Viral Hepatitis C-Related Care in Active Duty and Reserve Service Members: A Retrospective Review

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ABSTRACT

Introduction:
Hepatitis C Virus (HCV) infection is a leading cause of chronic liver disease and hepatocellular carcinoma, and universal screening of all adults is recommended. Treatment with new direct antiviral agents are well tolerated and highly effective and decrease morbidity and mortality from HCV. The timely treatment of active-duty Service members (SMs) is essential to prevent complications of HCV and to ensure medical readiness and safety of the Department of Defense blood supply. We performed a retrospective review of the quality of care of Navy Active Duty (AD) and reserve SMs diagnosed with HCV to assess rates of successful treatment and compliance with national guideline recommendations and identify potential challenges to receiving curative HCV therapy.

Materials and Methods:
A retrospective chart review was completed on the health records of 54 AD and reserve US Navy SMs diagnosed with HCV. The records were reviewed for timeliness of subspecialty evaluation, achievement of sustained virologic response (SVR), and documentation of the completion of HCV-associated recommendations from national organizations and guidelines. Challenges and barriers to care were identified.

Results:
Ninety-eight percent of AD and reserve Navy SMs diagnosed with HCV were prescribed treatment, 81% achieved an SVR after completing initial treatment, which reached 92% after initial nonresponders underwent a second round of treatment. Fifty percent of SMs experienced a delay in care due mostly to military-related obligations and patient noncompliance or both. There was a small number of delays in care as a result of prolonged notification of results and referral time.

Conclusion:
As HCV screening recommendations expand to include all adults, more HCV infections will be identified in both the active and reserve components. Modern HCV therapies are both relatively short in duration as well as curative, allowing for the restoration of medical readiness and military service retention. Despite these advantages, we identified challenges of effecting HCV cures in a mobile military population. We recommend centralized compliance monitoring of not only HCV force screening but also HCV treatment to ensure maximized military medical readiness.

INTRODUCTION

The hepatitis C virus (HCV) causes chronic liver diseases, such as cirrhosis and hepatocellular carcinoma, and is a leading cause for liver transplant in the United States. HCV currently affects an estimated 2.4 million people in the United States and the incidence is rising, largely as part of the opioid epidemic. HCV is spread parenterally, typically through IV drug use, needle stick injuries, and blood transfusions prior to universal screening.1, 2

The development of a cure for HCV has made rapid progress over the last 30 years. In the early years following HCV identification, treatments required interferon therapy, which had a limited response rate and many side effects. In 2014, the first interferon-free regimens, direct anti-viral agents (DAA), became available, which are both highly effective and well tolerated. The current standard of care treatment of HCV is typically an 8–12 week course of a once daily oral medication. Treatment options can vary based on the presence of cirrhosis and in special populations, such as patients who have undergone prior treatment for HCV or with patients concurrent infections such as human immunodeficiency virus (HIV) or hepatitis B virus (HBV). Twelve weeks following the completion of therapy, HCV RNA should be rechecked; a negative test indicates sustained virologic response (SVR). Those with cirrhosis will continue to undergo screening for hepatocellular carcinoma (HCC) and varices, and those without cirrhosis require no further follow-up. With
the development of DAAs, there has been widespread public health initiatives to identify and treat HCV with current Center for Disease Control guidelines recommending at least once in a lifetime testing of all adults over 17 years old.\(^3\),\(^4\)

In the U.S. military, operational readiness is a top priority and includes the health of Service members (SMs). We performed a retrospective review of the cases of U.S. Navy SMs diagnosed with HCV. With this review, we aimed to assess effectiveness of care, identify any potential challenges for SMs with HCV-related medical care, and determine possible strategies for future interventions and improvements.

METHODS
A retrospective review was completed of the health records of 54 AD and reserve U.S. Navy SMs diagnosed with HCV from 2000 to 2019 based on a positive HCV antibody and detectable viral load. The Hepatitis C laboratory data originate from Composite Health Care System (CHCS) facilities and arrive in health-level 7 (HL7) formatted messages from the Defense Health Services System Solutions Delivery System (DHSS-SDD). The DHSS-SDD receives HL7 messages on a daily basis from CHCS. These messages come directly from CHCS at the military treatment facilities (MTFs). Age, gender, race, genotype, prior HCV testing, year of diagnosis, and presence of co-infection with HIV and HBV were reviewed. Compliance with HCV-associated recommendations was assessed, including completion or not of an initial fibrosis assessment through the collection of laboratory tests that could be utilized in Fibrosis-4 (FIB 4) calculation, transient elastography, or a liver biopsy. We assessed, for liver imaging, the presence of immunity to HBV and hepatitis A virus (HAV), documented alcohol cessation counseling, and compliance with hepatocellular cancer screening and esophageal varices screening for SMs with cirrhosis. The amount of time until initial subspecialty care was measured and documented, and reasons for delays in care were reviewed. A delay in care was identified as greater than 1 year from diagnosis to evaluation until a discussion of treatment, greater than 6 months between recommendation for treatment and treatment initiation or a documented encounter where a delay was reported. The definition was broad and beyond TriCare Policy for Access to Care memorandum, which advises that patients should be offered an appointment within 28 days of referral. Therapy selection was reviewed, the number who obtained SVR, documented interruptions in care and reasons for interruptions in care or reasons for not obtained SVR were assessed. Follow-up care for those who did not obtain SVR on initial therapy was reviewed.

This case review was determined to meet the standards of a quality improvement assessment and approved by the Walter Reed National Military Medical Center Department of Research.

