Hepatitis C infection among pregnant women in central Poland: Significance of epidemiological anamnesis and impact of screening tests to detect infection

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Abstract

Background. Mother-to-child transmission is one of the main sources of hepatitis C virus (HCV) infection in children. However, because of the asymptomatic course of the illness, certain women may not be aware of their infection.

Objectives. The aim of this study was to estimate the significance of epidemiological anamnesis in diagnoses of HCV infection in women of reproductive age and to evaluate how screening among pregnant women impacts the detection of HCV infection.

Material and methods. Epidemiological interviews of 432 mothers infected with HCV (but free of human immunodeficiency virus (HIV)) were conducted in the Warsaw Hospital for Infectious Diseases (Poland) from 1998 to 2012.

Results. Complaints or abnormalities in laboratory tests were the reasons for anti-HCV antibody testing in 28.2% of mothers, whereas specific interview responses or occupational health care services group affiliation were the reasons for testing in 35.6%. However, in a large group of women, infection was only detected because of screening examinations. The introduction of routine screening for pregnant women (since 2010 in Poland) has led to the increased detection of HCV infection in women who did not present with infection risk factors (9.9% before 2010 vs 46.1% after 2010). This practice has also led to an increase in the percentage of women diagnosed during pregnancy (21.5% before 2010 vs 30.8% after 2010).

Conclusions. Establishing HCV infection risk factors during the interview process is the most common indicator for serological testing; however, not all infected cases can be diagnosed in this manner. Screening for anti-HCV antibodies in pregnant women increases the detection of HCV infection in this group.

Key words: pregnancy, HCV, screening, anti-HCV

Introduction

The hepatitis C virus (HCV) causes an inflammation of the liver that leads to chronic disease in 50–85% of cases. Hepatitis C virus infection is usually asymptomatic or sub-clinical for many years; however, after 20–30 years, it can lead to cirrhosis (in 5–25% of patients) and an increased risk of hepatocellular carcinoma. Transmission of the virus can occur during the transfusion of HCV-infected blood, the performance of medical and non-medical procedures (piercings or tattoos) using equipment contaminated with infectious material, and intravenous drug use (IVDU) with needles shared by an infected person. Infection through sexual contact with HCV-infected persons is possible, although the risk is low.^{1–4} Currently, one of the main routes for HCV infection in children in developed countries is vertical transmission from infected mothers. Anti-HCV antibodies (anti-HCV) in pregnant women in Europe are detected at a prevalence of 0.1–1.7%,^{5,6} and the risk of vertical HCV infection is estimated to be 3–10%.⁷ No specific methods of prevention (vaccination or specific immunoglobulin) are available to reduce the risk of transmission in children after birth. The main factor affecting vertical transmission is maternal viral load. The use of antiviral therapy before pregnancy can lead to the reduction or elimination of HCV viremia. However, because of the asymptomatic nature of HCV, women may not know they are infected. The diagnosis of HCV involves testing for anti-HCV (ELISA method), and a positive result is followed by an evaluation of viral replication using a reverse transcription polymerase chain reaction assay (RT-PCR).

The aims of the study were as follows: to estimate the significance of epidemiological anamnesis in diagnoses of HCV infection in women of reproductive age and to evaluate how screening among pregnant women impacts HCV infection detection.

Material and methods

The study group consisted of women who attended the Department of Children's Infectious Diseases (Medical University of Warsaw, Hospital for Infectious Diseases, Warszawa, Poland) in order to test for HCV infection in their infants. Epidemiological information was collected via questionnaires distributed to 432 mothers living in the Warsaw agglomeration area from 1998 to 2012. The Warsaw agglomeration is located in central Poland and it has an area of 6,200 km² and a population of 3 million, with 80% living in the cities and 20% living in the countryside. The average prevalence in this area is 10/1,000 live births per year. The Hospital for Infectious Diseases is the primary center for diagnosis and treatment of HCV-infected children in the agglomeration of Warszawa. The sample group of HCV-infected women were not selected using a screening population. The reasons provided for

undergoing the HCV diagnostic tests were the subject of the survey. The respondent group was not homogeneous, and all women who visited the clinic to have diagnostic HCV tests performed on their infants were qualified for the study.

