5,6%). Patients older than 40 years had a significant higher rate of declared risk factors compared with younger patients (p=0,038). The results of this study stress the need of strict adherence to universal precautionary measures. Because the quality of knowledge regarding hepatitis C is very poor among adolescents it would be beneficial for public health a strong intervention to present the most relevant risk factors for the acquisition of this virus.

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Keywords: Hepatitis C virus, risk factors

Introduction

Hepatitis C virus (HCV) is the most common cause of chronic liver diseases worldwide. Approximately 3% of the world population (200 million persons) is chronically infected with HCV. Three to four million new HCV infections occur each year, and about 250 000 annual deaths throughout the world result from HCV associated chronic liver disease. About 80% of infected persons will develop chronic hepatitis, and 20% of them will progress to cirrhosis in twenty years (WHO 2000, Kim et al., 2000). Although the liver is primary involved, with a frequent rate of asymptomatic cases, HCV could produce a variety of extrahepatic manifestations: hematological, dermatological, renal, endocrine and autoimmune. Moreover, final stages of chronic hepatitis C represent the main cause of liver transplants (Boyer et al., 2000). The prevalence rate of HCV infection is difficult to be estimated and has a consistent variability from one region to other. In Europe the prevalence rate is approximately 1%, being higher in southern regions (2% in Mediterranean countries) and lower in northern regions (0,5%). In France the prevalence rate of HCV antibodies is 1,2% (in adults between 29 and 59 years). A prevalence rate of 7% was reported in a subgroup of elderly in Sardinia; in southern Italy it was mentioned a rate of HCV carriage of 11%. The incidence of HCV infection in Poland is 5 per 1000 000 habitants (Boyer et al., 2000, Gross et al., 1998, Bielak, et al., 2003). Hepatitis C virus is the most common chronic blood borne pathogen in some region as United States of America; approximately 2,3% of adults more than 20 years of age are positive for anti-HCV antibody, between 55 and 84% of these have chronic infection and 5 to 50 % are thought to know their status (Armstrong et al., 2004).

Methods

We have conducted a prospective study in which have been included 286 patients with chronic hepatitis C hospitalized in the Clinic Hospital of Infectious Diseases Iasi between 2004 and 2007. The aim of this study was to investigate the risk factors for the acquisition of hepatitis C virus in patients with chronic hepatitis. It is difficult to determine the exact mechanism of HCV transmission, therefore we have considered the most probably risk factor that was reported by each patient. Data analysis was performed with SPSS and Excel softs. The measurement of associations was done with Cramer, Gamma and Lambda coefficients.

Results

Risk factors in patients with hepatitis C

Patients with hepatitis C reported potential risk factors in the past in 35,66% of cases (102 patients) (see table 1).

Table 1. Potential source of hepatitis C infection in 102 patients

Risk factors	Nr. cases	%
Transfusions	33	32,35
Surgery	17	16,66
Dental procedures	26	25,5
Hemodialysis	3	2,94
Tattooing	2	1,96
HCV partner	5	4,9
Accidental needlestick injury	16	15,69
Total	102	100,00

Analyzing the distribution of cases with risk factors we could confirm that the most relevant risk factors for the acquisition of HCV are transfusions of blood or blood products before 1993 (32,35%). Less frequently, transmission of HCV has been reported in patients who underwent a diagnostic or therapeutic procedure such as contaminated equipment during dental or surgery interventions, or in those whose wife or husband were HCV infected.

Gender distribution of risk factors

The majority of risk factors was registered in women (68,63%), the percentage exceeding two folds the males ($p=0,006$); female gender was preponderant to report dental procedures as risk factors (61,54% versus 38,46%), transfusions (72,72% versus 27,27%), health care related procedures (82,35% versus 17,65%) and professional risk (needlestick injury) (93,75% versus 6,25%). We found statistically significant differences only for the professional risk, more frequent in women compared with men ($p=0,021$) (see Table 2). Cramer coefficient (value of 0,483) indicates a moderate relation, statistically significant between risk factors and gender of patients.