RESULTS

Demographics
Of 54 patients with active infections, 45 were AD, 9 were reservists, 49 were male, and 5 were female. Six SMs were born in 1945–1965. Twenty-seven identified as Caucasian or white, 10 as African American or black, 4 as Asian, 2 as Hispanic, 1 American Indian, 3 identified as other race, and 7 had no race reported. Per 5-year periods, 6 cases were diagnosed in 2000–2004, 15 in 2005–2009, 19 in 2010–2014, and 14 in 2015–2019. There were 6 patients who had prior negative HCV tests before diagnosis, and 3 patients presented with suspected HCV due to results from blood donation screening.

Disease Characteristics
All 54 SMs were screened for both HBV and HIV. There were 5 SMs who were co-infected with HIV and one co-infected with HBV. HCV genotype 1a was present in 31 SMs, genotype 1b in 13 SMs, genotype 2 in 5 SMs, genotype 3 and genotype 6 affected 1 SM, and 6 SMs did not have their genotype documented. For an assessment of fibrosis, there were 6 SMs with advanced fibrosis or cirrhosis, 45 without advanced fibrosis and 3 with indeterminate assessment of fibrosis without definitive staging. Liver biopsy was completed in 29 SMs, blood-based fibrosis assessments such as Fibrosure or labs for a FIB-4 were available for 24 SMs, and 1 SM was assessed with transient elastography.

Treatment
Medications for the treatment of HCV were prescribed by gastroenterologists at an MTF for 27 SMs, by infectious diseases specialists for 18 SMs, by civilian gastroenterologist (non-MTF) for 6 SMs, by an OCONUS Internal Medicine specialist with tele-health support for 1 SM, and 1 SM was treated by both an infectious diseases specialist at an MTF and by a gastroenterologist at an MTF. One SM declined treatment. Of the 53 SMs who underwent HCV treatment, 43 had documented SVR 12 weeks after completing the initial treatment, 9 did not respond to initial treatment, and 1 SM is still undergoing treatment. Interferon-based therapies were used in 7 of the 9 treatment failures, and 2 were treated with DAAs. For the 2 SMs who were treated with DAAs, one was noncompliant with therapy and one was found to have genetic resistance to the initial DAA used but then obtained SVR with a different DAA. Of the 9 SMs that did not initially respond to treatment, 4 had documented noncompliance with their medications, 1 SM stopped due to side effects, and 4 were primary medication failures. Of the 9 that did not initially obtain SVR, 6 SMs were retreated and documented SVR, while 3 SMs left the military prior to retreatment.
Timing of Care
Of the 54 SMs diagnosed with HCV, 53 completed treatment aimed at curing HCV and 1 SM did not. Evaluation by a specialist occurred within 12 months of diagnosis for 44 SMs, it was greater than 12 months from diagnosis for 6 SMs, and it was unable to be assessed for 4 SMs due to the lack of documentation of the timing of evaluation by non-MTF specialists. There were 28 SMs who experienced a delay in receiving HCV treatment, 23 cases with no delays, and delays in care were unable to be determined in 3 cases. Cases that cited both noncompliance and military obligations or career concerns were the most common reasons for delay in care with 10 cases, military obligations alone were cited as the cause for delay in 7 cases, delay in diagnosis notification or delay in follow-up was cited in 6 cases, and SM noncompliance with medical recommendations was cited as the cause for delay in care in 5 cases. Upcoming permanent change of station (PCS) moves and deployments were completed were the primary reasons cited for not initiating therapy. Evaluation following PCS and deployment primarily relied on SMs self-referrals back to care.

Additional HCV Care Recommendations
All 54 SMs were assessed for immunity or documented immunizations to HAV and HBV except the 1 patient who had a concurrent HBV infection. For liver imaging, 45 SMs had documented liver imaging and 6 SMs did not. For alcohol cessation, 33 SMs had documented that they underwent alcohol cessation counseling and 21 SMs did not. Of the 54 SMs with HCV, 4 were recommended to undergo HCC screening and 2 completed screening and 2 did not with no follow-up care documented without reason provided.

DISCUSSION
HCV is an ongoing public health concern and untreated or delays in treatment resulting in significant morbidity and mortality and there have been recent recommendations to expand screening to all adults. With the availability of well-tolerated and highly successful DAA treatments, prompt identification and treatment of SMs diagnosed with HCV are essential to limit spread, decrease complications of chronic infections, and ensure the medical readiness of our military forces.

Our assessment shows that military health providers and MTFs have been overall very successful at providing medical therapies to SMs diagnosed with HCV with a 98% (53/54) treatment rate and a 94% (49/52) rate of ultimately obtaining SVR. Military providers demonstrated high compliance rate (100%) in screening for concurrent HIV and HBV infections and for assessing for immunity or immunizations to HAV and HBV. Challenges observed in this review were timeliness of care, with 43% (23/54) with a documented delay in receiving definitive therapy. The reasons for the delays were many but center around a central theme of either military obligations, including upcoming PCS and upcoming deployment or training, or SMs not complying with medical recommendations made by their providers or a combination of both. Education of providers among primary care about the newly available therapies and the ease of prescribing is one potential opportunity to decrease barriers to prompt therapy. Providing care coordination, specifically telemonitoring services, has been shown to be an effective strategy to improve compliance in large populations. To improve HCV-related care in the military, early identification of positive HCV tests, prompt linkage to care, and consistent documented follow-up are all potential targets for process and quality improvement projects. Studying this population among other military services would provide additional information on the care of patients with HCV and may shed light on additional strategies to optimize out SMs care. We propose that centralized monitoring of HCV diagnosis and treatment may identify SMs who are at risk of delayed or incomplete treatment. Based off of the data and areas for improvement we identified, consistent coordination of care will be the aim of our future projects for HCV-related care as the provision of HCV continues to advance.

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CONFLICT OF INTEREST STATEMENT
None declared.

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