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CROSS-SECTIONAL, ANONYMOUS SCREENING FOR ASYMPTOMATIC HCV INFECTION, IMMUNITY TO HBV, AND OCCULT HBV INFECTION AMONG HEALTH CARE WORKERS IN WARSAW, POLAND

PRZEKROJOWE, ANONIMOWE BADANIA PRZESIEWOWE BEZOBJAWOWYCH ZAKAŻEŃ HCV, ODPORNOŚCI NA HBV I UTAJONEGO ZAKAŻENIA HBV WŚRÓD PRACOWNIKÓW OCHRONY ZDROWIA W WARSZAWIE*

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STRESZCZENIE

WPROWADZENIE I CEL BADAŃ. Wyniki badań epidemiologicznych objawowych zakażeń HCV w Polsce wykazały, że ich częstość występowania wśród pracowników ochrony zdrowia (poz) może przewyższać odsetek notowany w ogólnej populacji. Ponieważ taka sytuacja epidemiologiczna byłaby podobna do zjawiska zwiększonej częstości występowania zakażeń HBV wśród poz w okresie przed wprowadzeniem szczepionki przeciw wirusowemu zapaleniu wątroby typu B (wzw B), wykonano w tej grupie zawodowej badania seroepidemiologiczne zakażeń HCV i odporności na HBV.

MATERIAŁ I METODY. Wszystkie osoby zaproszone do badań były zatrudnione jako poz w dwóch największych szpitalach klinicznych w Warszawie. Badane osoby oddały dobrowolnie próbkę krwi do badań serologicznych i jednocześnie były proszone o wypełnienie kwestionariusza z pytaniami odnoszącymi się do możliwych dróg zakażenia patogenami przenoszonymi drogą krwiopochodną, okresu zatrudnienia, i częściowo do ich stylu życia. Oba kierunki badań były anonimowe i wykonywane niezależnie. W pobranych próbkach krwi oznaczano także aktywność aminotransferaz.

WYNIKI. Otrzymano 961 próbek krwi od poz zatrudnionych w obu szpitalach. W zbadanych surowicach krwi wykryto anty-HCV w 16 próbkach (1,7%). HCV RNA wykryto w 3 spośród 16 (19%) próbek zawierających anty-HCV. W 2 próbkach surowic stwierdzono genotyp 2, a w jednej genotyp 1b HCV. Anty-HBs wykryto w 943 (98,1%) i anty-HBc (total) w 151 (15,7%) z 961 badanych surowic. Częstość występowania bezoobjawowych zakażeń HCV była więc podobna do częstości stwierdzanej w ogólnej populacji, natomiast częstość występowania anty-HBc przekraczała trzykrotnie wartość stwierdzaną w innych badaniach.

WNIOSKI. Ponieważ szczepienia przeciw wzw B są obecnie obowiązkowe dla poz, wysoki odsetek obecności anty-HBs wskazuje na skuteczną odpowiedź odpornościową po szczepieniach. Jednak obecność anty-HBs nie zawsze może być traktowana jako wskazująca na odporność przeciw zakażeniu HBV, ponieważ u niektórych osób może maskować utajone zakażenie HBV. Ze względu na powszechną odporność przeciw zakażeniu HBV młodej populacji Polski, po wprowadzeniu obowiązkowych szczepień przeciw wzw B u noworodków i szczepień wyrównawczych 14-latków, starsze pokolenie poz może stanowić grupę ryzyka utajonego zakażenia HBV.

SŁOWA KLUCZOWE: zakażenie HCV, odporność na HBV, utajone zakażenie HBV, pracownicy ochrony zdrowia

ABSTRACT

INTRODUCTION AND OBJECTIVES. Epidemiological data on symptomatic HCV infection in Poland has shown that its prevalence among health care workers (HCWs) may exceed the prevalence notified among general

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population. Since such epidemiological situation would be similar to the increased prevalence of HBV infection among HCWs before anti-hepatitis B vaccine era, a seroprevalence study on HCV infection and immunity to HBV was performed in the group of volunteering HCWs.

MATERIAL AND METHODS. All the persons employed as HCWs in the two largest clinical hospitals in Warsaw were invited to participate in the study. They voluntarily gave a sample of blood for serological examination and were asked to fill-in a questionnaire containing questions relevant to the possible routes of infection, period of employment, and in part also to their life style. Both were done anonymously and in the unlinked manner. The activity of aminotransferases has also been determined in all the samples.

