

Hepatitis C Infection in Louisiana

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Estimating a prevalence of 1.8% of hepatitis C in the general population, there are in Louisiana about 81,000 individuals who have been infected with the hepatitis C virus. In 2002, the incidence of reported cases of acute hepatitis C was 2.2 /100,000 versus 0.64 in the USA. The case register maintained by the Louisiana Office of Public Health has 22,000 cases. Building up a register of hepatitis C past or present infections is an important tool that may be used to resolve some important questions about the epidemiology of hepatitis C or be used for future preventive actions. Physicians and hospitals are encouraged to report hepatitis C infection including sufficient information to distinguish acute hepatitis C from hepatitis C past or present infection.

Hepatitis C is an important public health problem in the USA and particularly in Louisiana. The goal of this article is to provide Louisiana physicians a description of the hepatitis C prevalence, incidence, mortality, distribution among the Louisiana population, and main risk factors.

Hepatitis C virus (HCV) was discovered in 1988 as the main agent responsible for nonA-nonB post-transfusion hepatitis. Since then we have come to understand that hepatitis C constitutes a major public health problem, with much broader implications than post-transfusion non-A non-B hepatitis.

National data on the prevalence of hepatitis C from the Third National Health and Nutrition Examination Survey (NHANES III), conducted during 1988–1994, have indicated that an estimated 1.8% of all Americans and 2.3% of those age 20 years and older have been infected with HCV.¹ There are no data on the prevalence of HCV infection in Louisiana. Prevalence has been more accurately determined in selected populations.

Accurate data on the incidence of new infections has been a challenge because no serologic marker for acute infection exists, and most health departments do not have the resources to investigate positive laboratory reports for hepatitis C virus and to determine whether they represent a new or old infection. National estimates suggest that the annual number of new infections in 1998 was 13.3 /100,000.² In the past sentinel surveillance systems provided the most reliable information on HCV incidence. However, in recent years the health department's passive surveillance for acute, symptomatic hepatitis has yielded similar results as those from sentinel surveillance, suggesting that the quality of national surveillance data for acute hepatitis C has improved. In 2002 the national incidence of acute hepatitis C was 0.64 /100,000.

POPULATION AND METHODS

Prevalence

Because of a lack of resources, no attempt has been made to estimate the prevalence of HCV infection in the entire Louisiana population. The approach used was to compare prevalence in some specific groups with national prevalence data in similar risk groups.

Three limited studies were carried out to estimate the prevalence of hepatitis C among populations at high-risk for hepatitis C:

- Persons with a history of substance abuse
- Sexually transmitted disease (STD) clients at a city STD clinic
- Clients seeking Human Immunodeficiency Virus (HIV) testing and counseling

The Infectious Disease Epidemiology Section established a collaborative relationship with an inpatient drug-treatment facility wherein hepatitis C counseling and testing services were offered to all residents.

In order to estimate the prevalence of HCV among persons seeking HIV and STD counseling and testing services, 100 samples submitted to the state public health laboratory for HIV and syphilis testing were blindly tested for the presence of hepatitis C antibody.

Testing was done using a third generation enzyme-linked immunosorbent assay (ELISA) method. No confirmation with recombinant immunoblot assay (RIBA) was done.

Incidence

Hepatitis C is one of the diseases whose reporting is mandated by law in Louisiana. Reports are received by phone, fax, and mail-in cards but in recent years mostly

by using the web based Louisiana Reportable Disease Database, which was initiated in 2001. Reported cases must meet the Centers for Disease Control case definitions to be counted in the state and in the national surveillance system.³

All cases having a positive hepatitis C result, ie, enzyme immunoassay (EIA), RIBA, realtime-polymerase chain reaction (RT-PCR), are entered in the surveillance database in one of two definitions:

1-Acute Hepatitis C

Clinical case definition: An acute illness with discrete onset of symptoms and jaundice or elevated serum aminotransferase levels: AST \geq 280 and ALT \geq 350.

