Hepatitis A

Hepatitis A is a Class B Disease and must be reported to the state within one business day.

Reportable cases of hepatitis A virus (HAV) infections are those newly infected individuals who are symptomatic, or who have elevated liver enzymes and have IgM antibodies to hepatitis A. IgM antibodies to HAV are the main indicator of recent infection, but there may also be false positive test results. To meet the case definition, a person has to meet both the clinical and the laboratory criteria.

Pre-vaccine Era

Reporting of HAV started in 1970. During the 70s and early 80s the number of cases varied between 500 and 700 a year, for a reporting rate ranging from ten to 20 per 100,000 population. National incidence models showed that the number of cases may have been ten times higher. The U.S. prevalence of infection was 31% during the National Health and Nutrition Examination Survey (NHANES) by the Centers for Disease Control and Prevention (CDC) (1988-1994). Most cases were due to person-to-person transmission for sporadic cases and small community outbreaks. In the late 1980s, the number of cases started to decline sharply to five to ten per 100,000 population. This decline may have been the consequence of better sanitation and stricter application of case definitions.

Vaccine Era

An inactivated HAV vaccine was approved in 1995. In subsequent years, there was a further decline to very low rates. However, vaccination rates still remain lower than for other common vaccines. It is recommended that any household or sexual contacts of confirmed cases receive the vaccination as post-exposure prophylaxis.

Nationally, hepatitis A cases were decreasing dramatically, but then saw an increase in 2012 and 2013 due to a large multi-state outbreak. Since 2014, the national case counts have continued to slowly rise. Cases have been linked to contaminated foods and spread among at-risk populations, such as men who have sex with men and individuals with behaviors associated with injection drug use. International travel is the most common risk for HAV infection.

In 2015 in the United States there were 1,390 cases of hepatitis A reported to the CDC, resulting in an incidence of 0.4 cases per 100,000 population. By comparison, in 2015 Louisiana had an incidence of 0.13 reported cases per 100,000 population. In 2017, Louisiana had an incidence of 0.17 cases per 100,000 population (Figures 1 and 2).

Figure 1: Incidence of Acute HAV Infections - Louisiana, 1970-2017
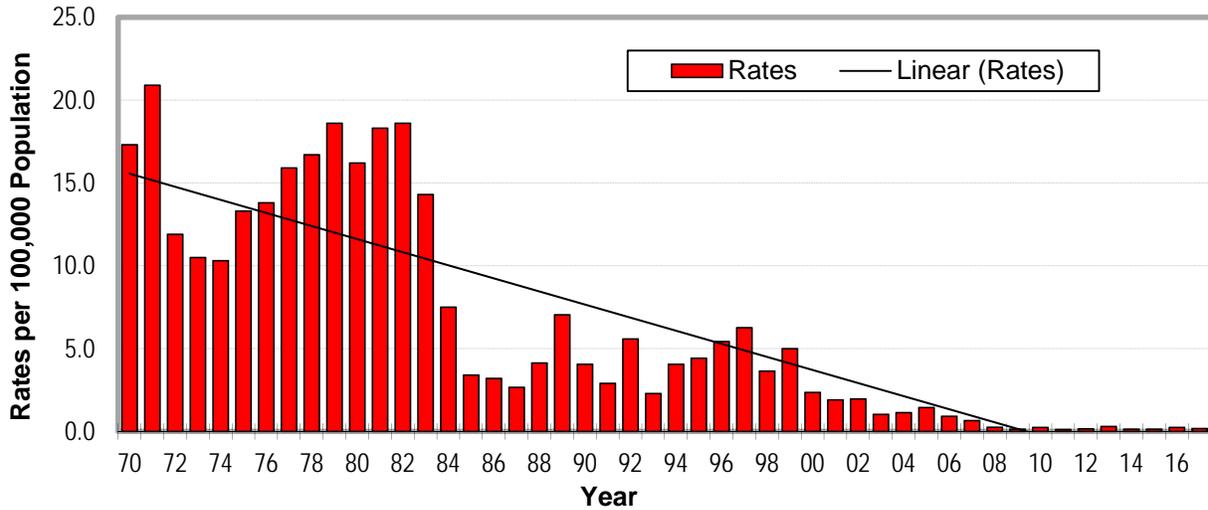
Since 1999, when routine HAV immunization of children was recommended by the Advisory Committee on Immunization Practices (ACIP) of the CDC, the number of reported cases of hepatitis A fell from over 200 cases to only 8 cases reported in 2017 in Louisiana (Figure 2).

