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RAPID COMMUNICATION

Known and probable risk factors for hepatitis C infection: A case series in north-eastern Poland

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Abstract

AIM: To describe the risk profile of patients in hospital with hepatitis C virus (HCV) infection in Poland.

METHOD: Using a structured questionnaire, all patients with confirmed HCV infection were interviewed about the risk factors.

RESULTS: Among the 250 patients studied, transfusion before 1993 was the primary risk factor in 26%, intravenous drug use setting in 9% and occupational exposure in health-care in 9%. Women were more likely to have a history of occupational exposure or transfusion before 1993 and less likely to undergo minor surgery. Known nosocomial risk factors (transfusion before 1993, dialysis) were responsible for 27% of infections, probable nosocomial factors (transfusions after 1992, minor surgery) for 14% and further 9% were occupationally acquired infections.

CONCLUSION: A careful history investigation can identify a known or probable risk factor for HCV acquisition in 59% of patients with HCV infection. Preventive activities in Poland should focus on infection control measures in health-care setting.

Key words: Hepatitis C; Risk factors

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INTRODUCTION

Hepatitis C virus (HCV) is the most common chronic blood-borne infection in developed countries and the major cause of chronic liver disease, cirrhosis and hepatocellular cancer. Since no effective vaccine against HCV infection is available, reducing the spread of the disease relies on primary prevention activities that can cut the transmission routes and reduce or eliminate the risk of acquiring infection. Since its discovery in 1989, much has been learnt about the ways in which HCV is transmitted. Well-known and common modes of transmission involve transfusions received before the routine screening of blood donors was implemented (in Poland since July 1992), intravenous drug use (IVDU), hemodialysis, and occupational exposure to the infected blood in health-care facilities[1-3]. Sexual transmission of HCV has also been demonstrated, but it is known to occur with less frequency compared to hepatitis B or HIV. Other risk factors are considered, but their role has not been established convincingly. Some case-control studies linked HCV infection to surgical or dental procedures, endoscopies, tattooing, body piercing, acupuncture, household contact with an anti-HCV person, and intranasal cocaine use. The results of the studies are, however, conflicting and some expert groups have found no associations between those exposures and HCV infections. In fact, there may be geographical differences in predominance of certain routes of transmission over others. Although the data on HCV epidemiology in Eastern Europe are scarce, the available literature and experts' opinions indicate that surgical and parenteral procedures (independent from blood transfusions) account for 40%-71% of HCV infections[4].

The precise data on HCV prevalence in the general population in Poland is lacking since no population-based study was carried out. According to WHO estimates about 1.4% of general Polish population may be infected with HCV, which means about 560 000 persons in the whole country[5]. At the same time, statistics of the National Institute of Hygiene in Warsaw registered about 13 000 infections in the years 1997-2003 (compulsory registration of HCV started in 1997)[6]. It is clear that most people with HCV infection in Poland are unaware of their status, even if we assume under-reporting by medical and laboratory services.

In Poland, in contrast to USA or UK, where drug use prevails, many HCV cases are presumed to be nosocomial infections. Previous studies based on the samples of patients hospitalized for acute or chronic hepatitis C linked as many as 59%-71% of HCV infections to medical procedures[7]. Our recent case-controlled study aiming at identifying medical procedures associated with exposure to HCV found that transfusions (OR = 3.7, 95%CI = 2.2-6.3), minor surgery (OR = 3.2, 95%CI = 1.5-6.7) and dental care (OR = 2.3, 95%CI = 1.4-4.0) were independently associated with HCV infection[8]. In Poland, hepatitis B virus (HBV) infection, which spreads in a similar way to HCV, is also frequently a medically linked disease[9].

Identifying risk factors is important in order to plan preventive activities and is also necessary to target screening for people with higher pre-screening probability of the disease.

We undertook this study in order to describe the risk profile in a population of patients seeking care in a tertiary care level hospital in a defined region of Poland.