Laboratory confirmation: 1- IgM anti-HAV negative, and 2- IgM anti-HBc negative (if done) or HBsAg negative, and 3- Antibody to hepatitis C virus (antiHCV) positive, or RT-PCR or any other test showing viral presence.

2-Hepatitis C Past or Present Infection

Clinical case definition: Most cases are asymptomatic.

Laboratory confirmation: EIA positive with signal to cut off ratio \geq 3.8,

Or RIBA positive,

Or quantitative RT-PCR,

Or any nucleic acid positive test.

Confirmed: A case that meets the lab case definition.

Probable: antiHCV EIA positive with ALT above normal.

Suspect: antiHCV EIA positive only.

National reporting of "hepatitis past or present infection" has been instituted only recently (2003) while "acute hepatitis C infection" has been nationally notifiable since 1990. Louisiana was collecting data on HCV past and present infection long before this condition became nationally reportable. Those reports of acute hepatitis C which did not meet the "acute" case definition, were entered in a register of hepatitis C cases.

Data collected for the case surveillance includes basic demographic and locating information on the case to enable a follow-up interview, basic clinical and laboratory data to allow accurate classification, and epidemiologic and risk factor data to determine the extent of the investigation and preventive course to be taken. Clinical information is collected during primary surveillance.

Data entered in the Reportable Disease Database (RDD) web-based system are stored in an Oracle® database. Data was extracted to a Microsoft Access® database and analyzed using MS Access® and MS Excel® statistical tools.

Laboratory Diagnosis of Hepatitis C

Serologic Assays

Enzyme immunoassays (EIA) are the tests most often used for the diagnosis of HCV infection. They detect antibod-

ies to HCV in 97% of infected patients, but do not distinguish between acute, chronic, or resolved infection.⁴

Recombinant ImmunoBlot Assays (RIBA) use the same antigens as EIA but in an immunoblot format. Supplemental testing with a more specific assay, such as RIBA, of a specimen with a positive EIA result prevents reporting of false-positive results, particularly in settings where asymptomatic persons are being tested.

An anti-HCV-positive person is defined as one whose serologic results are EIA-test-positive and supplemental-test-positive. Persons with a negative EIA test result or a positive EIA and a negative supplemental test result are considered uninfected, unless other evidence exists to indicate HCV infection (e.g. abnormal ALT levels in immunocompromised persons or persons with no other etiology for their liver disease). Indeterminate supplemental test results have been observed in recently infected persons who are in the process of seroconversion, as well as in persons chronically infected with HCV. Indeterminate anti-HCV results also might indicate a false-positive result, particularly in those persons at low risk for HCV infection.

Nucleic Acid Detection

The diagnosis of HCV infection also can be made by qualitatively detecting HCV RNA using gene amplification techniques (e.g. RT-PCR). Although not FDA-approved, RT-PCR assays for HCV infection are used commonly in clinical practice. Because of assay variability, rigorous quality assurance and control should be in place in clinical laboratories performing this assay, and proficiency testing is recommended.

Mortality

Data on death due to acute hepatitis C and chronic hepatitis C were obtained and reviewed.

RESULTS

Prevalence

In the inpatient drug treatment facility, among 118 residents who sought testing for hepatitis C, 38 (35%) were HCV positive. Among persons seeking HIV and STD counseling and testing services, the initial testing showed that 10% of the HIV client samples were HCV positive and 8% of the STD client samples were HCV positive.

Analysis of surveillance data

There was a steady increase in case reporting from 1991 to 2000. In 2001 there was a notable decrease in the number of reported cases, due most likely to a CDC-mandated change in the case definition for acute hepatitis C (Figure 1). There is an increasing preponderance of cases among males, from 60% in 1991 to 70% in 2003, with a slope of 1%/year (c^2 for trend =14.25, $p=0.00016$). Inci-

