REPORTED PAST/PRESENT HEPATITIS C CASES IN ALLEGHENY COUNTY, PENNSYLVANIA, FROM 2007-2016: A DESCRIPTIVE ANALYSIS

by

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Hepatitis C virus (HCV) is a bloodborne infection that causes both acute and chronic hepatitis that may lead to liver disease, cirrhosis, or liver cancer. Hepatitis C is a national and global public health problem. About 71 million people globally are chronically infected with hepatitis C and an estimated 3-4 million people are chronically infected with hepatitis C in the United States. Annually, about 399,000 people die worldwide from hepatitis C infection and approximately 20,000 people die from HCV-related liver disease in the U.S. Most people with hepatitis C infection are asymptomatic and about half of people do not know that they are infected. Hepatitis C is a reportable disease in Pennsylvania; therefore, the Allegheny County Health Department (ACHD) receives reports of hepatitis C for residents of Allegheny County, Pennsylvania. Starting in 2015, ACHD conducted enhanced surveillance activities for hepatitis C cases which included faxing one-page questionnaires to healthcare providers who had patients with at least one HCV positive laboratory test and conducting patient phone interviews to collect risk factor and exposure information. Disease surveillance is important to public health because it helps identify which populations need interventions to prevent transmission of the disease, morbidity, and mortality. The purpose of this study is to describe the trends in hepatitis C cases
from 2007 to 2016 and the reported past/present hepatitis C cases from 2015 to 2016 in Allegheny County, Pennsylvania.
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PREFACE

I would like to thank Jennifer Fiddner for assisting with the surveillance process and datasets. Thank you to my committee members for reviewing my thesis and providing valuable feedback. Lastly, I would like to thank the Allegheny County Health Department for allowing me to use their data.
1.0 INTRODUCTION

Hepatitis C virus (HCV) is a bloodborne infection that causes both acute and chronic hepatitis C that may lead to liver disease, liver cancer, or cirrhosis. Hepatitis C is a public health problem. About 71 million people globally are chronically infected with hepatitis C and about 3-4 million are chronically infected with hepatitis C in the United States. Each year, approximately 399,000 people worldwide die from hepatitis C infection. Of those infected with hepatitis C, 75%-85% will develop chronic infection, 60%-70% will develop chronic liver disease, 5%-20% will develop cirrhosis, and 1%-5% will die from chronic infection. About 15%-25% of people infected with HCV spontaneously clear the infection without treatment. The reason for this is still unknown to researchers. Development of acute hepatitis C infection is less common, and about 20%-30% of newly infected HCV cases develop acute illness symptoms such as fatigue, abdominal pain, jaundice, and loss of appetite.

Hepatitis C is most commonly transmitted through the use of injection drugs, sharing drugs and equipment, and reusing needles or syringes. It can also be transmitted from the use of unsterilized medical equipment or from transfusions of blood and other blood products. Additionally, HCV can be transmitted sexually or through maternal transmission but is not as common. Sexual transmission of HCV has been shown to be about 3%. According to the Centers for Disease Control and Prevention (CDC), approximately 6 out of every 100 infants born to an HCV positive mother will become infected. Before blood screening began in the U.S.
in 1992, HCV was most commonly transmitted through blood transfusions.\textsuperscript{1} For this reason, the CDC recommends HCV testing for all people born between the years 1945 and 1965.\textsuperscript{1} In resource limited countries, HCV is mostly transmitted from the use of unsterilized needles, syringes, and medical equipment.\textsuperscript{2}

Hepatitis C virus is a bloodborne infection, which has many risk factors. People at high risk include those who have used injection drugs even just once in their life, recipients of blood clotting factors made prior to 1987, recipients of blood transfusions or solid organ transplants before July of 1992, patients who have received long-term hemodialysis, people who are infected with HIV, people who have received tattoos or body piercings with unclean needles, and children who were born to HCV positive mothers.\textsuperscript{1,3} People who have known exposures to HCV, such as healthcare workers with needlesticks from HCV positive blood and recipients of blood products or organs from HCV positive donors, are also at risk of contracting HCV.\textsuperscript{1} Ways to reduce the risk of HCV infection include not using injection drugs, using clean needles and equipment if injecting drugs, not sharing needles and equipment if injecting drugs, not sharing personal items that may have blood on them (i.e. toothbrushes, razors), and refraining from sex or contact of blood with people who are HCV positive.\textsuperscript{1}