Figure 2: Incidence of Acute HAV Infections - Louisiana, 1990-2017

$y = -10.793x + 235.71$
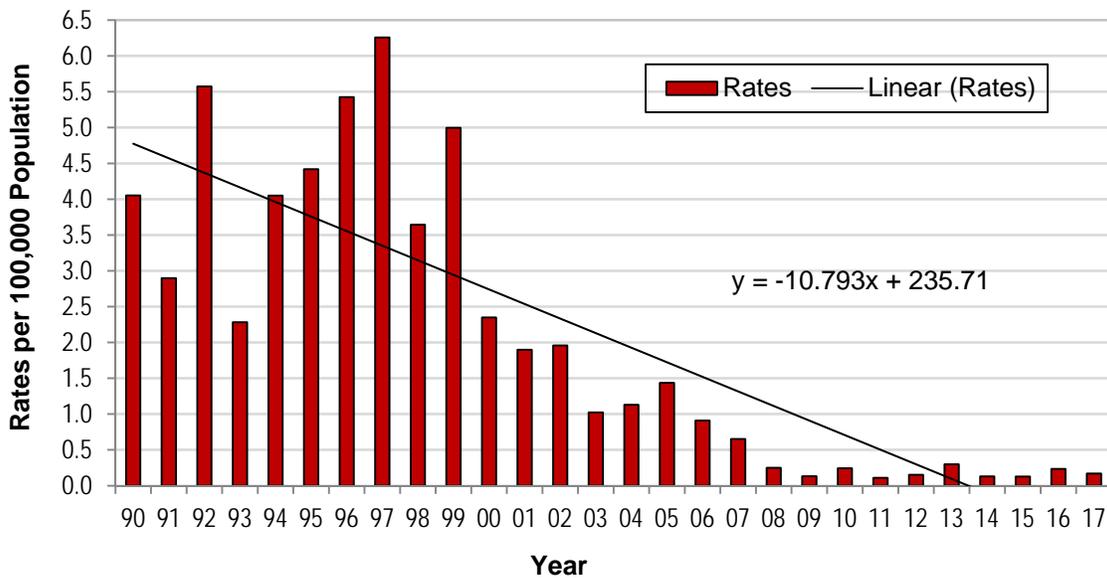
The trend line shows a decrease in reported cases over time. This decrease is probably due to a true decrease in new cases rather than an artifact of reporting.

The proportion of young adults ever infected with hepatitis A was estimated to be 25% in 2004 by a survey done by the Louisiana Department of Health (LDH), Office of Public Health (OPH) Laboratory among young adults whose blood was tested for other purposes.

Age Group, Race Distribution

Less than 10% of children younger than six years of age infected with hepatitis A display symptoms, compared with 40% to 50% of those from six to 14 years of age and 70% to 80% of those older than 14 years of age. Because the percentage of hepatitis A cases with symptoms increases with age, the age group distribution of reported cases does not reflect the actual age group distribution of infections.

The age group distribution shows two peaks, one among children aged 10 to 14 years and another among females, ages 20 to 24 years. Men who have sex with men are also at high risk, which may explain the comparatively high rates among males, ages 20 to 44 years (Figure 3).