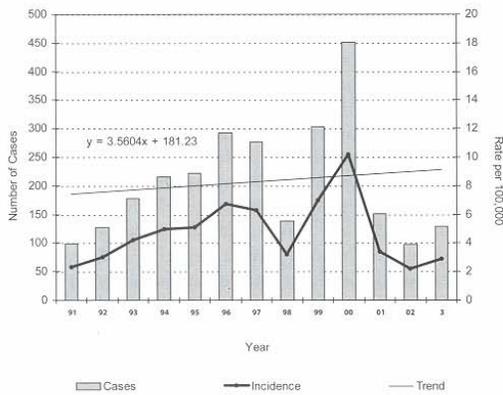


Figure 1. Hepatitis C. Reported cases and incidence rates, Louisiana, 1991-2003.

dence rises from the age group 15 to 19 years old to peak in the group 35 to 44. For the five year period 1999 to 2003 the highest incidence is 16 /100,000 for males and 7 /100,000 for females in the age group 35 to 44 (Figure 2). Incidence rates are higher among African Americans than among whites (Figure 3). The peak incidence among African Americans is 17/100,00 for the age group 45-54, and for whites the peak is 8 /100,000 for the age group 35-44.

Among new acute HCV infections for which symptomatology was known 25% had jaundice; others had other symptoms and elevation of hepatic enzymes. Only 2.5% were hospitalized.

The systematic collection of risk factors for reported cases is too labor intensive to be reliable. Data collected is limited. Examination of known risk factors for hepatitis C showed that a few cases (3%) were intravascular drug users, had dental procedures or surgery in the six weeks to six months prior to disease report (<1%), or had been tattooed (3%). The majority of cases (for whom sexual preference was known) are heterosexual.

Analysis of register data

Over the 13 years from 1991 to 2003, 22,203 cases were entered in the register, a mean of 1708 cases added per year, standard deviation 1186, range 193 to 3655. The age group distribution of cases entered in the register is similar to that of incident acute cases (Figure 4). The distribution by race also shows a pattern similar to that of incident acute cases. The proportion of co-infection hepatitis B and hepatitis C is 1.9% among those in the register.

Mortality

The total numbers of deaths attributed to hepatitis C as a primary cause were 83 in 1999, 111 in 2000, 142 in 2001, and 131 in 2002. The majority were male (60%). The

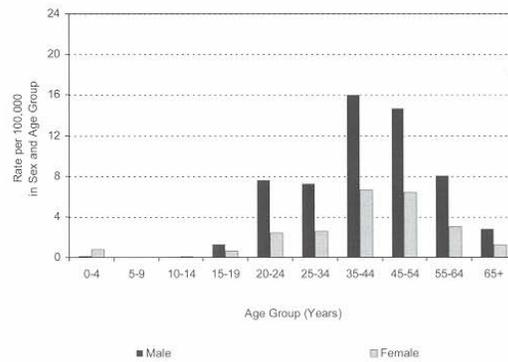


Figure 2. Hepatitis C. Average annual incidence rates by gender and age, Louisiana, 1999-2003.

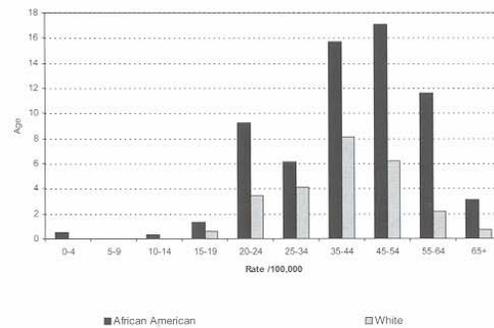


Figure 3. Hepatitis C. Average annual incidence rates by race and age, Louisiana, 1999-2003.

youngest death was at 15, and the oldest was at 94 years. The age group distribution is presented in Figure 5. The mortality rate increases with age.