Several diagnostic tests can be performed to determine whether a person is HCV positive. Tests that can be used are the antibody HCV test (anti-HCV), enzyme immunoassay (EIA), enhanced chemiluminescence immunoassay (CIA), and the HCV RNA polymerase chain reaction (PCR) test.\textsuperscript{1} The PCR test is referred to as the confirmatory test because it can detect the absence or presence of HCV and the amount of the virus.\textsuperscript{1} The most common tests that are conducted are the anti-HCV test and the confirmatory RNA PCR test.\textsuperscript{1} The confirmatory test is always recommended even if the antibody test has been done because someone can have a
positive HCV antibody test but not currently be infected with hepatitis C. The RNA test can determine whether a person is currently infected with hepatitis C. Testing is recommended for people born between 1945-1965, anyone who has ever injected drugs, people with chronic liver disease or abnormal liver tests, and people infected with HIV or AIDS. Testing is also recommended for people who received or donated blood products prior to 1992, those who have been exposed to blood in their workplace via needlestick or puncture, people who have received hemodialysis, and those who were born to HCV positive mothers.

Approximately 20,000 people die each year from HCV-related liver disease. There is a cure for hepatitis C with several treatment options available. Advancements in hepatitis C treatment have been made, particularly within the past five years. In fact, the U.S. Food and Drug Administration (FDA) approved two new drugs this year for treatment of hepatitis C. Drugs for hepatitis C treatment have vastly improved with regard to the number of side effects and the length of treatment. Newer treatments have shorter duration from about 8 to 12 weeks, work for a variety of HCV genotypes, and only need to be taken once a day. Despite the great successes in hepatitis C treatment, a small percentage (16%) of patients infected with hepatitis C receive treatment. A significant barrier to hepatitis C treatment is access and the cost of treatment.

HCV has been a nationally notifiable disease since 2003 and is also a reportable disease in Allegheny County, PA. Therefore, it is required by law that healthcare providers, hospitals, and laboratories report HCV cases for residents of Allegheny County, PA to the Allegheny County Health Department (ACHD). Prior to 2015, ACHD did not have the staff to conduct thorough HCV surveillance. However, starting in 2015, ACHD staff conducted enhanced surveillance for all HCV positive cases. These activities included faxing one-page questionnaires...
to healthcare providers for patients with a positive HCV laboratory test and conducting phone interviews to collect more patient information. An interview script and guide were developed by ACHD staff using a template from the CDC to obtain patient risk factor/exposure information. Routine follow-up calls are normally conducted for reportable diseases in Allegheny County, PA. Hepatitis C cases were classified in Pennsylvania’s Electronic Disease Reporting system, PA-NEDSS, using the current CDC case definition. In 2016, ACHD staff conducted similar surveillance activities but only for people with positive HCV laboratory tests between the ages of 18-34 and greater than 75 years old. The 18-34 year old age group was chosen because they were suspected to be newly infected hepatitis C cases. The purpose of this study is to describe the reported past and present hepatitis C cases in Allegheny County, PA from 2007-2016.
2.0 METHODS

All information was collected and stored on an electronic database maintained by ACHD. HCV case classification was determined by using the case definition for that year that was created by the CDC. Prior to 2015, ACHD did not have the staff to conduct enhanced surveillance activities. The hepatitis C data collected from 2007-2016 in Allegheny County, PA were used to show trends in the data from this ten-year period. More rigorous hepatitis C surveillance was conducted in 2015 and 2016 for the county. The 2015 HCV case definition classified chronic hepatitis C cases as past or present hepatitis C cases while the 2016 case definition classified them as chronic cases. Figure 1 shows the HCV class classification algorithm for the new 2016 case definition. All HCV cases were classified in the state electronic disease surveillance system PA-NEDSS.