Figure 3: Acute HAV Average Annual Incidence Rates by Gender and Age - Louisiana, 2005-2017
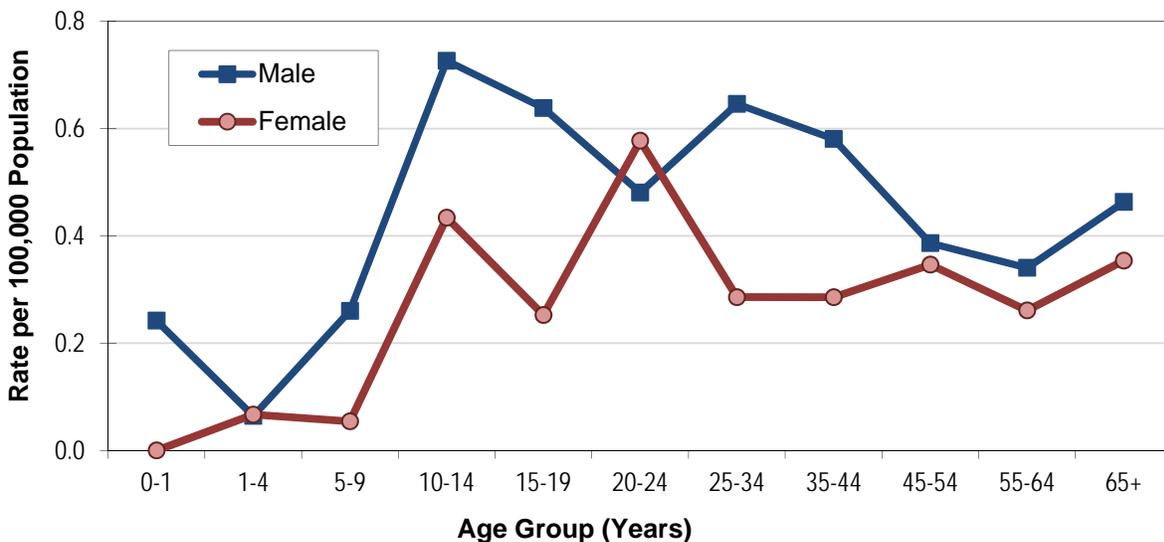
Transmission of hepatitis mainly occurs via the fecal-oral route. Children and toddlers (newborn to four-years-old) are most at the risk of infection, but the majorities of those infected at a very young age are asymptomatic, and therefore not recognized or reported.

The average incidence by age group shows a slightly different pattern by race. For the White population, there is a slight peak for the five to nine-year-old age group, a slight peak for young adults (20 to 34 years), and another peak in the older age group (65+ years). For African-Americans, there is a peak in children between the ages of 10 to 14 years due to six cases being reported in 2006. If the 2006 cases were excluded, the average incidence for 2005-2017 would be 0.34 per 100,000 for African-Americans 10 to 14-years old. Including the 2006 cases, the rate for that demographic is 0.78 per 100,000. Also, a slight peak occurs in young adults, between the ages of 20 and 44 years (Figure 4).

Figure 4: Acute HAV Average Annual Incidence Rates by Race and Age - Louisiana, 2005-2017
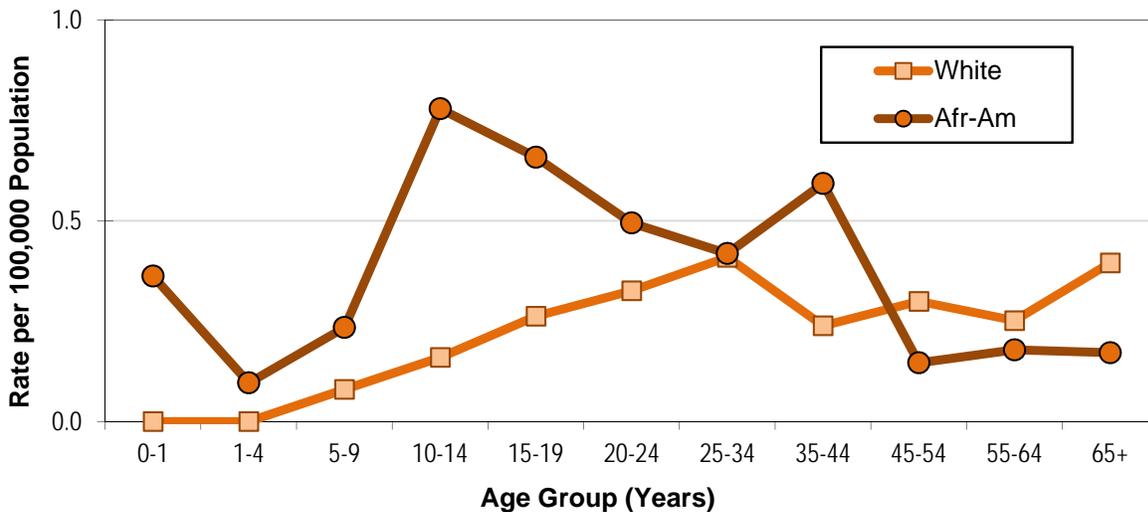
Geographical Distribution

The geographical distribution is unremarkable. Large numbers of cases are reported in heavily populated areas like Orleans and Jefferson parishes with other parishes reporting fewer cases. A five-year average shows that the only parishes with high rates are low population parishes who reported high number of cases for short periods (for example, St. Landry - 15 cases in 2006; West Baton Rouge – two cases in 2006; St. James - two cases in 2007; Acadia – three cases in 2007). There do not seem to be parishes which are continuous hotbeds of hepatitis A.

