Injecting drug users, MSM and people at the older age should be routinely tested for HCV in Poland – data derived from a post-exposure prophylaxis population

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Abstract

Objective. The aim of the study was to identify risk factors for HCV infection and thus identify groups for routine HCV testing in the group of people consulted for post-exposure prophylaxis (PEP).

Materials and methods. A retrospective analysis was performed of cross-sectional data available from consultations due to post-exposure prophylaxis in HIV Out-patient Clinic and Emergency Department (ED) of Hospital for Infectious Diseases in Warsaw, Poland. Data were obtained from the electronic database, from 2008-o 2016. For statistical analysis, χ2 and t-tests were used for group comparisons, as appropriate. A total of 3,593 persons were included in the study, 60 (1.7%) were anti-HCV positive. In the first step, univariate models were estimated for each of predictors separately.

Results. The results showed that odds of infection are significantly higher in males (OR=1.92), people after non-professional exposure (OR=3.82), and increase with age (OR=1.03). In the next step, a multivariate logistic model was fitted in the group of participants after non-professional exposure with gender, age, and route of exposure as predictors. Obtained results revealed significantly higher odds of infection, both in IDU (OR=162.6) and gender exposure (OR=3.59) groups. After including routes of exposure, effects of age remained significant (OR=1.05), while the effects of gender did not (OR=1.12).

Conclusions. Based on the study results, it is recommended that routine testing for HCV should be provided for people at older age, and for individual with behavioural risk factors, such as history of injecting drugs use or sexual exposure, particularly among men having sex with men (MSM).

Key words

professional exposure, pos-exposure prophylaxis, risk factors for HCV infection, HCV testing, non-professional exposure

INTRODUCTION

According to the data provided by the World Health Organization (WHO) in 2017, up to 71 million people worldwide and 3.9 million in Europe were chronically infected with HCV[1, 2]. Despite this, the testing rates for hepatitis C are still relatively low due to the lack of possible general screening in the risk groups. Finding a solution to this problem constitutes one of the most relevant challenges as it will allow overcoming the difficulties and potential for the missed opportunities for the HCV and HIV testing [1, 3–5]. Moreover, this could prevent late presentation as the missed opportunities for the HCV and HIV testing [1, 3–5]. Furthermore, many individuals are unaware of their status due to insufficient awareness or lack of knowledge regarding the potential sources or risks of infection, which constitute the leading and most frequent causes of the low rates of the HCV and HIV detection in the general population [7, 8].

Poland belongs to the countries with low seroprevalence of HCV infection, thus the entire ‘population-based screening strategy’ is not recommended as it is not cost-effective. It is said that the strategies aimed at preventing new infections should be ‘tailored to address the most common modes of transmissions’ [7, 9, 10]. In Poland, more than 1,400 new cases of HIV and more than 3,500 of HCV were diagnosed in 2018 [11, 12]. Current statistics indicate that one in five persons infected with HCV are aware of their status [11, 13].

Similar to international data, in Poland the risk groups are quite well understood and include: people who inject drugs (PWID), migrants, people in prison, transfusion recipients prior to universal donation screening before 1992, HIV positive men who have sex with men, and patients who have been hospitalized more than three times in their lives [14–19].

The lack of possibility to find an appropriate testing strategy to reach the risk groups is still problematic and constitutes one of the most relevant issues in the area of public health in Poland [20]. Unfortunately, the major problem is still the lack of a national screening programme for HCV infection in Poland. The remaining patients are an anonymous reservoir of the virus, which influences the dynamics of the epidemic of the viral hepatitis [21, 22]. Research in this area is scarce.
Many projects involving routine screening failed to identify new infections and guide behavior-based testing, because no appropriate regulations have been made at government level [23].

**OBJECTIVE**

The aim of the study was to identify the risk factors for HCV infection, and thus identify groups for routine HCV testing in people consulted for post-exposure prophylaxis (PEP) -patients attending the Out-Patient Clinic of the Hospital for Infectious Diseases in Warsaw.

**MATERIALS AND METHOD**

A retrospective analyses was performed of data available from consultations due to post-exposure prophylaxis in the HIV Out-patient Clinic and Emergency Department (ED) of the Hospital for Infectious Diseases in Warsaw. The data presented and analysed in this study were obtained from an electronic database prospectively designed to collect all medical information for PEP patients since 2008. A manual review of medical charts was carried out in the case of ambiguous data. The data analyzed included information about type of exposure, age, gender, exposure source (if available), and only baseline laboratory tests. Type of exposure was categorized as occupational and non-occupational exposure. The Hospital for Infectious Diseases provides post-exposure prophylaxis according to Polish AIDS Society Recommendations [24]. Blood samples for baseline serology are taken according to Polish AIDS Society Recommendations [24].