RESULTS. 961 serum samples were collected from HCWs employed in both hospitals. Anti-HCV were detectable in 16 out of 961 sera (1.7%). HCV RNA was detected in 3 out of these 16 (19%) sera; in 2 serum samples – genotype 2, in 1 – genotype 1b HCV. Anti-HBs were detected in 943 out of 961 (98.1%) sera. Anti-HBc (total) were detectable in 151 out of 961 (15.7%) sera. Out of 151 sera with anti-HBc in 149 (98.7%) samples anti-HBs were also detected. HBV DNA was detected in 6 (4%) samples out of 151 sera containing anti-HBc. While the prevalence of asymptomatic HCV infection among HCWs is similar to that seen in general population in Poland, the 15.7% prevalence of anti-HBc exceeded almost three times the percentage found in another study.

CONCLUSIONS. Since vaccination of health care personnel against HBV is at present obligatory, a large percentage of anti-HBs positive persons indicates for a high rate of immune response to vaccination. However, it seems that the presence of anti-HBs may not always be taken as indicating for immunity to HBV, but in some persons it may mask occult HBV infection. Since a younger population is immune to HBV infection due to universal vaccination of newborns and catch-up vaccination program for teenagers, older generations of HCWs may constitute a risk group for occult HBV infection.

KEY WORDS: *HCV infection, immunity to HBV, occult hepatitis B, health care workers*

INTRODUCTION

It is well known that one of the major threats for health care workers (HCWs) is the exposure to blood-transmitted pathogens. It is a continuous risk factor deserving different approaches, from observing universal precautions to those based on raising awareness (1,2). If such an infection occurs, it can theoretically be transmitted to patients, other personnel or after-duty contacts. The major bloodborne pathogens present worldwide include viruses, such as hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV). These infections in the health-care setting are mainly transmitted through direct contact between body surfaces of which one is the source of infection, through splashes of infected body fluids, or through contaminated intermediary like sharps, tubings or other medical devices (3).

HBV infection is currently vaccine-preventable, but HCV and HIV infections are still lacking specific immunoprophylaxis. Nevertheless, universal precautions provide guidance for prevention of all occupational bloodborne infections. It may be taken for granted that nowadays in a vast majority of health-care settings worldwide vaccination against HBV is a routine procedure for HCWs. However, legal requirements concerning HCWs infected with HBV, HCV or HIV are diverse among the European Union (EU) countries, and in some of them may require change of occupation. In addition,

not everywhere in the EU the screening tests for these infections are required for HCWs before starting up the work, or as a part of periodical health check-up (4,5).

Epidemiological surveillance of HCV infection among general population started in Poland in 1997, and it was based on notifications of symptomatic hepatitis C cases positive for anti-HCV. The year 2006 was the last for obligatory notification of only symptomatic hepatitis C cases, and beginning from 2007 asymptomatic persons carrying anti-HCV were also reported. The prevalence of anti-HCV in risk groups (dialysis, hemophilia, injecting drug use) is well recognized (6).

However, a discrepant results can be observed in data related to HCWs in Poland. A study on anti-HCV prevalence among HCWs in Gdańsk and surrounding area revealed a 1,3% prevalence among 4238 asymptomatic persons during 2005-2007 (7). But among 2947 persons notified in 2006 in Poland as new symptomatic hepatitis C cases, the major risk groups – in addition to hospitalized patients undergoing invasive procedures like surgery or dialysis – were HCWs constituting 3,9% (8). In presented study we were interested in finding out how prevalent is asymptomatic HCV infection as well as the prevalence of HBV immunity markers among HCW employed in two major hospitals in Warsaw, Poland. In addition to voluntary, unlinked, anonymous blood screening tests for HBV and HCV markers, more information were sought to be collected on the basis of anonymous questionnaires.

MATERIAL AND METHODS

All 4 836 persons employed in two major clinical hospitals at the Medical University of Warsaw (MUW) were invited to participate through an invitation displayed at information tables for employees and letters mailed to the supervisors of all the hospitals wards and units. Both hospitals are located 3 km apart in the downtown Warsaw and have in total over 1,700 beds serving the whole Warsaw population (over 1.8 mln inhabitants) as well as an advanced clinical support to total population of Mazovia Region (5.2 mln inhabitants).

Blood samples were obtained after informed and written consent of HCWs according to the rules set by the Ethical Committee at MUW and after its agreement to perform the study. Blood samples were obtained in December 2008/January 2009 and all the samples were coded. After laboratory determinations all personnel wishing to receive results of their testing could have them by quoting their respective code number. All the persons were also asked to fill-in anonymously the questionnaire voluntarily. In order to increase the participation rate, HCWs were informed that the data from the anonymous questionnaire and blood samples are unlinked and the questionnaire was self-administered. Such a design was inevitable in a context of close relations among workers and potential anonymity fraud, however the data from questionnaires filled-in voluntarily and completely anonymously are less reliable than collected by a trained researcher.