Table 1 Prevalence of all known and probable risk factors among 250 chronic hepatitis C patients (*n*, %)

Risk factors	All *n* = 250 (100%) *n* (%)	F *n* = 92 (36.8%) *n* (%)	M *n* = 158 (63.2%) *n* (%)
Known risk factors			
IVDU	22 (8.8)	4 (4.4)	18 (11.4)
Transfusion <1993	67 (26.8)	31 (33.7)	36 (22.8)
Hemodialysis	5 (2.0)	3 (3.3)	2 (1.3)
Occupational exposure - health-care	34 (13.6)	21 (22.8)[1]	13 (8.2)[1]
Sexual exposure to HCV	2 (0.8)	0 (0.0)	2 (1.3)
Probable risk factors			
Transfusions after 1992	17 (6.8)	6 (6.5)	11 (7.0)
Minor surgery	36 (14.4)	5 (5.4)[2]	31 (19.6)[2]

[1]$P<0.05$, F *vs* M in occupational exposure - health-care group; [2]$P<0.05$, F *vs* M in minor surgery group.

MATERIALS AND METHODS

Patients

The study took place in the Department of Infectious Diseases, Medical University of Bialystok (north-eastern Poland) between June 1, 1998 and December 31, 2004. All consecutive adult patients with acute or chronic hepatitis C admitted to the department were invited to participate. This department is the biggest hepatologic center in Podlaskie Region (1 200 000 inhabitants, north-eastern Poland), where the majority of patients with chronic viral hepatitis from the whole region are referred for evaluation and antiviral treatment.

The diagnosis of hepatitis C was based on the presence of anti-HCV antibodies (ELISA, third generation test, IMx MEIA, Abbott, Chicago, USA) and was confirmed by means of HCV-RNA testing (qualitative nested RT-PCR). The standard procedures with a suspected case of chronic hepatitis C include initial testing for anti-HCV and determination of ALT levels, and repeating the tests for anti-HCV and ALT levels after 6 mo. If anti-HCV is repeatedly positive and ALT levels remain elevated above the normal range, patients are tested for HCV-RNA, and liver biopsy is performed. Since confirmatory tests using immunoblotting were not available, only the patients who were positive for anti-HCV and HCV-RNA were included in the present study.

Methods

All patients were interviewed extensively by one of the two doctors with the use of a structured questionnaire. The questionnaire covered demographic data (age, sex, education, job, place of living) and information about the possible risk factors. The risky exposures considered in our study were as follows: (1) known risk factors, such as IVDU, transfusions of blood or blood products before 1993, employment as a health-care worker with exposure to blood or other fluids, hemodialysis, and sexual contact with an anti-HCV positive person; (2) probable risk factors, such as household (non-sexual) contact with an anti-HCV positive person, transfusion after 1992, and minor surgery; and (3) other potential risk factors for HCV infection, such as surgeries, endoscopies, tattoos, previous hospitalizations, and acupuncture. In further analysis, the patients with more than one risk factor were classified as having only the risk factor according to the hierarchy. The hierarchy of risk factors used in our study was based on the data from medical literature as well as on the results of our previous study indicating the link between history of minor surgery, transfusion after 1992 and increased risk for HCV infection in Poland. We did not include dental care (which had also been associated with HCV infection) into probable risk factors because of the low specificity of that exposure with nearly 90% of the study group providing history of dental treatment. For comparisons between groups, the patients were stratified by age (<45 or ≥ 45 years) and by gender.

Statistical analysis

The statistical calculations were performed with the use of statistical package, Statistica Pl. Fisher's exact test was used for the analysis of differences in risk factors between groups (males *vs* females, younger *vs* older and younger *vs* older patients of the same sex). A P value < 0.05 was considered statistically significant.

RESULTS

A total of 420 anti-HCV positive individuals were evaluated during the study period and 250 were eligible for the study. In the remaining 170 cases, the results of HCV-RNA testing were either negative or unavailable. Among the study group, there were 92 females (36.8%) and 158 males (63.2%). Patients' age ranged from 18 to 70 years with the mean age of 39.7 (± 2.8) years. Females were found to be obviously older compared to males (mean age, 43.4 *vs* 38.4 years, $P < 0.05$). Majority of the patients came from urban setting (219 patients, 87.6%) and had secondary (120, 48.0%) or elementary (80, 32.0%) education.