Table 2. Gender distribution of risk factors

Risk factors	Total	Male		Female		p
		Nr.	%	Nr.	%	
Transfusions	33	9	27,27	24	72,72	0,537
Surgery	17	3	17,65	14	82,35	0,181
Dental procedures	26	10	38,46	16	61,54	0,366
Hemodialysis	3	3	100	-	-	-
Tatooing	2	2	100	-	-	-
HVC partner	5	4	75	1	-	0,032
Accidental needlestick injury	16	1	6,25	15	93,75	0,018
Total	102	32	31,37	70	68,63	0,0069

Risk factors repartition on groups of age

Risk factors have been registered in almost a half of patients belonging to tranches of age: 21-30 years (57%), 41-50 years (47%) and 61- 65 years (47%). Less frequently these factors have been reported by patients aged of 51-60 years (30%) or by patients of 31-40 years (23%). We have found a significant higher rate of reported risk factors in patients older than 40 years (40,32%) compared with younger patients (27,55%, p=0,038) (OR=0,57; IC=0,33–1,01). Risk factors for HCV infection have been reported in higher proportion in patients aged 21-30 years (57%) compared with those of 31-40 years (23%) (p=0,013); similar differences were observed between tranches of age 41-50 years (47%) and 51-60 years (30%) (p=0,023). The study of risk factors distribution related of age showed an increasing tendency, directly proportional with age until 50 years and a subsequently decreasing after this age (fig 1).

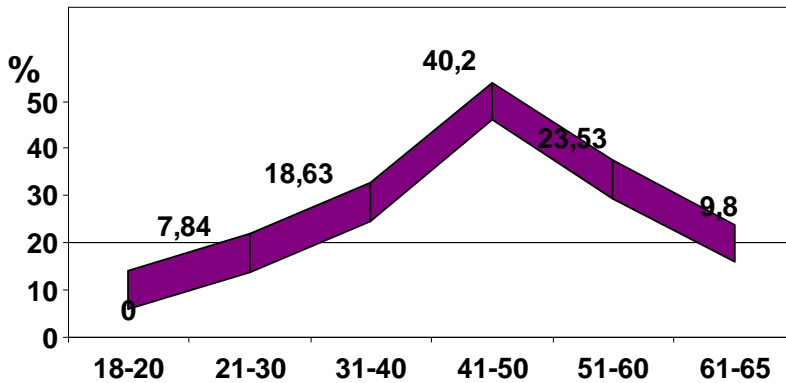


Fig. 1: Frequency of risk factors related with age

Risk factors and relation with initial value of liver enzymes

Low levels of liver enzymes (transaminases – TGP) were decelated more frequently in patients with reported risk factors than in those who could not indicate any favourizing factor for infection either for groups with <50 and >50 u.i./l (50,59% versus 22,69%, p=000001), or for groups with transaminases levels of <100 and >100 u.i./l (40,32% versus 27,55%, p=0,038). Normal values of transaminases have been noted especially in patients with surgery antecedents (58,82%), in patients receiving transfusions in the past (42,42%) and in those with dental procedures as risk factor for infection (42,3%) (see table 3).

Table 3: Level of transaminases in patients with potential risk factors

Risk factors	Total	Mean value (u.i./l)	Normal TGP < 50 UI/l	High level TGP > 50UI/l	p
Transfusions	33	70,66	14 (42,42%)	19 (57,58%)	0,96
Surgery	17	52,2	10 (58,82%)	7 (41,18%)	0,127
Dental procedures	26	86,88	11 (42,3%)	15 (57,7%)	0,98
Hemodialysis	3	163	-	3	-
Tatooing	2	58	1	1	-
HCV partner	5	61,25	2	3	0,647
Accidental needlstick injury	16	86	5 (31,25%)	11 (68,75%)	0,335
Total	102	71,26	43 (42,15%)	59 (57,85%)	0,00001

The value of Lambda coefficient of association - 0,183, with sig. \hat{a} 0,000, indicates a low relation between transaminases and risk factors, but statistically significant.

Discussion

HCV epidemiology has suffered important changes during last years. The introduction of HCV antibody testing in 1990 made transmission of HCV by these routes rare (could be considered entirely disappeared in developed countries), but recipients of blood transfusions and organ transplants before this date remain at particular risk. Implementation, in some countries of some programmes such as those supporting changes of the syringes/needles and methadone maintaining therapy generated an important reduction of HCV and HIV transmission among drug users. By consequences, it is possible that the relative impact of

nosocomial transmission of HCV to be higher than a few years ago (Martinez-Bauer et al., 2008).