Child qualification criteria for the vertical infection tests changed over the course of this study. Between 1998 and 2009, children born to mothers with detectable anti-HCV antibodies (anti-HCV+) were tested regardless of HCV-RNA status. However, from 2010 to 2012, the tests were only performed on children born to anti-HCV(+) mothers that were positive for HCV-RNA – HCV-RNA(+), which resulted in a change in the recruitment of respondent mothers.

The survey questions were related to the putative source of infection, infection risk factors, and reasons for performing the diagnostic tests.

The data obtained was summarized into 3 time intervals according to the following 2 events that could have had a significant effect on the epidemiology of hepatitis C and the detection of HCV infection: the introduction of the RT-PCR HCV-RNA test for blood donation in Poland in 2002 and the introduction of the recommended anti-HCV test for pregnant women in 2010. In the 1st period (1998–2002), data was obtained from 54 women; in the 2nd period (2003–2009), data was obtained from 300 women; and in the 3rd period (2010–2012), data was obtained from 78 women. The putative sources of infection and the reasons for undergoing HCV infection testing were compared with respect to the women's age (<24, 25–35, >35 years) and place of residence (urban and rural). Women living in towns with more than 10,000 residents or fewer than 10,000 residents but with non-agricultural labor forces that commuted to work in larger cities were considered residents of urban areas.

The Local Ethics Committee of the Medical University of Warsaw gave its approval for the study. Each patient and/or parents/guardians gave written informed consent for the study. The study complies with the principles outlined in the Declaration of Helsinki.

Statistical analysis

Categorical variables were compared using either the χ^2 test or Fisher's exact test as appropriate. A p-value of <0.05 was considered statistically significant. All of the statistical analyses were performed using MedCalc Statistical Software v. 12.1.4.0 trial software (MedCalc, Mariakerke, Belgium).

Results

The questionnaire data on 432 HCV-infected mothers was analyzed. From 1998 to 2009, the analysis involved 354 anti-HCV(+) mothers: 182 (51.4%) were HCV-RNA(+), 59 (16.7%) were HCV-RNA(–), and 113 (31.9%) had an unknown HCV-RNA status. From 2010 to 2012,

epidemiological information was gathered from 78 women: 59 (75.6%) were HCV-RNA(+) and 19 (24.4%) had an unknown HCV-RNA status (children who were adopted and in foster families (biological mother unavailable)). Epidemiological data on the mothers of adopted children was obtained from the children's medical records. Almost all of the women (431/432) were Caucasian (427 of Polish nationality and 4 of Ukrainian nationality), while 1 woman was Asian. The average age of the mothers was 29.85 years (range: 18–50), including 37 women younger than 24 years, 346 women between 24–35 years of age, and 49 women older than 35 years. In addition, 367 women (85%) lived in urban areas and 65 women (15%) lived in rural areas.

Events in the women's history that might have increased the risk of HCV infection are presented in Table 1.

Table 1. Events in the women's history that could increase the risk of HCV infection and characteristics of the group

Risk event in the history	Number of women	%
Surgical procedure	106	24.5
Blood product transfusion	94	21.8
IVDU	74	17.1
age of women		
<24 years	(8/37)	(21.6)
24–35 years	(63/346)	(18.2)
>35 years	(3/49)	(6.1)
Multiple hospitalizations	39	9.0
Health care workers with needlestick/scarification in history	24	5.6
Infected sexual partner	11	2.5
Infected other family member	5	1.2
Tattoo or piercing	5	1.2
Mother infected with HCV	3	0.7
Unknown source of infection	71	16.4
Total	432	100

IVDU – intravenous drug use.