The voluntary questionnaire consisted of a general demographic questions regarding gender, occupation and experience. Additional questions referred to specific occupational and behavioral risks such as surgical procedures, blood transfusions, history of jaundice, hepatitis or HIV/AIDS, or drug addictions.

Sera were tested for the presence of anti-HCV, anti-HBs, anti-HBc and activity of aminotransferases was determined. For qualitative determination of anti-HCV in serum the chemiluminescence method on ECI analyzer (Ortho Clinical Diagnostics) was applied using commercial diagnostics kits. Electrochemiluminescence immunoassays on Cobas Modular Analytics E 170 (Roche Diagnostics) were used for qualitative determination of human anti-HBs in serum by sandwich principle, and for human IgM and IgG anti-HBc by competition principle using commercial test kits. Alanine (ALT) and aspartate (AST) aminotransferases catalytic activity were measured by standard reaction of NADH oxidation on Cobas Integra (Roche Diagnostics). All laboratory methods were calibrated and controlled according to manufacturer's recommendations.

The presence of HBV DNA in sera with anti-HBc was tested for using GeneProof® Hepatitis B virus PCR kit (GeneProof a.s., Brno, Czech Republic). HCV RNA in sera with anti-HCV was detected using Cobas® AmpliCor® Hepatitis C Virus test version 2.0. Both methods of nucleic acid testing (NAT) were performed at the commercial diagnostic laboratory "Synevo" in Warsaw.

RESULTS

Demographic data. The overall participation rate ranges from 21.9% as regards blood sample collection to 18.1% of those who provided data in the questionnaire (table I). The highest participation rate was observed among administrative personnel and nurses (37 and 17% respectively). Physicians and other HCWs were less likely to participate or to declare their occupation in the questionnaire.

Table I. Total study participation rate

Tabela I. Liczba (%) osób, które wypełniły kwestionariusz i dostarczyły próbki krwi do badania wg grup zawodowych

Total study population	Number of cases (% of all employees)	Participants who voluntarily filled the questionnaire (participation rate)	Participants who delivered a blood sample (participation rate)
All employees	4386 (100%)	794 (18.1%)	961 (21.9%)
Physicians	1370 (31.2%)	91 (6.6%)	N/A* (blood samples and questionnaires were unlinked)
Nurses	1580 (36.0%)	269 (17.0%)	
Other HCWs	1174 (26.8%)	91 (7.7%)	
Administration	262 (6.0%)	97 (37.0%)	

*N/A = nieznane (próbki krwi były niepowiązane z kwestionariuszem ankiety)

*N/A = not available (blood samples were unlinked with questionnaire)

794 questionnaires with complete or incomplete information were returned. Therefore, the data presented below are based on the proportion of answers concerning a particular question. Thus, a sum of numbers could differ for each question. 167 questionnaires were non-answered and they were discarded. The data collected in questionnaires are presented in tab. II.

Laboratory data. 961 serum samples were collected from HCWs employed in both hospitals. The main observations are summarized in tab. III. Anti-HCV were detectable in 16 out of 961 (1.7%) serum samples. HCV RNA was detected in 3 out of these 16 (19%) sera. Anti-HBs were detectable in 943 out of 961 (98.1%) sera. In the remaining 18 (1.9%) serum samples anti-HBs were undetectable. The distribution of anti-HBs levels is shown in tab. IV. Anti-HBc were detectable in 151

Table II. Distribution of a valid answers in a voluntary questionnaire.

Tabela II. Odpowiedzi w dobrowolnie wypełnianym kwestionariuszu ankiety wg grupy pytań

Variable and number of valid answers	Categories	Number of cases	%
Gender (n=794)	Male	695	87.5
	Female	99	12,5
Occupation (n=548)	Physician	91	16.6
	Nurse	269	49.1
	Other HCWs	91	16.6
	Administration	97	17.7
Experience (n=784)	0-9 years	216	27.6
	10-19 years	209	26.7
	20-29 years	208	26.5
	30 years and more	151	19.3
Specific risk factor (n=794)	Performing surgical procedures at work	88	11.0
	History of an invasive surgical procedure	451	56.8
	History of a needle stick injury	415	52.2
	History of blood transfusion before 1993	39	4.9
	History of jaundice	35	4.4
	History of hepatitis B	15	1.9
	History of a family member with hepatitis B	57	7.8
	History of a family member with hepatitis C	5	0.6
Sensitive risk factors (n=612)*	History of intravenous drug addition	4	0.65*
	History of HIV/AIDS	2	0.32*
HCV test in the past (n=794)	Declared YES	126	16.2

*Pytania dotyczące problemów uznanych za osobiste były zawarte w osobnym kwestionariuszu.