Transfusions

Approximately 90% of post-transfusion non-A non-B hepatitis are due to HCV and history of transfusion are found in 19-36% of patients infected with this virus. The risk of HCV infection associated with transfusions has decreased once the screening methods of the blood were introduced (1990 in developed countries): in United States the risk of HCV following blood transfusions HCV-negative is <1 per 103000 units of transfusion (the blood being in the period infection-aparition of antibodies, period of almost 12 weeks). In these conditions the risk of post-transfusional HCV is 5 folds higher than the risk of HIV-1 transmission. PCR (polymerase chain reaction) used as a screening methods for the blood have reduced the post-infection risk period of the donated blood to approximately 3 weeks. Introduction of the steps for viral inactivation in frozen plasma diminished as well the risk of post-transfusion HCV infection; before this procedure was generalized 100% of persons with hemophilia were HCV infected (Serfaty et al., 1993, Dubois et al., 1997). In our study transfusions were administrated mainly in women, this fact being related with a higher rate of surgical procedures, most frequently involving genital tract, as other Romanian authors reported (Calistru et al., 2003).

Intravenous drug users

The drug addicts represent the population category most affected by HIV infection, the prevalence of infection being almost 50%, but it can reach 90% after 6 years of intravenous drug use. Most usual, HIV infection occurs in the first months from the initialization of intravenous drug injection. In some groups of people who use injecting drugs prevalence of HCV infection was higher than that of HIV or HBV (Garfein et al., 1996). In USA, at least 2/3 of newly HCV infections are associated with drug consumption (Sulkovski et al., 2005). Intravenous drug use represents one of the principal present-day ways for transmission of some important infections for the public health, especially the Hepatitis B and C viruses. In England, where it is estimated that less than 1% of population is intravenous drug consumer, approximately 35% of laboratory positive HBV results and 95% of the HCV positive are determined by intravenous drug consumption (de Angelis et al., 2004).

Health care personnel

The risk of transmitting virus C through accidental percutaneous inoculation from an HCV infected patient varies from a study to another between 1, 5% and 10%, different dates being attributed to the differences of viral load in these patients (Hernandez et al., 1992). In France, prevalence of HCV infection in medical dentists which have numerous drug addicted patients is 9, 3%, and in dentists - 1, 8%, in comparison with those who didn't have such patients (Dubois et al., 1997). The studies made in USA in stomatologists have revealed the presence of HCV serology in variable proportions depending by years of service: 0, 7% in those who worked maximum 23 years and 4% in those who have at least 24 years of practice (global prevalence is 2%). The virus B infection markers were present in 21% of medical dentists and in 7% of dentists (Hernandez et al., 1992, Spencer et al., 1997, Piazza et al., 1997).

Iatrogenic non-transfusional contamination

Hemodialysis and transplant

The prevalence of HCV antibodies among hemodialysis patients varies between 10 and 50%, value straight proportional with procedure frequency; in this case the infection is presumed to have been transmitted by inadequate infection control practices.

The risk of HCV transmission during an organ-transplant is 100% (Allander et al., 1994, Pereira et al., 1992).

Surgical interventions and other invasive diagnostic procedures

It is estimated that 15% of chronic hepatitis C diagnosed between 1991 and 1993 were, most probable, nosocomial transmitted. This modality of transmission involves endoscopy, gynecological procedures and surgical interventions. Per-endoscopic biopsy has a higher risk of HCV transmission (7,2% of patients with biopsy were seropositive for HCV), in comparison with the ones which underwent endoscopy, but without biopsy (4% seropositivity among patients with endoscopies maneuvers) (Bronowicki et al., 1997). Comparing the data from our study with data reported from other authors, we have noted a lower frequency of reported HCV transmission through invasive procedures in our region (12,6%). Accidental inoculation of the sanitary personnel was the potential way of contamination in 16 patients with hepatitis C (5,6% of all patients) followed by us, level which is similar with that mentioned by Martinez et al (7%)(Martinez-Bauer et al., 2008).