Based on the place of residence, we found a higher incidence of IVDU among urban residents compared with rural residents (70/367 (19.1%) vs 4/61 (6.1%); $p = 0.01$). Information on the type, duration, and number of the doses of intravenous drugs was not collected, recognizing that even a single incidence of drug use with HCV-contaminated equipment carries a risk of HCV infection. Among the children of mothers with a history of IVDU, 25/74 (33.8%) remained in foster care (adoption or orphanages), 49/74 (66.2%) were in the care of their mothers, 28/74 of the mothers (37.8%) declared abstinence, and 21/74 of the mothers (28.4%) participated in methadone programs.

The characteristics of anti-HCV-positive mothers stratified by intravenous drug use status are presented in Table 2.

In addition, the history of HCV-infected women was analyzed for changes in risk events in the periods: 1998–2002, 2003–2009 and 2010–2012. We observed an increasing incidence of IVDU (3.7%, 17.7% and 24.4%, respectively; $p = 0.007$) and decreasing history of blood transfusion among HCV infected women (31.5%, 22.3% and 12.8% in the subsequent periods; $p = 0.03$). All of the blood transfusions leading to HCV infection in this study were performed prior to 1992.

An event with the probability of increasing the risk of HCV infection was not determined in 71/432 women (16.4%), including 35/354 (9.9%) from 1998 to 2009 and 36/78 (46.1%) between 2010 and 2012 ($p < 0.001$).

The reasons for undergoing diagnostic tests are presented in Table 3.

In 77/432 cases (17.8%), tests were performed according to a planned gynecological recommendation before or during pregnancy. Changes in the responses in subsequent years are presented in Fig. 1.

The women were divided into 3 groups according to the time of HCV infection diagnosis: 287/432 (66.4%) were

Table 2. Characteristics of anti-HCV-positive mothers stratified by intravenous drug-use status

Characteristics of mothers	Mothers without IV drug use; n = 358 n (%)	Mothers with IV drug use; n = 74 n (%)	In total; n = 432 n (%)
Maternal hepatitis C RNA status*			
HCV-RNA positive	191 (53.4)	50 (67.6)	241 (55.8)
HCV-RNA negative	57 (15.9)	2 (2.7)	59 (13.7)
HCV-RNA not done	110 (30.7)	22 (29.7)	132 (30.5)
Place of living			
urban area	297 (83.0)	70 (94.6)	367 (85.0)
rural area	61 (17.0)	4 (5.4)	65 (15.0)
Age of women			
<24 years	29 (8.1)	8 (10.8)	37 (8.6)
24–35 years	283 (79.1)	63 (85.1)	346 (80.1)
>35 years	46 (12.8)	3 (4.1)	49 (11.3)
Time of HCV infection diagnosis			
before pregnancy	238 (66.5)	49 (66.2)	287 (66.4)
during pregnancy	89 (24.9)	11 (14.9)	100 (23.2)
after parturition	31 (8.6)	14 (18.9)	45 (10.4)

*HCV-RNA status tested with RT-PCR; P – NS for all comparisons; IV – intravenous; HCV-RNA – hepatitis C virus ribonucleic acid; RT-PCR – reverse transcription polymerase chain reaction.

Fig. 1. Percentage contribution of gynecologists and obstetricians in HCV infection detection in women

Table 3. Reasons for performing HCV diagnostics in women

Reason for HCV testing	Number of women	%
Interview response (risk factor for HCV infection in anamnesis)	125	28.9
Gynecologists' recommendation (planned, without recognized risk factors in history)	77	17.8
Acute hepatitis C or other complaints	48	11.1
Blood donor examination	45	10.4
Increased aminotransferases activity	44	10.2
Obstetric cholestasis	30	7.0
Periodical examination of health care worker or after occupational exposure	29	6.7
Detection of anti-HCV antibodies in child or HCV-RNA in umbilical cord blood or placenta	19	4.4
During other examination	11	2.6
Examination at the patient's initiative	4	0.9
In total	432	100

HCV-RNA – hepatitis C virus ribonucleic acid.

diagnosed before pregnancy, 100/432 (23.1%) were diagnosed during pregnancy, and 45/432 (10.4%) were diagnosed after parturition. A comparison of the periods 1998–2009 and 2010–2012 showed that the proportion of women with diagnosed infection during pregnancy increased from 76/354 (21.5%) to 24/78 (30.8%), respectively.