Table 1 presents the overall prevalence of the considered

Table 2 Distribution of known and probable primary risk factors (one per person according to the hierarchy) stratified by age and gender

Risk factors	All *n* (%) 250 (100%)	F *n* (%) 92 (36.8)	M *n* (%) 158 (63.2)	F < 45 *n* (%) 43 (46.7)	M < 45 *n* (%) 109 (69.0)	F > 44 *n* (%) 49 (53.3)	M > 44 *n* (%) 49 (31.0)
Known risk factors	112 (44.8)	49 (53.3)[a]	63 (39.9)[a]	26 (60.5)[c]	43 (39.4)[c]	23 (46.9)	20 (40.8)
IVDU	22 (8.8)	4 (4.4)	18 (11.4)	3 (7.0)[e]	18 (16.5)[e]	1 (2.0)[e]	0 (0.0)[e]
Transfusion before 1993	65 (26.0)	31 (33.7)[g]	34 (21.5)[g]	18 (41.9)[i]	19 (17.4)[i]	13 (26.5)	15 (30.6)
Occupational exposure – health-care	22 (8.8)	13 (14.1)[k]	9 (5.7)[k]	5 (11.6)	6 (5.5)	8 (16.3)	3 (6.1)
Dialysis	3 (1.2)	1 (1.1)	2 (1.3)	0 (0.0)	0 (0.0)	1 (0.0)	2 (4.1)
Sexual contact with HCV	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Probable risk factors	35 (14.0)	6 (6.5)[m]	29 (18.4)[m]	4 (9.3)	17 (15.6)	2 (4.1)[o]	12 (24.5)[o]
Transfusion after 1992	13 (5.2)	4 (4.4)	9 (5.7)	2 (4.7)	3 (2.8)	2 (4.1)	6 (12.2)
Minor surgery	22 (8.8)	2 (2.2)[a]	20 (12.7)[a]	2 (4.7)	14 (12.8)	0 (0.0)[s]	6 (12.2)[s]
No known or probable risk factors	103 (41.2)	37 (40.2)	66 (41.8)	13 (30.2)	49 (45.0)	24 (49.0)	17 (34.7)

[a]$P < 0.05$, known risk factors F *vs* M; [c]$P < 0.05$, known risk factors F < 45 *vs* M < 45; [e]$P < 0.05$, IVDU all < 45 *vs* all > 44; [g]$P < 0.05$, transfusions before 1993 F *vs* M; [i]$P < 0.05$, transfusions before 1993 F < 45 *vs* M < 45; [k]$P < 0.05$, occupational health-care F *vs* M; [m]$P<0.05$, probable risk factors F *vs* M; [o]$P < 0.05$, probable risk factors F>44 *vs* M>44; [q]$P<0.05$, minor surgery F *vs* M; [s]$P < 0.05$, minor surgery F > 44 *vs* M > 44

Table 3 Potential sources of exposure to HCV among 103 persons without known or probable risk factors

Risk factors	All *n* (%) 103 (100%)	F *n* (%) 37 (35.9)	M *n* (%) 66 (64.1)
Surgery (other than minor)	49 (47.6)	24 (64.9)[a]	25 (37.9)[a]
Endoscopies	52 (50.5)	22 (59.5)	30 (45.5)
Hospitalizations (more than 5)	22 (21.4)	15 (40.5)[c]	7 (10.6)
Tattoo	11 (10.7)	0 (0.0)	11 (16.7)
Dental care	91 (88.3)	33 (89.2)	58 (87.9)
None of above	1 (1.0)	0 (0.0)	1 (1.5)

[a]$P < 0.05$, surgery (other than minor) F *vs* M; [c]$P < 0.05$, hospitalizations (more than 5) F *vs* M; [c]$P < 0.05$, tattoo F *vs* M.