Ambulatory iatrogenic contamination

Studies conducted by Dubois and Serfaty didn't mentioned a statistically significant association between the presence of dental procedures in antecedents and HCV infection (Dubois et al., 1997, Serfaty et al., 1993). Piazza et al have detected the presence of HCV in 6% of the biological samples taken from dental technics used for the treatment of HCV infected patients, fact that confirms the possibility of HCV contamination during dental procedures (Piazza et al., 1997). Takata have evaluated the presence of HCV and HBV in hospitalized patients with oral diseases (cancers, oral cysts), and they reported a seropositivity rate of 6% and, 1,2% respectively (Takata et al., 2003). In a Swedish study, antecedents of tattooing were retrieved at 19% of HCV infected persons, compared with 3% detected in witness lot (Shev Set et al., 1995, Seeff et al., 2000). Tattooing and body piercing are practices that often begin during adolescence. In a recent study Gardella et al found that body piercing was more frequent among girls than boys (20% versus 3%, $P < 0.001$) and tattooing more frequent among boys than girls (3% versus 2%, $P < 0.02$) (Gardella et al., 2007, Carroll et al., 2002). Only 2 of our patients (1,96%) had the tattooing as potential risk factor for HCV contamination. This low level is probably attributable to the fact that in many cases clinical manifestations are unremarkable (patient generally asymptomatic) and therefore will not be identified if specific diagnostic tests are not performed. The involvement of dental treatments in acquisition of this viral infection, in a period when decontamination and sterilization techniques, as well as mass-media and sanitary education of medical personnel and population have increased considerably, seems to be overestimated. This fact could be attributed to the unrecognized by the patients of some risk factors, as sexual transmission, provoked abortion, ambulatory maneuvers and invasive treatments performed by unauthorized persons, non-respecting elementary asepsis and antisepsis rules. The group of patients with chronic hemodialysis was relatively low represented in our study (2, 94%), in comparison with other studies, in which is reported a seroprevalence rate between 9, 3% and 17, 7% (Rockville, 2004). This fact is probably due to the low addressability of these patients to our service, majority of them being diagnosed and treated in nephrology service. To be remarked, as well, the higher incidence of professional risk (16%) and the very low incidence of drug consumption – just 2 patients have declared this practice.

Vertical transmission from mother to infant

It has been reported that transfusion antecedents of the mother rise the risk of HCV transmission (10%), comparing with intra-venous drug use (8%) or in the case of unidentified risk factors (Resti et al., 2003). The prevalence of anti-HCV antibodies in pregnant women is between 0, 9 and 4, 6%. In a study conducted by

Hutchinson et al, 24% of infected women with Hepatitis C virus were diagnosed before the gestation and 46% were diagnosed before the moment of birth (Hutchinson et al., 2004).

Sexual transmission

The risk of sexual transmission of HCV is very low (approximately 0, 2-2% per year of relationship or 2-11% in case of long-term relationship). The virus was inconstantly isolated in saliva and seminal fluid, but was not isolated from the urine, feces or vaginal secretions (Liou et al., 1992). Global prevalence of HCV infection in sexual partners of the infected persons varies between 4% and 10%. The risk of sexual contamination is increasing as the infected person has a higher viral load, as hepatitis is much severe or as there is an associated HIV infection. Also, it looks like the number of contacts potentially infected has some importance, as well as the antecedents of sexually transmitted diseases (Dubois et al 1997, Kao et al., 1996).

Intra-family non-sexual contamination

However this modality of transmission was much controversial, the studies of sequence of isolated HCV within the members of the same family, which live together, have demonstrated the homogeneity of viral sequences, fact that argues intra-family non-sexual transmission. The value of viral load is a very important factor; thus, it was observed that in the group of an infected person, symptomatic, 1 of 10 persons were infected, while not any person of the family contacts of a HCV positive person, non-symptomatic, has been identified (Puoti et al., 1995).

Age-related epidemiological data

The mean age of patients who reported risk factors in our study was 45,7 years, value which is similar or exceeds with a few years mean age reported by other authors: Heathcote (46,5 years) and Zeuzem (41,1 years) (Zeuzem, 2004, Heathcote et al., 2000).