Hepatitis A - Related Hospitalizations

In 1997, the Louisiana Legislature mandated the reporting of hospital discharge data. The Louisiana Hospital Discharge Database (LaHIDD) serves as the state registry containing inpatient discharge data submitted to LDH, OPH by Louisiana hospitals. Yearly LaHIDD datasets contain parish, age, admit date, demographic and diagnosis information on all inpatients. These datasets are a tremendous resource allowing epidemiologists to examine absolute numbers and trends due to infectious diseases, for example, hepatitis related disease. However, most of the hospitalizations which include a diagnosis of hepatitis A (ICD 9 Codes 07.00 or 07.01) do not fit the profile of an acute fulminant hepatitis A infection. They appear to be positive results on serologic panels that are performed for a variety of reasons, so the patients do not necessarily fit the case definition of acute infections.
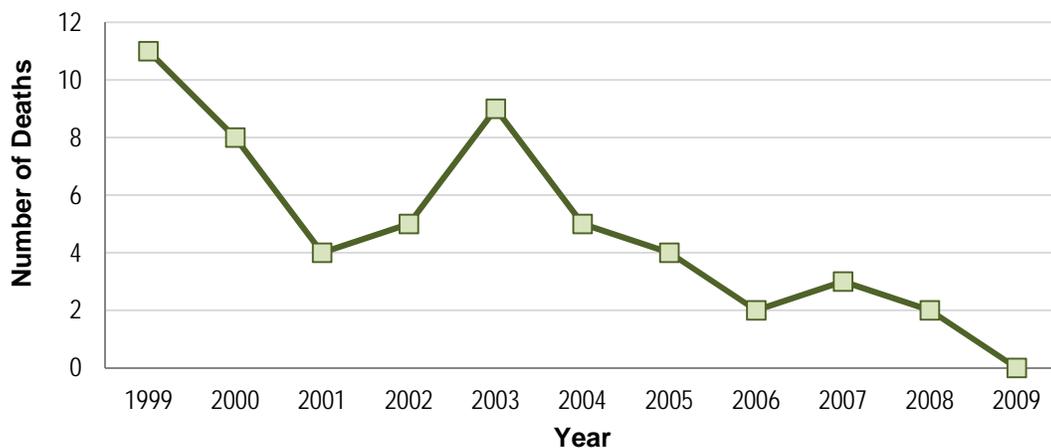
Hepatitis A – Related Deaths

The ICD 10 codes for hepatitis A are:

Code	Disease
B15	Acute Hepatitis A
B150	Hepatitis A with Hepatic Coma
B159	Hepatitis A without Hepatic Coma

At the time of this report, death data was available for the years of 1999 to 2009. A low number of hepatitis A related deaths are reported each year. The highest number of deaths related to hepatitis A occurred in 1999 with 11 deaths. Since 2003, the numbers of hepatitis A related deaths have been decreasing (Figure 5).

Figure 5: Hepatitis A - Related Deaths - Louisiana, 1999-2009

There is a higher number of hepatitis A related deaths in males compared to females. With the exception of 2006 and 2007, the average age of death between 1999 and 2009 ranged between 51 and 65 years of age. In 2006, the average age of death was 73 years and in 2007, the average death age was 34 years. The younger average death age in 2007 was due in part, to the death of a 25 year-old male with liver cell carcinoma listed as the primary cause of death and hepatitis A (ICD 10 code B159) listed as a secondary cause of death. The 53 deaths between 1999 and 2009 related to hepatitis A were among people with various occupations; there seemed to be no obvious association between the infection and the person's line of work.

Hepatitis A Virus (HAV) Reporting: An Evaluation of Non-Cases – Louisiana, 2013

In Louisiana, From January 1, 2013 to August 30, 2013 there were 125 case reports of hepatitis A. Of these cases, only six could be confirmed, while 119 were not confirmed. These 119 unconfirmed cases were reviewed to determine if they were properly classified and to understand the reasons for which they would not meet the case definition established for surveillance purposes.

Cases of hepatitis A infection are reported through the LDH, OPH, Infectious Disease Epidemiology Section's Infectious Disease Reporting Information System (IDRIS). Case definitions are established by the Council of State and Territorial Epidemiologists in collaboration with the CDC.

Although confirmed case reports are low, LOPH still receives from doctors, clinics, hospitals and labs, a significantly larger amount of possible cases that need to be reviewed.