At baseline visit, serological tests were performed for all patients (anti-HCV test, HBsAg and HIV DUO test). It should be noted that risk contacts included occupational exposure, defined as exposure to potentially infectious material as a result of a needle-stick injury or other devices contaminated with blood that occur during work (e.g. medical doctors, dentists, nurses, laboratory staff, cleaning staff, firemen, policemen, city guards and prison staff). The so-called non-occupational exposure refers to exposure to a particular infectious factor – ‘an infectious agent’ which occurs outside the professional environment (e.g. during sex; when sharing needles used to inject drugs, or after incidental contact with a needle or other devices contaminated with blood). Routes of exposure were defined in five categories: contact with blood, contact with other infectious material, needle injury, sexual contact (heterosexual or men having sex with men), as well as intravenous drug use (IDU).

For statistical analysis, χ2 and t-tests were used for group comparisons, as appropriate. Positivity rates of tests were reported with 95% confidence intervals. Analyses concerning types of exposure were performed using univariate and multivariate logistic regressions with profile-likelihood. In each analysis, the category with the lowest infection rate was selected as reference. Logistic regression models were used in order to identify factors associated with a positive anti-HCV test (all with p<0.1 in univariate included in the final model). Due to the low positivity rate, the HIV test status was not included in the presented model. All p-values were calculated using two-sided tests. All computations were performed with the use of the R version 3.4.2 (R Core team, 2017)

**RESULTS**

The initial database included 5,195 patients aged 18–80 years at the time of visit (routine check-ups of medical stuff were not included into this database) from 7 January 2008 – 17 May 2016. All the cases with unknown route of exposure (1,594 cases, 30.7% of the sample) and eight cases with inconclusive HCV-antibody test results (0.2% of the sample) were excluded. Patient data concerning the results of serological tests performed during the first visit were finally included in the analysis.

A total of 3,593 persons were included in the study, 60 (1.7%) were anti-HCV positive, thirty four (1.0%) HBsAg positive, and four (0.1%) anti-HIV/p24 positive. Among them, two persons were both anti-HCV and HBsAg positive, one both anti-HIV/p24 and HCV positive.

Comparison of basic demographic characteristics indicated that the anti-HCV positive group included fewer females (41.7 vs 57.8%) and were older (40.0 vs 35.7 years of age) when compared with anti-HCV negative group. The proportion of occupational exposures in the HCV+ group was markedly lower than in the HCV- sample (31.7 vs 63.9%) (Tab. 1).

| Table 1. Comparison of demographic characteristics of HCV- and HCV+ groups [1] |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Gender N (% of females)         | 2,066 (57.5)    | 2,041 (57.8)    | 25 (41.7)       | 0.018           |
| Age in years (M +/- SD)         | 35.72 (11.6)    | 35.7 (11.5)     | 40.0 (12.9)     | 0.013           |
| Professional exposures N (%)    | 2277 (63.4%)    | 2258 (63.9%)    | 19 (31.7%)      | <0.001          |

**Distribution of exposure routes across HCV negative and HCV positive groups are shown in Table 2.**

| Table 2. Distribution of exposure routes across HCV- and HCV+ groups |
|---------------------------------------------------------------------|
| Route of exposure:                                                |
| N (%)                                                              |
| N (% within group)                                                |
| N (% within group)                                                |
| Infection Rate (95% CI)                                           |
| Contact with infectious material                                  |
| 235 (6.5%)                                                        |
| 233 (6.6%)                                                        |
| 2 (3.3%)                                                          |
| 0.85% (0.15-3.37%)                                                |
| IDU                                                                 |
| 28 (0.8%)                                                         |
| 14 (0.4%)                                                         |
| 14 (23.3%)                                                        |
| 50.0% (32.6-67.4%)                                                |
| Needle                                                             |
| 2027 (56.4%)                                                      |
| 2007 (65.8%)                                                      |
| 20 (33.3%)                                                        |
| 0.99% (0.62-1.54%)                                                |
| Blood                                                              |
| 590 (16.4%)                                                       |
| 584 (16.5%)                                                       |
| 6 (10.0%)                                                         |
| 1.02% (0.41-2.32%)                                                |
| Sex                                                                |
| 713 (19.8%)                                                       |
| 695 (19.7%)                                                       |
| 18 (30.0%)                                                        |
| 2.52% (1.55-4.04%)                                                |