DISCUSSION

Prevalence

Among persons with a history of drug abuse and those seeking HIV and STD counseling and testing services, HCV showed respective prevalences of 35%, 10% and 8%. Larger and random samples would be necessary in order to determine a truly reliable estimate for the HCV seroprevalence in these populations. However, funding for such surveys probably will not be forthcoming. These small opportunity samples serve only to provide estimates that may be compared with more definitive data. In a study to determine incidence and prevalence for various US populations, subpopulations and risk groups,⁵ the prevalence of HCV among heterosexuals attending STD clinics was estimated at 3 times that of the general population (an estimated 5.4%). The prevalence of anti-

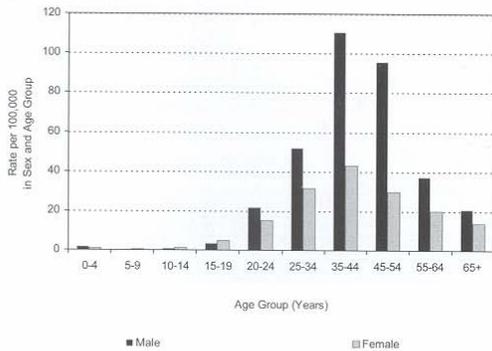


Figure 4. Hepatitis C Register: Average annual rates of additional cases by gender and age, Louisiana, 1991-2003.

body to HCV (anti-HCV) for those who were screened was 9.8% in Connecticut.⁶

Assuming that the Louisiana prevalence of hepatitis C infection is similar to that of the USA (1.8% of the population), there are about 81,000 individuals with hepatitis C infection. The case register includes more than 22,000 cases, about one fourth of all infections. Having 25% of all cases registered is a high proportion for public health registers of this kind.

There is a need for a better understanding of the disease burden associated with hepatitis C among high-risk populations in Louisiana. In addition, the preliminary studies, while limited, clearly indicate that the prevalence of hepatitis C is much higher among persons with a history of substance abuse and persons seeking HIV and STD services than among the general population.

Incidence

Based on comparison with national data, we estimate that there are approximately 500 to 600 new (acute) infections each year in Louisiana. The incidence of reported new acute cases of HCV is around 100 to 150 per year. It appears that about 20 to 25% of new infections are reported. However, data on new acute HCV infection reports must be interpreted with caution because of misclassification, eg, acute hepatitis of other etiology occurring in a patient with past HCV infection may be reported as acute HCV infection.

The steady increase observed from 1991 to 2000 may not reflect a true increase in HCV incidence. Whenever a new disease emerges, laboratory tests improve steadily in sensitivity, specificity and in simplicity, physicians request testing more often; and in the end, disease-reporting increases as the result of improving recognition. The decrease observed in 2001 resulted from a change in case definition. Beginning in 1990, the designation for elevated liver enzymes was established by the CDC as 2.5 times the upper limit of normal. In 2001, however, the CDC increased the level required for elevation to seven

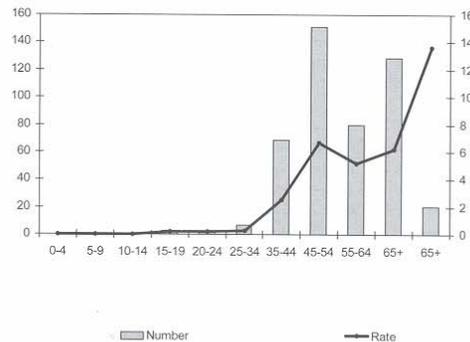


Figure 5. Hepatitis C mortality by age, Louisiana, 1999-2002.

times the upper limit of normal, thus excluding a large number of cases that previously would have been considered reportable.

The age distribution observed in Louisiana is similar to that reported in the USA.² The higher rates observed for African Americans in Louisiana are also observed at the national level.²

Direct reporting of positive serologic test results by laboratories will increase the completeness of reporting of HCV infected persons to the health department, but reporting other available laboratory or clinical data would improve surveillance for hepatitis C by providing information to identify patients with acute disease. Improving the accuracy of hepatitis C surveillance data continues to be a priority because monitoring hepatitis C incidence trends provides information needed to evaluate the effectiveness of preventive efforts and identify opportunities for prevention.

Many questions remain unanswered about the natural history of untreated patients, progression from asymptomatic to symptomatic HCV infections, and morbidity related to untreated HCV infections.⁷ Building up a case register of HCV past or present infections is an important tool that may be used to resolve some of these questions.

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