Discussion

Complaints or abnormalities in laboratory tests (symptoms suggesting acute hepatitis, cholestasis during pregnancy, elevated aminotransferases, etc.) were the reasons for anti-HCV testing in 28.2% of the participants.

Specific interview responses or employment in health care services was the reason for testing in 35.6% of the cases (154/432) (Table 3). Extended and complementary interviews conducted during the survey were used to determine risk events in the women's histories in an additional 48% of cases (207/432). Knowledge of the epidemiology of HCV infection specific to the given population and appropriately conducted interviews by the general

practitioner were likely to increase the detection of HCV infection.^{8,9} Events that could carry a risk of HCV infection in the respondents' histories are presented in Table 1.

The most important changes in HCV sources in recent years are related to blood donation centers, with the safety of transfused blood products increasing significantly because of the introduction of HCV testing in blood donation centers in Poland (anti-HCV since 1992 and HCV-RNA RT-PCR since 2001/2002).^{10,11} It is estimated that 1.4% of blood donors in Poland were anti-HCV(+) before the introduction of routine serological tests.¹² All blood transfusions resulting in HCV infection in this study were performed prior to 1992. It is likely that a history of blood transfusion will not be a risk factor for HCV infection in women of reproductive age within 25 years.

Intravenous drug users represent a significant group among the HCV-infected population, and multiple exposures to HCV and a lower incidence of spontaneous HCV-RNA clearance are found among intravenous drug users.^{13–15} The prevalence of IVDU among the interviews of HCV-infected women increased from 3.7% (1998–2002) to 17.7% (2003–2009) and to 24.4% (2010–2012) ($p = 0.0075$). Young women (under 24 years old) living in cities accounted for the majority of IVDU ($p = 0.01$). From a reproductive health perspective, an increase in the percentage of teenagers reporting at least 1 contact with an intravenous drug is a worrisome problem; according to Sieroslawski, this percentage was 0.3–0.6% in 2003 and 0.6–1.2% in 2011 (higher in the group of 15- and 16-year-olds than in those aged 17–18 years).¹⁶

A mother actively using drugs is not able to care for her child responsibly. Among children born to IVDU mothers, 33.8% remained in foster care and 66.2% remained in the care of mothers who reported abstinence or participation in a methadone program.

Determining a direct relationship between surgical procedures or multiple hospitalizations and HCV infection is difficult unless the patient presented with symptoms of acute hepatitis after a period corresponding to HCV incubation.⁴ Such time-dependence was not demonstrated in any of the women; thus, it is likely that hospitalizations in most of these cases had no effect on HCV infection. However, the data for these women should be analyzed against a control group with no risk factors.

Health care workers may be a group with an increased risk for HCV infection.^{4,17–20} The risk of infection after incidental occupational exposure is less than 2% on average (range 0–10%). Flisiak et al. analyzed the presence of anti-HCV among health care workers in Poland and found significant differences depending on the workplace, with anti-HCV detected in 0.98% of basic health care employees, in 2% of employees in multi-profile hospitals, and in 3.28% of employees in specialist centers.²¹ All of the HCV-infected health care workers in our study confirmed that they had been stabbed with a needle or sharp instrument while dealing with a patient.

Postgraduate training in HCV epidemiology may improve the effectiveness of HCV detection, and such courses for gynecologists and obstetricians led to the following results: among women examined from 1998 to 2002, HCV infection was diagnosed based on gynecologists' recommendations in 1.8% of cases, whereas in 2003–2009 HCV infection was diagnosed based on gynecologists' recommendations in 17.3% of cases (Fig. 1). A further statistically significant ($p < 0.001$) increase in gynecologist involvement in HCV diagnosis after the year 2010 (30.77%) was related to the implementation of the Act on Pregnant Woman Care, which recommends anti-HCV examinations for all pregnant women in Poland.²² This act also led to an increase in the percentage of women diagnosed during pregnancy after 2010.