**Logistic regression models.** The predictors associated with anti-HCV positive test were investigated by fitting a series of logistic regression models. In the first step, univariate models were estimated for each of the predictors separately in the whole sample (Tab. 3). The results showed that odds of infection were significantly higher in males, people after non-professional exposure, and increase with age. Analysis including routes of transmission revealed significant change in odds when IDU group was compared to the reference category, i.e. patients who had contact with infected material.
The multivariate analysis including exposure (Tab. 5.) showed a similar pattern, confirming that non-professional exposure was related to higher infection odds, as was participant's age, whereas the effects of gender were no longer significant.

Table 3. Univariate logistic regressions models predicting positive results of anti-HCV positive test

| Route of exposure: | 95% profile-likelihood CI | OR  | LL | UL | p    |
|--------------------|--------------------------|-----|----|----|------|
| Infectious material | -                        | -   | -  | -  | -    |
| IDU                | 116.50                   | 29.03 | 791.16 | <0.001 |
| Needle             | 1.16                     | 0.34 | 7.30 | 0.838 |
| Blood              | 1.20                     | 0.27 | 8.21 | 0.824 |
| Sex                | 3.03                     | 0.86 | 19.07 | 0.089 |
| Sex (male)         | 1.92                     | 1.15 | 3.25 | 0.013 |
| Age (in years)     | 1.03                     | 1.01 | 1.05 | 0.006 |

Type of exposure (non-professional) 3.82 2.24 7.76 <0.001

OR – odds ratios, LL – lower limit, UL – upper limit

The study presents high rates of anti-HCV positive test results among persons consulted for post-exposure prophylaxis, 1.7% compared to the general population rate of 1.0% in Poland. While the rate of the positive anti-HCV tests was higher among non-occupational exposures (3.11%), it was slightly lower among occupational exposures (0.83%) when compared with the rate observed in the general Polish population [13].

According to a recent systemic review from 2017 in the EU/EEA countries, the prevalence of anti-HCV in the general population of individual Member States is estimated to vary from 0.1% – 5.9% [25]. Compared to Polish data, countries in Eastern and South-Eastern Europe have higher prevalence estimates. On the other hand, people who were consulted for the post-exposure prophylaxis might be at higher risk for HBV, HCV or HIV infection due to the earlier exposures for blood-borne viruses.

In addition, the current study, based on a large population of persons consulted for post-exposure prophylaxis, shows several significant risk factors of HCV infection. First of all, the reported data indicated that positive HCV test was associated with injecting drugs. These data are consistent with the findings of a recent systemic review of hepatitis C sero-prevalence in the EU/EEA countries, which indicated that the most commonly reported route of transmissions among all disease categories was injecting drugs (55% among chronic and 40% among acute cases) [26]. Therefore, it is unquestionable that currently sharing of needles and other equipment in the process of injecting drugs remains the most relevant factor for HCV transmission in developed countries [27]. In Poland, people who inject drugs (PWID) are one of the important groups at risk for HCV infection, with geographical variation in particular regions (univariable and adjusted ORs with respect to the region with the lowest prevalence varied up to 2.8 and 3.8 for HCV infection, respectively). Data point to the need for a stronger investment in preventive measures [28]. In addition, recent research indicates the quick need for changes in harm reduction programmes in Poland. Besides, it is worth emphasizing that drug users, especially those who inject drugs, are one of the most vulnerable groups in the population, because in countries with a high standard of medical care, people who inject drugs are the main group determining the dynamics of HCV epidemics [29, 30].

Additionally, the presented analysis showed association between positive HCV test result and sexual exposures, as well as older age. Reported data also indicated that hepatitis C infection predominantly affects men between 35–44 years. The results of the current study showed similarly that odds...
of infection were almost twice as high for men and 160 times higher for injecting drugs.