The prevalence of anti-HCV in USA, in general population >6 years is 1,6%, and the lowest level of seropositivity for HCV is noticed in population < 29 years (0,4%). The highest rate of infection is reported in the group of age 45-49 years (7,1% of men and 2,3% of women). In the category of elderly (>60 years) 1% has antibodies against HCV (Armstrong et al., 2004). In Japan, the prevalence of HCV seropositivity is 3% (1 among 38 persons) for the group of age 20-29 years and increases to 41% (13 among 32 persons) in elderly of 80-89 years old (Okayama et al., 2002).

Contamination of unknown origin

This way of contamination remains unknown in 20-40% of HCV infected persons (Dubois et al., 1997, Conry–Cantilena et al., 1996). Socioeconomic status also plays an important, although indirect, role in the transmission of HCV infection. In the study conducted by Kawachi prevalence of anti-HCV was inversely related to educational levels and positively related to the number of medical injections. This might be because people of lower socioeconomic status are more likely to have an unhealthy lifestyle and lack access to health care, and be less well informed about the prevention of diseases (Kawachi, 1998). Those persons who habitually smoked had a higher prevalence of HCV infection and were at significant risk for frequent medical injections (as outpatient or in hospital) (Nina et al., 1999). In the study of Gardella, students demonstrate a poor quality of knowledge regarding hepatitis C and among factors associated with better knowledge about hepatitis C were identified: female gender, employed parents, and type of educational institution (Gardella et al., 2007).

In our study the initial value of transaminases (at the initiation of treatment) was low in a third of cases, mainly in female and in young persons. Higher level of transaminases in men could be correlated with alcohol consumption, drugs or sexual transmitted diseases, behaviors generally undeclared by patients. Moreover, heavy alcohol intake (50 grams per day) in patients with chronic HCV has been shown to increase fibrosis progression, rates of cirrhosis, and risk of death (Peters et al., 2002). In table 4 are shown different ways of HCV infection and their frequency in recent studies.

Table 4. Risk factors associated with hepatitis C (recent studies)

Author	N	Nosocomial transmission	Contaminated needlesticks	Injecting drugs	Sexual transmission	Other	Unidentified
Delawaide (2004)	44	45%	9%	32%	-	-	14%
Wiegand (2006)	89	19%	11%	22%	22%	8%	17%
Sanantonio (2006)	214	32%	5%	30%	7%	13%	13%
Martinez (5)	109	73%	7%	9%	6%	5%	5%
Katsoulidou (2006)	1229	5%	-	30%	-	28%	37%

Educational and medico-social measures to limit the prevalence rate of risk factors for hepatitis C in population

Attitudes and medical activities

Primary prevention (to avoid Hepatitis C virus contamination). It has main importance and regards the circumstances that could favor the infection of an innocent person (blood transfusions, surgical interventions, therapeutic and diagnostic procedures). The iatrogenic primary prevention use now efficient and verified tools which can decrease to the minimum level the iatrogenic infection risk. *The blood test* (for transfusions) done in the Regional Centres for Blood Transfusion, the protocols for proper sterilization and disinfection which use *modern and efficient techniques*, the usage of effective disinfection *solutions* in ambulatory medicine that nullify the risk of fortuitous contamination, the using of single-utility surgical instruments (needles and syringes, for infusions, for basic surgery), represents the best methods and techniques intended for this aim.

Population screening. It has the role to discover the infected persons with HCV which doesn't know about their contaminations and have no symptoms. Today, the situation in Romania could be considered as satisfactory taking into account the increasing accessibility and addressability of the population to laboratory exams. Nowadays, the serological tests for HCV infection it is not mandatory but it is strongly recommended for certain socio-professional categories: the pregnant women (the exam is for free), medical personnel (physicians and nurses), and the care-workers from closed communities (hospitals for aged people, houses for abandoned or orphan children, nurseries etc), military personnel and tourism – workers (WHO 2000).

Specific medical education, focused on this subject, must be done by qualified medical experts with certain responsibilities. The Family Medicine Network, the Scholar Medicine services, the WorkMedicine, the specific medical services from Army and Homeland Affairs, represents resorts and tools to disseminate informations concerning prevention through population at risk. These informations can be given using scholar's sexual education activities, educative meetings for future couples, and workshops for target groups (institutionalized teenagers, detainees, prostitutes).