*Questions on sensitive issues were collected on separate sheet.

out of 961 (15.7%) sera. Additional 4 serum samples reacted within „grey zone” and showed undeterminate results for the presence of anti-HBc. Out of 16 sera with anti-HCV in 4 (25%) anti-HBc were also detected. Out of 151 sera with anti-HBc in 149 (98.7%) samples anti-HBs were simultaneously detectable. In 2 (1.3%) out of these serum samples anti-HBs were undetectable. Out of 149 sera containing both anti-HBc and anti-HBs in 9 (6%) samples anti-HBs were below 10 IU/ml, 6 (4%) sera contained anti-HBs within the range 10 – 100 IU/ml, and in 134 (88.7%) sera the levels of anti-HBs exceeded 100 IU/ml. HBV DNA was detected in 6 (4%) samples out of 151 sera containing anti-HBc.

Increased activity of ALT or AST was detectable in 51 samples out of 961 (5.3%) sera. In 19 (2%) sera both values were increased, while in 22 (2.3%) only AST was increased, and in 10 (1%) the activity of ALT alone exceeded normal value.

Out of 16 sera with anti-HCV in 3 (18.3%) the activity of ALT/AST was increased, while in the remaining 13 (81.3%) sera ALT/AST values were within the normal range. Out of the 151 sera containing anti-HBc the increased activity of ALT/AST was detected in 10 (6.6%) sera. These all 10 sera with anti-HBc and increased ALT/AST activity has also contained anti-HBs. Increased ALT/AST activity with anti-HBs alone has also been found in 34 (3.6%) out of 943 sera containing

these antibodies. Moreover, 4 sera out of 961 samples (0.4%) had ALT/AST values above normal range without any markers of HBV nor HCV infection.

DISCUSSION

A large number of studies on populations and geographical distribution has helped to evaluate the HCV burden in the world (9). One of the risk factors for HCV infection in developed countries is connected with medical procedures (10). For example in Spain, the major cause of acute hepatitis C responsible for 67% of all cases was hospital admission (11). For comparison, hospitalization during the last 6 months was responsible for 51% of symptomatic HCV infections noted in 2006 in Poland (8). In the Spanish study, 5 out of 109 (4.6%) nosocomial cases of HCV infection occurred among HCWs and were due to accidental needlesticks (11). The results of study conducted in Hannover, Germany over a period of 2000 – 2005 revealed that despite 1 431 occupational exposures with 166 index cases infected with HCV there were no cases of HCV seroconversion in HCWs (12). However, among 2947 persons notified in Poland in 2006 as newly diagnosed, symptomatic hepatitis C cases, 115 (3.9%) out of them were HCWs, although their source of infection was not obvious (8).

Table III. Serological markers of HBV and/or HCV infections in a study sample (n=961)

Tabela III. Wyniki badań i serologicznych w kierunku zakażeń HCV lub/i HBV w badanym materiale n=961

Positive results	Number of cases	%	NAT*
Anti-HCV	16	1,7	HCV RNA in 3 out of 16 (19%)
Anti-HBc	151	15,7	HBV DNA in 6 out of 151 (4%)
Anti-HBs	943	98,1	
Anti-HCV and anti-HBc	4	0,4	
Anti-HBc and anti-HBs	149	15,5	

*NAT= badanie kwasu nukleinowego

*NAT = nucleic acid testing

Table IV. Distribution of anti-HBs levels in a study sample (n=961)

Tabela IV. Poziomy stwierdzonego anty-HBs w badanym materiale (n=961)

Level of anti-HBs [mIU/ml]	Number of cases	%
0	18	1,9
0.1 - 9.9	119	12,4
10 - 99.9	126	13,1
100 and more	698	72,6

One of the problems faced by a person with HCV infection working as HCWs is his employment. Legally, different measures are followed in the EU countries (4). In Poland, there are suggestions for restriction for such person from contacts with patients, until his HCV infection is eliminated (5). Similar restrictions concerns personnel infected with HBV. Therefore, the design of the study as a voluntary, anonymous screening had the purpose to enhance HCWs to participate without any threat that their possible HCV positivity or any other relevant information may jeopardize their current occupation. However, anti-HCV seropositivity among the studied group of HCWs did not exceed the values seen in the general population of Poland (6). It seems that data on symptomatic hepatitis C among HCWs should more carefully be evaluated, and there could be a possibility of additional to occupational risk factors for acquiring HCV infection.