Population and Methods

The definition of a confirmed case of acute hepatitis A must meet both the clinical description and the laboratory criteria, or be a case that meets the clinical case definition and occurs in a person who has an epidemiologic link with a person who has laboratory confirmed hepatitis A (i.e., household or sexual contact with an infected person during the 15 to 50 days before the onset of symptoms).

   1- Clinical Description: An acute illness with a discrete onset sign or symptom consistent with acute viral hepatitis (e.g., fever, headache, malaise, anorexia, nausea, vomiting, diarrhea and abdominal pain), and either (a) jaundice, or (b) elevated liver function tests (LFT) serum alanine aminotransferase (ALT >200 IU/L) or aspartate aminotransferase (AST) levels.

   2 - Laboratory Criteria for Diagnosis: Immunoglobulin M (IgM) antibody to hepatitis A virus (anti-HAV) positive.

It is important to remember that a case definition is not a diagnosis. A case definition has to be standardized so as to have a consistent and standardized reporting throughout all jurisdictions. A diagnosis is a more flexible tool; it is made by a clinician and serves as the basis for the patient management.

Results

Four (4) cases met the case definition. The breakdown of the 119 unconfirmed cases follows:
   80 reports included positive anti-HAV IgM test results
    - three reports included high ALT >200 IU/L and could have been considered acute hepatitis A, but there were no recent symptoms consistent with acute viral hepatitis

- three reports included LFTs that did meet the laboratory confirmation levels, but had other severe hepatitis conditions that could explain their high ALT (biliary obstruction or cirrhosis)
- 74 reports included only anti-HAV IgM test results with no elevated ALT, or ALT levels not measured
- 39 reports were considered unconfirmed due to 11 reports of negative or indeterminate anti-HAV IgM antibody
- 28 reports with no anti-HAV IgM test results.

Total anti-HAV antibody test results were reported for 30 individuals, including 23 where no anti-HAV tests were performed, four with positive anti-HAV IgM positive and three with anti-HAV IgM negative. Total antibody does not allow a differentiation between recent or old infection. The main purpose for identifying acute cases is to conduct contact investigations and to prevent disease occurrence among contacts. Investigations around "old" cases would be pointless. In summary, testing for total anti-HAV seems to be useless to diagnose recent infection.

Discussion

It was found that almost all of the cases were correctly labeled as "unconfirmed cases". In examining the data for the reasons why a suspected case was reported, by and large, the evidence suggests that cases were reported due to a false-positive lab result. Eighty of the 119 cases were IgM positive. Anti-HAV IgM positivity has been observed to remain positive in patients for more than 200 days in one study; in another study, anti-HAV IgM was detected more than 30 months after the onset of symptoms. With any test, no matter how sensitive or specific, the positive-predictive value of a test will diminish if the disease prevalence is low. Therefore, testing of anti-HAV IgM antibody should be performed only if clinical signs and symptoms strongly point toward acute hepatitis.

The 39 remaining cases could be attributed to the reporting of total hepatitis A antibody or even IgG antibody. A total hepatitis A antibody or even the IgG antibody, do not indicate infection; rather, they show past infection, or that immunity is present. Furthermore, the data collected showed that in the newborn to 19-year-old age group as compared to the adult group (30 years and older), a significant amount of the children had a total antibody test positive at 50% as opposed to 21% in the adult (OR=3.68 p-value: 0.01). Observation of the database, confirms this finding to a degree showing that many of the children were solely tested for total antibody. One possibility is that much of the positive total antibody in this group is due to vaccination, which will confer positive total immunity. Vaccination status and date of vaccination, unfortunately, were not reported in the IDRIS system during this search. The answer may also be due to asymptomatic infection. Most hepatitis A infections in children present with no discernable symptoms and are often incidental findings.

Recommendations

Similar findings were discussed in a CDC Morbidity and Mortality Weekly Report (MMWR) (May 2005). The article found similar results, and its suggestion should be reiterated. The hepatitis A IgM serology test is a confirmatory test that should be performed when hepatitis A is suspected, specifically when signs and symptoms of acute hepatitis are present, or a patient has been in close contact to a confirmed hepatitis case already. The greatest utility of the laboratory test is when the prevalence is deemed higher, allowing the positive predictive value of the test to be high as well. Reflexive viral hepatitis panel testing is therefore both harmful and costly. It should be recommended to physicians and hospitals to only test for hepatitis A when it is clinically probable.