Since HCV is a reportable condition, patient and provider contact information was obtained and accessed from PA-NEDSS. A one-page questionnaire was faxed to healthcare providers who had patients with at least one HCV positive laboratory test to collect information on symptoms, other laboratory results, and risk factors. The questionnaire was faxed to healthcare providers a second time if they did not return it to ACHD. To find additional risk factor/exposure information for HCV positive patients, ACHD staff created an interview guide based off of a template provided by the CDC and an introductory script to conduct phone interviews. ACHD staff trained two interviewers and a group of graduate students before they
started conducting the phone interviews. The graduate students were used due to the large number of HCV cases that needed to be contacted for the follow-up calls. In 2015, all HCV cases were investigated but this was unsustainable due to the large amount of cases. Consequently, in 2016, only the HCV cases between the ages of 18-34 and greater than 75 years old were investigated. Data were analyzed using Microsoft Excel for descriptive statistics.
### 3.0 RESULTS

Between 2007 and 2016, there were 11,475 reported probable and confirmed hepatitis C cases in Allegheny County, PA. Out of 11,475 cases, 9745 (85%) were classified as confirmed and 1730 (15%) were probable. The number of reported probable and confirmed hepatitis C cases increased throughout this ten-year period from 643 cases in 2007 and 606 in 2008 to 2123 in 2015, and 2824 in 2016 (Figure 2).

As shown in Figure 3, the majority of probable and confirmed hepatitis C cases from 2007 to 2016 were male (61%). The age distribution was bimodal with peaks between the ages of 25-39 (25%) and 50-64 years old (43%). The distribution of race for these cases from 2007 to 2016 was 41% unknown, 40% White, 16% Black, 2% other, 0.4% Asian, and 0.1% Pacific Islander. The majority of probable and confirmed hepatitis C cases from 2007 to 2016 had unknown ethnicity (84%).

The number of pediatric hepatitis C cases for children less than 2 years old and between ages 2-9 peaked in 2010 with 7 cases and 2 cases respectively and in 2016 with 6 cases for each age group (Figure 4). The number of hepatitis C cases in women of childbearing age (ages 15-44) increased from 2007 to 2016 where the number of cases in 2016 is almost four times higher than the number of cases in 2012 (Figure 5).

As shown in Figure 6, acute hepatitis C cases peaked in 2015 with 23 cases. There were 11 acute cases in 2016 which is almost half as many cases in 2015. This may be due to the more
aggressive surveillance that ACHD conducted in 2015. ACHD did no follow-up investigation for acute cases in years prior to 2015, which explains the minimal number of cases for those years.

In 2015, there were 2123 reported probable and confirmed hepatitis C cases in Allegheny County, PA. Out of 2123 cases, 2012 (95%) were classified as confirmed cases and 111 (5%) were probable. The majority of cases were male (61%). The age distribution was bimodal with peaks between the ages 20-39 (35%) and 50-69 years old (49%). Out of the 2123 cases, 46% were White, 34% had unknown race, 17% were Black, 2% had a race of other, 0.3% were Asian, and 0.1% were Pacific Islander. The most common risk factor for interviewed cases was needle usage for injection drugs.

There were 25 acute hepatitis C cases in 2015 and the majority were White (68%) males (64%) with a peak between ages 30-39 years old (40%). The age of acute cases is older than previously thought. More investigation is needed to explain the peak of acute cases in this 30-39 year old age group.

In 2016, there were 2824 reported probable and confirmed hepatitis C cases in Allegheny County, PA. Out of 2824 cases, 1628 (58%) were classified as confirmed and 1196 (42%) were probable. The majority of cases were male (60%). Case numbers peaked between the ages 20-39 (34%) and 50-69 years old (50%). Out of the 2824 cases, 47% had unknown race, 34% were White, 15% were Black, 5% had a race of “other,” 0.3% were Asian, and 0.1% were Pacific Islander. A total of 832 hepatitis C cases between the ages 18-34 years were investigated in 2016. Out of these cases, 105 (13%) were non-cases, 126 (15%) were incarcerated, 348 (42%) had invalid or missing phone numbers, 148 (18%) were left voicemails and did not respond, 86 (10%) were interviewed, 17 (2%) refused to be interviewed, and 2 (0.2%) were deceased. The interview response rate was low at about 10%. Shown in Figure 7, the most common risk factors
for the 86 probable and confirmed hepatitis C cases between the ages of 18-34 years old that were interviewed were needle usage for injection drugs (74%), tattoos (70%), dental work or oral surgery (66%), contact of a hepatitis C case (43%), surgery (42%), employed in field involving contact with human blood (12%), received blood or blood products/transfusions (7%), puncture with needle or other object contaminated with blood (6%), and acupuncture (5%). Out of the 86 interviewed cases, only 8 (9%) reported receiving medical treatment and 14 (16%) reported receiving medical care specifically for hepatitis C infection. A total of 53 hepatitis C cases aged 75 years or older were investigated in 2016. Out of these cases, 14 (26%) were non-cases, 15 (28%) had invalid or missing numbers, 7 (13%) were left voicemails and did not respond, 11 (21%) were interviewed, 2 (4%) refused to be interviewed, and 4 (8%) were deceased. The interview response rate was better for this age group than those aged 18-34 years old at about 28%. The fax return rate from providers was about 68% while the fax return rate for second attempts was lower at about 45%.