known and probable risk factors. In the studied hepatitis C group, there were no cases of household (non-sexual) exposures to HCV and that factor is not presented in the table. The most prevalent reason was transfusion before 1993 in 67 (26.8%) cases, followed by minor surgeries in 36 (14.4%) cases, occupational exposure in 34 (13.6%) cases during health-care and IVDU in 22 (8.8%) cases. Table 2 displays hierarchical distribution of primary risk factors for HCV infection (each case is represented only once). Overall known risk factors could be identified in nearly 45% of patients and probable in further 14%. About 41.0% had no known or probable risk factors according to the criteria established in our study. Three factors, such as history of transfusion before 1993, occupational exposure and minor surgery, were significantly associated with gender. The first two factors occurred more frequently in females while minor surgery was more common among males. There was a clear tendency towards more frequent occurrence of IVDU among males, but the difference did not reach statistical significance.

Overall females were more probable than males to have known risk factors (53.3% *vs* 39.9%, $P < 0.05$). The prevalence of drug use in the younger group (21/152, 13.8%) was significantly higher than that in the older group (1/98, 1.0%, $P < 0.05$). IVDU in our study was almost limited to males under the age of 45 with 82% (18/22) of patients.

In our study, females ≥45 years were the group with the highest frequency (49%) of unidentified (without known or probable risk factors) source of HCV infection, but the difference was not statistically significant.

Table 3 depicts the overall prevalence of other potential exposures to HCV among 103 patients without known or probable risk factors. Only one person denied all of the considered risk factors.

Known nosocomial risk factors (hemodialysis, transfusion before 1993) were responsible for 27% of all infections, while probable nosocomial risk factors (transfusion after 1992, minor surgery) were responsible for 14% of infections. Further 9% were occupationally acquired infections in health-care workers. Altogether at least 50% of all HCV infections in our study were associated with a health-care sector.

DISCUSSION

Hepatitis C infection affects approximately 560 000 people in Poland. Difficulties in identifying risky exposures result from the fact that most cases are clinically silent and remain undiagnosed for many years. In addition, some potential risk factors (e.g., dental care, hospitalizations) are very common and their non-specific nature hinders

establishing their role in HCV transmission and makes targeting prevention measures difficult.

The demographic characteristics of our sample were comparable to the data collected by National Institute of Hygiene in Warsaw for all 2 255 new hepatitis C cases registered in Poland in 2003 (incidence 5.90/100 000 inhabitants)[6]. In our group, males constituted 63% of cases and males under the age of 45 made up nearly 44% of all HCV infections. The national statistics for 2003 indicate that 57% of HCV infections occurred in males, and younger males between 20 and 24 years of age had the highest incidence of infection (10.8/100 000 inhabitants). Similarly, as in our findings, majority of the registered new cases came from urban setting (80.0%). Currently, there are no national reports on the distribution of risk factors among registered HCV cases in Poland.

In our study, known risk factors could be identified in nearly 45% of HCV infections. As expected, transfusions before 1993 represented the most prevalent known exposure. Transfusion before 1993 could be documented in more than 60% of HCV infected females under the age of 45. In a majority of cases, the infection was the iatrogenic effect of postpartum iron-deficiency anemia treatment. Blood transfusion was frequently used to raise the hemoglobin levels and to allow earlier discharge from hospital.

Primary prevention activities have been already undertaken and current procedures have virtually eliminated the risk of HCV infection from blood transfusion. The knowledge of history of transfusion is important for secondary prevention, which means target screening for HCV infection. Testing should be routinely offered to the persons with the history of transfusions before 1993, accompanied by appropriate counseling and medical management.