In Poland since 1990 vaccination against hepatitis B is obligatory for HCWs as well as for students of medical, dental, nursing and medical technologies disciplines. The prevalence of anti-HBs among HCWs at the level of 97.6% is indicative for the efficacy of employees vaccination programme. However, since no testing for HBV markers is required before vaccination, it seems that quite a number of vaccinated HCWs were unaware that they had earlier acquired HBV infection and they have detectable anti-HBc. The detection rate of anti-HBc among HCWs was in the current study almost three times higher up than among 19-20 years old military recruits (13). Persons with anti-HBc detec-

table together with anti-HBs after vaccination against hepatitis B have earlier been reported in vaccinated Chinese children, some of them born to HBV-infected carrier mothers (14,15). Nevertheless, the detection of HBV DNA in sera containing anti-HBc is indicative for the possibility of occult HBV infection masked by the presence of anti-HBs, even in persons with inactive or resolved hepatitis B who may have eliminated HBsAg. In Poland, testing for the presence of HBsAg and other HBV markers is not obligatory for HCWs, unless there are defined indications, such as occupational exposure to material containing blood-transmitted pathogens (5). The high proportion of HCWs with anti-HBc requires future action, like for example an offer for HCWs to determine the presence of anti-HBc if there is a history suggesting possibility of earlier exposure to HBV. Since hepatitis B is currently viewed upon as a long-life disease, persons with anti-HBc should then be advised on the possibility of spontaneous or chemo- or immunosuppressive therapy-triggered HBV reactivation (16,17). It seems that such indications should be targeted at the HCWs belonging to the older age groups. In Poland, after WHO call in 1992 for universal vaccination of newborns against hepatitis B (18), beginning from 1994-1996 all newborns have been vaccinated against HBV, with catch-up vaccination of children 14-years old between 2000-2010. It may be taken for granted that at the end of 2011 the young population aged less than 25 years is immune to HBV infection. However, earlier studies on the prevalence of hepatitis B in some Eastern European countries in 1993 has shown that HBV infection was at that time rampant there, with 50 - 60% of nosocomially transmitted cases (19), which underlines the possibility of older HCWs generation as a risk group for occult HBV infection.

A proportion of HCWs had elevated aminotransferase levels without any serologic evidence of viral hepatitis. It has also been observed in different population groups (20,21). These reports have shown that chronically elevated aminotransferase levels may be caused by disorders that affect organs or tissues other than the liver. Nevertheless, it may not be excluded that medications, excessive use of alcohol or nonalcoholic steatohepatitis could be responsible for ALT/AST elevation in studied group of HCWs (22).

It is of interest that out of 794 persons who answered the question on earlier HCV testing, 16.2% had earlier been tested and current testing provided them with opportunity for a new check-up. Therefore, the present results may have a volunteer bias that a detection of anti-HCV was in fact confirmation of earlier diagnosis, and the results may show not really a true proportion of anti-HCV positivity among HCWs as a total of randomly tested persons. The true anti-HCV positivity among HCWs tested for the first time will probably be

lower after exclusion of persons already knowing their serologic status. This is supported by testing more than 4 million blood donors in Poland, who have anti-HCV detectable in the range of 0.23-0.52% or 0.86-1.10% among first-time or multiple donors, respectively (mean=0.48%) (23,24).

Key occupational health aspects of blood-transmitted pathogens are related to surveillance, transmission and primary prevention. The effective vaccines against HCV and HIV remains elusive, but the possible preventive strategies against these and other blood-transmitted pathogens were postulated and deployed in health care institutions. Hepatitis B can at present be prevented through vaccination, but it seems that HCWs might be one of the risk groups for occult HBV infection. It seems that it might also be a case in other countries, where HBV infection was not uncommon before universal vaccination against hepatitis B was introduced, and therefore the possibility of occult HBV infection among HCWs in these countries may not be ruled out.

CONCLUSIONS

1. The prevalence of asymptomatic HCV infection among studied group of HCVs is similar to that seen in general population in Poland, which may indicate for epidemiological heterogeneity of infection.
2. The high prevalence of anti-HBs positive HCWs indicated for efficient vaccination program of employees.
3. The simultaneous presence of anti-HBc in anti-HBs positive sera may indicate for occult HBV infection, which probably was acquired before vaccination against hepatitis B.

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