There were less acute hepatitis C cases in 2016 than in 2015, which may be due to the more aggressive surveillance that was conducted in 2015. There were 11 acute cases in 2016 and the majority of them were male (55%) and between the ages 20-29 years old (55%). The age group for these cases has shifted to a younger population than the acute cases in 2015, which may be due to not investigating cases for people over the age of 34 years old. The most common races were White (45%) and unknown (45%).


4.0 DISCUSSION

Hepatitis C cases in Allegheny County, PA have increased from 2007-2016. This finding is consistent with national hepatitis C data. Another finding that is consistent with national data is that injection drug use was the most common risk factor for hepatitis C cases in both 2015 and 2016. These findings are not surprising due to the opioid epidemic that is affecting the U.S. and Allegheny County in particular. In fact, the CDC reported that hepatitis C related deaths in the U.S. reached an all-time high in 2014 surpassing deaths from any other infectious disease. In 2016, Allegheny County had 422 opioid overdose deaths, which were the most overdose deaths the county has ever reported. The peak in hepatitis C cases for ages 25-39 years old in Allegheny County is also the same age group with a significant increase in overdose deaths in the county. This warrants attention because as the opioid epidemic continues to grow, the number of hepatitis C cases will likely continue to increase. Another study finding that is consistent with national data is the peak in hepatitis C cases from ages 50-64 years old, or the baby boomer population. The large number of cases in this age group could be due to the HCV screening recommendation by the CDC for this population. Screening is recommended for people born between 1945-1965 because they are five times more likely to be infected with hepatitis C than any other adult age group. This may be due to blood not being screened for HCV before 1992. A study finding that is inconsistent with national data is that White individuals are the most common race for hepatitis C cases in Allegheny County. National data
show that chronic hepatitis C infection and hepatitis C-related deaths are most prevalent among African Americans. This difference in race could be attributed to the large majority of Whites in Allegheny County (80.5%) compared to the small percentage of African Americans (13.4%).

Hepatitis C surveillance activities need to be improved in Allegheny County to ensure collection of accurate data. A large portion of hepatitis C cases in 2016 had unknown race and it was the second most common response for race in 2015. Ethnicity was often missing as well. These data could be collected more accurately if the healthcare personnel who tested the individuals for HCV completed them. Due to the small number of cases who were interviewed, it is imperative that healthcare personnel complete as much information on the questionnaire as possible about demographic, symptoms, previous laboratory tests, and risk factor information to ensure accurate data collection. Consequently, this would create less work for the investigation of cases by ACHD staff, which does not have the resources to investigate all hepatitis C cases in the county. However, this may not be of interest to the healthcare personnel because they often are too busy to complete the information on the questionnaire. Another part of the surveillance process at ACHD that needs to be improved is contacting the hepatitis C cases for follow-up interviews. Phone interviews proved to be unsuccessfull with an interview response rate of only 10%. Surprisingly, the cases aged 75 years or older had a higher interview response rate than cases aged 18-34 years old. People in the younger generation are considered to be frequent mobile phone users; therefore, it would be expected that more cases from this age group would participate in phone interviews than the cases in the older age group. However, it was not determined whether the phone numbers provided were mobile phones or landlines, which could make a difference in the phone interview response rate. Other forms of communication could be used for the follow-up interviews, such as sending text messages, emails, or online surveys to
complete. Since phone calls are not successful for the younger population, using updated technology may help to improve the interview response rate. Another improvement that could be made to the ACHD surveillance process is making it completely electronic. Eliminating faxes would save the ACHD staff time that could be used for conducting follow-up interviews. Surveillance is an important process with the goal of describing the burden of disease for infectious diseases so interventions can be made to stop the transmission of the disease. Attention is warranted to prevent HCV transmission in Allegheny County, especially as the opioid epidemic continues to grow. Therefore, concerted effort needs to be given to provide accurate and thorough surveillance of hepatitis C cases in Allegheny County. Data collected from surveillance can be used to develop and implement interventions to decrease HCV transmission and ultimately reduce morbidity and mortality in Allegheny County, PA.