IVDU was responsible for 9% of infections and was almost exclusively limited to males under the age of 45. At the same time, younger males made the group with high frequency of no known or probable risk factors. It may be speculated that, at least in some of those cases, incidental drug use could be responsible. Many of American blood donors found to be positive for HCV infection revealed the history of drug use, despite initial denial of such exposure[10]. In our study, the rate of HCV infections resulting from drug use among males <45 years of age (17%) was still much lower than that reported in similar groups in the United States (59%-60%)[11,12]. This finding confirms the primary role of nosocomial HCV spread in Poland and may reflect lower numbers of drug users in Poland compared to USA or other Western European countries. Estimates of the prevalence of problem drug use (defined as injecting drug use or long duration, regular use of opiates, cocaine and/or amphetamines) range in European Union countries between 2 and 10 cases per 1 000 of the population aged between 15 and 64 years, and Poland remains in the low range[13]. As in many Central and Eastern European countries, the major problem regarding drug use in Poland concerns heroin. Opiate users represent the biggest proportion of persons admitted to residential treatment due to drug addiction. Shared usage of contaminated needles and syringes results in high prevalence of HCV antibodies. Among 100 parenteral drug users in Warsaw, 76% were found to be seropositive for anti-HCV[14]. Another possible explanation for relatively low percentage of intravenous drug users in our study might be failing secondary prevention of HCV infection among drug-dependant population in Poland. In this respect, it is possible that drug users are under-represented in the hospital samples because of the hindered access to screening procedures, health-care services and long-term antiviral treatment.

Occupational infections constituted nearly 10% of primary risk factors in our study and occurred mostly in women in both age groups. Nurses are the predominant occupational group injured by needles and other sharp-edged instruments, because they are the largest segment of the workforce in health-care, and also because they may have a higher rate of injury. This group sustains about 50% of all needle-stick injuries. The accidents typically happen when workers are recapping needles, transferring body fluids from one container to another, or when they do not dispose the used needles properly[15,16]. In 2001, hepatitis C constituted the major cause of all occupational blood-borne infections in health-care workers in Poland[17].

In this study, known nosocomial and probable nosocomial risk factors were responsible for 27% and 14% of all infections, respectively. Fortunately, the major nosocomial risk factor, transfusion of contaminated blood, has been virtually eliminated. After the introduction of screening of all blood donations for HCV-RNA, the calculated risk of HCV infection resulting from the transfusion of blood during window period is about 1/1 000 000 blood units[18].

In 102 out of 103 HCV-infected individuals without known or probable risk factors, other potential exposures could be found and most of those were medically linked.

Our study confirms that hospital setting remains as an important source of infection. This seems to be a common feature in Eastern European countries. Nosocomial transmission of HCV is possible if infection-control techniques or disinfection procedures are inadequate and contaminated equipment is shared among the patients. Diagnostic or treatment procedures (surgical or parenteral procedures without blood transfusions) in hospitals were indicated as the source of infection in approximately 59%-65% cases in Poland, 59% in Latvia and 46% in Hungary[4].

Our study had certain limitations as follows: the patients with IVDU or hemodialysis were under-represented in the sample; the percentage of patients with probable risk factors was related to our definition of those factors; and we did not include certain medical procedures or events into that category because previous case-control study did not confirm their relation to HCV infection and because some of them could not be the cause but the result of HCV infection (endoscopies, hospitalizations). In our previous study, we found an increased risk associated with minor surgery[8]. Including that exposure into probable risk factors category could overestimate the percentage of patients in our study with known or probable risk factors. The possible overestimation was almost limited to men.

In our experience, a careful history can elicit a risk factor in nearly 60% of hepatitis C infections. The study reveals that overall of at least 50% of HCV infections are associated with health-care sector (transfusions, occupational exposure, other nosocomial exposures). Among the remaining 40% of patients without known or probable risk factors, almost all individuals provided a history of contact with health-care sector preceding diagnosis of hepatitis C. There is a clear tendency towards association of risk factors with age and gender. IVDU occurs mainly in younger males, whereas transfusion before 1993 was more common in younger females. Females are more probable to acquire the infection performing occupational activities in health-care. The two groups with the highest rates of risk factors were women > 44 years and men < 45 years. We speculate that hospitalization and surgery are responsible for some of those infections in older females and IVDU in the younger males.

We conclude that preventive activities against HCV spread in Poland should focus on infection control measures in health-care setting.

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