Attitudes and social activities

Identification of persons at risk who are not registered in the health services records (healthy people, without contact with medical institutions). The target-groups can be people who use intravenous drugs, detainees, prostitutes, (Preda, et al., 2009), people with particularly sexual behaviors, and teenagers (Ingrand et al., 2004, Lindsay et al., 1999). These population categories can represent an infectious reservoir also for HCV and HBV (hepatitis B virus) or HIV.

Acces facilitation to health care services for persons founded at risk, by counseling and steering them to specialized services (Cojocaru, 2005). A major effectiveness could be obtained by inter-disciplinary teams composed from physicians, nurses, social workers, psychologists and sociologists, having the aim to identify the population risk groups, to analyzing the social, familial, professional features and environment habits in order to manage it by versatile manner (including health and social bearings).

Educational activities and interventions

It includes a large trowel of actions and we can specify the *child's basic education* (health, private sanitation or human relationship hygiene) (Dimitriu-Tiron, 2009), *the sexual education of teenagers* (relationship between both genders, affective and emotional hygiene) (Gabor, 2004), health education of young adults (using the protective means against sexual transmitted diseases, encouragement of the monogamic sexual life, fidelity and respect for life partner).

The core principles of these educative activities concerns the personal protection skills learning, keeping an effective private hygiene, informations about risk status (accidental/ignorance exposing by cosmetic procedures, tattooing or piercing) (Gardella et al., 2007), training about protection methods and skills against sexually transmitted diseases (using the condom, couple fidelity, knowing the sexual history of the new partner), female education concerning the risk of propagation to fetus of sexually transmitted diseases).

Conclusions

The present study confirms that the most relevant risk factors for the acquisition of HCV in north-east of Romania are transfusions of blood or blood products before 1993 followed by dental procedures (25,5%) and health care related procedures (diagnostic or therapeutic procedures in hospital). The results of this study stress the necessity of strict adherence to and enforcement of safe and standard medical practices and to universal precautionary measures to prevent further transmission of HBV and HCV.

Because the quality of knowledge regarding hepatitis C is very poor among adolescents would be beneficial for public health a strong intervention to present the most relevant risk factors for the acquisition of this virus, activities with implications in prevention and early recognition of suggestive manifestations of liver disease.

Rezumat

Virusul hepatitic C (HCV) este principala cauză a afecțiunilor hepatice cronice peste tot în lume. Estimativ, 3% din populația globului (200 milioane persoane) este cronic infectată cu HCV; infecția cu HCV este responsabilă de aproximativ 20% din hepatitele acute și de 70% din hepatitele cronice. Boală lent progresivă, hepatita cronică C se dezvoltă la 75% dintre pacienții infectați acut. Am realizat un studiu prospectiv care a inclus 286 pacienți cu hepatită cronică cu virus C spitalizați în spitalul clinic de Boli Infecțioase Iași. Scopul studiului a fost investigarea factorilor de risc potențiali pentru infectarea cu virusul hepatitei C în regiunea de nord-est a României. Pacienții incluși în studiu au declarat existența în antecedente a unor factori de risc potențiali în 35,66% din cazuri, cei mai frecvenți fiind: antecedentele transfuzionale (32%), intervențiile stomatologice (25,5%) și procedurile invazive cu scop diagnostic sau terapeutic (20%). Înteparea accidentală a fost raportată de 16 pacienți (5,6%). Pacienții cu vârsta peste 40 ani au prezentat o rată mai mare de raportare a factorilor de risc față de cei tineri ($p=0,038$). Rezultatele acestui studiu subliniază necesitatea respectării stricte a măsurilor universale de asepsie și antisepsie precum și a respectării metodelor de prevenție a bolilor cu transmitere sexuală.

Intervențiile de tip informativ asupra adolescenților ar putea avea un impact pozitiv privind nivelul cunoașterii acestei patologii cu implicații asupra prevenției și depistării precoce.

Cuvinte cheie: Hepatita cu virus C, factori de risc.

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