4.1 LIMITATIONS

The results of this study are limited to the work and resources that the ACHD allocates toward the HCV surveillance process as well as the number of laboratory reports that were sent to ACHD. Therefore, the increase in hepatitis C cases could have been influenced by the enhanced surveillance activities that the ACHD conducted, particularly in the year 2015 where all cases were investigated as opposed to in 2016 where only certain age groups were investigated. Additionally, the risk factor data for 2015 and 2016 need to be interpreted with caution because multiple risk factors were reported for each person. Due to the small sample size of hepatitis C cases that were interviewed in 2016, the results cannot be generalizable to the population of Allegheny County, PA.
4.2 CONCLUSION

Hepatitis C cases in Allegheny County, PA have increased within the past decade. The majority of these cases in Allegheny County were males aged 25-39 and 50-64 years old and the most common risk factor was injection drug use. Interventions need to be developed for these populations to decrease the number of hepatitis C cases and prevent transmission of HCV in Allegheny County. Particular attention is warranted to injection drug users due to the opioid epidemic that has been occurring throughout the U.S. and significantly impacting Allegheny County. Improvements need to be made for HCV testing and linkage to care to decrease the number of hepatitis C cases and deaths. However, many upstream factors influence these issues making interventions harder to develop and implement. Enhanced HCV surveillance conducted by ACHD can aid this process but more resources are needed for it to be sustainable.
APPENDIX: FIGURES
HEPATITIS C: CASE CLASSIFICATION ALGORITHM (CDC 2016)

Note: Previously reported and/or counted cases of “Hepatitis C, Past or Present” should have a new PANEDSS investigation initiated when:
- A previous PANEDSS investigation for “Hepatitis C, Past or Present” from a closed-out MMWR year exists AND
- A newly received hepatitis C report in PANEDSS upgrads the case classification (e.g., from probable to confirmed)

Otherwise, newly received hepatitis C reports in PANEDSS for patients with existing investigations should be linked to the old investigation.

Evidence of acute hepatitis C?
- Acute onset of viral hepatitis symptoms\(^{4}\); AND
- Jaundice \(\text{OR} \)- serum ALT levels >200 IU/L; AND
- No evidence of acute hepatitis A or B (Negative IgM anti-HAV, IgM anti-HBe-if done)

Positive nucleic acid test result for HCV RNA?
- Qualitative, viral load, or genotype

Positive anti-HCV result?
- Not a case
- Documented negative anti-HCV or HCV RNA result ≤12 months before the date of the current positive result?
  - Documented negative anti-HCV or HCV RNA result ≤12 months before the date of the current positive result?
    - Documented negative HCV RNA result with collection date on or after positive anti-HCV specimen collection date?
      - Probable, Hepatitis C Chronic\(^{6}\)
      - Not a case (resolved HCV infection)
    - Probable, Hepatitis C Chronic\(^{6}\)
    - Documented negative anti-HCV or HCV RNA result ≤12 months before the date of the current positive result?
      - Confirmed, Hepatitis C Acute
      - Confirmed, Hepatitis C Chronic\(^{6}\)

Positive anti-HCV result?
- Confirmed, Hepatitis C Acute
- Not a case

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Figure 1- HCV 2016 case classification algorithm
*The case definition changed, which may be the reason for the increase in probable cases and decrease in confirmed cases.

Figure 2- Number of reported past/present hepatitis C cases in Allegheny County, PA from 2007 to 2016 by year
Figure 3- Distribution of reported past/present hepatitis C cases in Allegheny County, PA by age and sex
Figure 4- Number of reported past/present pediatric hepatitis C cases by year for ages less than 2 years and ages 2 to 9 years in Allegheny County, PA from 2007 to 2016
Figure 5- Number of reported past/present hepatitis C cases in women of childbearing age (15-44 years old) by year in Allegheny County, PA from 2007 to 2016
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