The presented analysis of the PEP population shows that the odds of infection are almost four times higher among male participants (OR=3.59, CI 1.01–22.87), but after including the routes of exposure, the effects of gender were no longer significant (OR=1.12, CI0.60–2.07). The HCV was pre-selected as a result of the characteristics of patients who reported (patients after sexual exposure with HCV-infected partners). It is worth emphasizing that many studies have shown that heterosexual intercourse plays a relatively insignificant role in transmission of hepatitis C [31]. A majority of the said studies indicated that the risk factors responsible for transmission included vaginal mucosal damage, genital erosive lesions, traumatic sexual intercourse with abrasion of the genital mucosa, via reuse of razors, medical devices and manicure devices contaminated with blood [32–34]. Transmission occurs very rarely through vaginal intercourse compared to anal intercourse (particularly among men who have sex with men – the group also referred to as ‘MSM’), when HCV infection happen several times more frequently [35].

According to the findings presented in the ECDC report, the prevalence of anti-HCV antibodies in the men having sex with men group had a higher than expected prevalence in the general population across the European Economic Area Countries (highest prevalence – 4.7%) [2]. The higher possibility of infections occurring during anal intercourse may be connected with co-infection with HIV or other sexually transmitted diseases with disruption of mucosal tissue [36]. Therefore it is viable to screen for HCV all persons diagnosed with sexually transmitted disease [37]. Recent studies strongly suggest that the epidemic of sexually transmitted HCV infections in MSM Has continued to spread during recent decade [38, 39]. It is worth emphasising that targeted and preventive measures are essential to stop the transmission of HCV, including increased testing to prevent the transmission of HCV in the MSM community [40].

Although associations with sexual exposures were noted, and the spread in this population was demonstrated, the nature of these and the burden of HCV among MSM remains unclear [41, 42]. Due to the limitations of the available data, it was not reliably possible to separate MSM vs MSW exposures for direct comparison in the presented sample. However, based on incomplete declarative responses, it was possible to confirm that at least 193 out of 451 (42.8%) non-occupational sexual exposures in males were MSM contacts. To the best of the authors’ knowledge, the results they obtained are the first to present in Polish population that sexual exposure in MSM poses a risk of HCV infection. The study also identified that people with older age are at greater risk for HCV. Similar results have been shown in several different studies, e.g. in the United States, Canada and Argentina. According to a study conducted in the USA, everyone who was born between 1945 – 1965 should undergo testing for HCV infection without prior ascertainment of HCV risk; similarly, in Canada persons born between 1945 – 1975, and in Argentina persons born before 1973 [43–45]. Similarly, in other studies conducted in Poland, the highest percentage of HCV antibodies occurred in the population aged over 50 (2.93%) [46, 47]. The increased prevalence of anti-HCV is probably associated with several factors, including contaminated blood or blood products (before 1992), as well as use or reuse of contaminated medical devices (e.g. in haemodialysis or for other purposes, such as tattooing devices, acupuncture needles, razors, and manicure devices) [15, 48]. However, it is estimated that in Poland people who have undergone non-medical invasive procedures, such as tattoos or small esthetic treatment, are still at great risk of HCV infection [16, 19].

In different studies in various countries, the prevalence of anti-HCV positivity among healthcare workers fluctuated from 0% – 9.7% [49]. The current study has shown rates of anti-HCV slightly lower in occupational exposures (0.83%) than the rates estimated to occur in the general population (1%), but similar to those seen in other studies [50, 51]. According to a study conducted by experts from the University of Antwerp in Belgium, the transmission of HCV infection may vary depending on the HCV load of the source (HCV RNA positive patient), and may occur among almost 10% of the healthcare workers after parenteral exposure to blood [52]. To achieve the goal of elimination of the public health problem of this disease in healthcare sites across Europe, it is necessary to increase testing rates and the number of new diagnoses [53].

The introduction of highly effective direct-acting anti-virals have changed the perspective of HCV treatment, but the major problem in Poland is the lack of a national screening programme searching for potential candidates for therapy. The presented study identified the populations with the highest antibody prevalence rate, and therefore should be considered as an optimal target group for improvement in the national strategy for HCV infection in Poland [54].

Some limitations to the study need to be mentioned. As this was a retrospective study, it was not possible to eliminate selection bias, as people at greater risk of HCV might be more likely to be referred to specialists care. Moreover, although data were collected in a standardized manner, some of the information was available only in doctors’ notes. It was also not possible to retrieve information on the route of exposure for 30% of the consulted patients. Additionally, patients with anti-HCV reactive results were referred to another outpatient care department, resulting in data on HCV RNA results not being available.

CONCLUSION

Based on the results obtained, it is recommended that routine testing for HCV should be provided for people at older age and individuals with behavioural risk factors, e.g. a history of injecting drugs or sexual exposure particularly among MSM.

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