There is a large group of women for whom infection was only detectable because of screening examinations. The introduction of screening recommendations for pregnant women in 2010 led to an increase in the percentage of HCV infections detected in women who did not disclose risk factors in an interview (9.9% before 2010 vs 46.1% after 2010; $p < 0.001$). Certain women may not disclose risk factors in their history for reasons of moral and social censure. A study by Lamber et al. determined that infection risk factors were not observed for 27% of Irish women infected with HCV, over half of whom were immigrants from Eastern Europe.⁶ In an examination of pregnant women in Austria, Diab-Elschahawi found that 21% of them learned about their infection from a screening examination, despite a lack of risk factors.²³

A significant number of women of reproductive age who are infected with HCV are unaware of their infection and will not qualify for examination because of a lack of disclosed risk factors or clinical abnormalities. This group may only be detected through screening examinations.^{24,25} In our study, 36.1% of women were diagnosed without presenting risk factors in the interview, physical examination, or laboratory results.

Because of its cost-effectiveness, universal/antenatal screening is primarily considered in populations in which the prevalence of anti-HCV is higher than 1–2%.^{24,26,27} Such rates of infection significantly increase the risk of contact with HCV through casual sexual contact and non-sterile medical and non-medical procedures. Currently, the United States has implemented a routine examination for anti-HCV in people born 1945–1965, regardless of other

risk factors. Anti-HCV antibodies are detected in 3.5% of people in this group age, with the estimated average for the whole population at 1–1.5%.²⁸ The prevalence of anti-HCV in Europe is in the range of 0.4–5.2% and Flisiak estimated the prevalence in Poland at 1.9%.^{5,21}

The most beneficial method of reducing the risk of vertical infection is to detect infection in the pre-reproduction period and to use antiviral therapy to eliminate or reduce HCV viraemia.^{29–31} Because of toxicity, drug therapies that are applicable during pregnancy are not available.⁴

Among the women included in the study, 287/432 (66.4%) knew of their infection prior to pregnancy, whereas the remaining participants (145/432 (33.6%)) did not. The results of this study confirm the low awareness of HCV infection, which is consistent with findings from studies conducted among various European populations.^{23,32} The data presented here suggests the benefits of performing screening examinations for HCV infection in young women of reproductive age, although detecting infection during pregnancy also has benefits. For example, therapy is more effective when performed shortly after birth because of changes in the immune system,^{33,34} effective therapy provides benefits for subsequent pregnancies, and maternal infection awareness programs provide recommendations on slowing the course of the disease, such as avoiding alcohol and receiving vaccinations against other hepatotropic viruses (HAV, HBV). Detecting HCV infection in mothers will promote diagnostic testing in their children, and children infected with HCV will benefit from early treatment.²⁴

The authors are aware of the following study limitations: 1. the group of women infected with HCV was not selected from the population based on screening examinations, and 2. the study group was not uniform and included respondents who were anti-HCV+, though HCV replication was not confirmed in all cases. (It is estimated that an active replication of the virus occurs in 31% of Polish anti-HCV(+) individuals on average, with 44% of cases occurring in patients <25 years old and 27% of cases occurring in patients >40 years old).²¹

Although the authors have acknowledged these limitations, they believe that the study presents new information on HCV infection among women of reproductive age in Poland. To our knowledge, this is the only work of this type concerning women in Poland.

Conclusions

Establishing HCV infection risk factors by analyzing interview responses is the most common indicator for serological testing. However, performing examinations on women according to their interview responses alone will not lead to a diagnosis of all infected cases. Screening for anti-HCV in pregnant women increases the detection of HCV infection in this group. Universal screening of women of reproductive age should be considered.

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