HCV Universal Test-and-Treat With Direct Acting Antivirals for Prisoners With or Without HIV: A Prison Health Care Workers–Led Model for HCV Microelimination in Thailand

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Background: This study investigated the sustained virologic responses (SVRs) among prisoners with hepatitis C virus (HCV) using universal test-and-treat approach by prison health care workers in a central male prison in Thailand.

Methods: A universal HCV screening was conducted in a maximum-security central prison (Klong Prem Central Prison) in Thailand. HCV RNA–confirmed prisoners were treated with generic sofosbuvir/velpatasvir by prison health care workers, regardless of their HCV genotypes and duration of prison sentences. We evaluated the SVR rates at 12 weeks after completing direct acting antivirals (DAA) treatment.

Results: A total of 68 prisoners with detectable HCV RNA received DAA treatment. The median age and duration of prison sentences were 44 years (interquartile range, 41–53) and 25 (interquartile range, 19–33) years, respectively. Twenty-five percentage of the participants was coinfected with HIV, and 6% of the participants was coinfected with hepatitis B virus. Among all prisoners who received DAA treatment, 20 (29%) had genotype (GT)-1a, 3 (4%) had GT-1b, 22 (32%) had GT-3a, 3 (4%) had GT-3b, and 7 (10%) had GT-6. Overall, improvements in liver biomarkers were seen after HCV treatment, and SVR was achieved in 97% of the participants with per-protocol analysis and in 90% of the participants with intention-to-treat analysis.

Conclusions: HCV treatment using DAA among prisoners through universal test-and-treat approach led by prison health care workers is highly effective and safe, and such model can potentially help to facilitate the goals of HCV microelimination among prisoners in Thailand.

Key Words: HCV, DAA treatment, prisoners, microelimination

INTRODUCTION

Hepatitis C virus (HCV) infection remains a major burden for liver-related mortalities globally. The World Health Organization has set ambitious goals to achieve HCV elimination by 2030. Microelimination, which prioritizes focused interventions on specific populations, is seen as a crucial approach to reach the elimination targets. Settings such as prisons, which have a high HCV prevalence, consequently, have been considered as opportunities for establishing interventions to achieve HCV microelimination.

Because people who inject drugs (PWID) are vulnerable to incarceration due to social barriers and criminalization of drug use, using the opportunity to provide HCV treatment as prevention in the prisons is an important approach for preventing ongoing transmission in prisons or after returning to the communities. Recent modeling studies suggest that prison-based interventions such as HCV “test-and-treat” approach with scale-up of direct-acting antivirals (DAAs) in prison combined with postrelease linkage to community public health services would facilitate microelimination among PWID.

Injection drug use remains a continuing risk for HCV transmission in Thailand. Long duration of prison sentences exposes the prisoners to HCV acquisition risks.
limited data on HCV prevalence and treatment outcomes with DAAs in prisons in Thailand. In addition, DAA treatment outcomes among prisoners in the Asia-Pacific region are limited. Most of the data are from high-income settings reporting very high sustained virologic response (SVR) rates for prisoners treated with DAA therapy. This study evaluated SVRs among prisoners with HCV receiving DAA treatment in a central male prison in Thailand.

MATERIALS AND METHODS

Study Population
Prisoners from 2 sectors of a central male prison (Klong Prem Central Prison) in Thailand were recruited from March 2018 to September 2019. During the study period, universal screening for HCV and HIV was implemented. Klong Prem Central Prison is a maximum-security central prison in Thailand, and it has 9 separate sectors that house more than 6000 male prisoners. Two sectors were chosen by the prison authorities to participate in the study because they are geographically close to the Central Correctional Hospital where the study procedures and treatment were provided. These 2 sectors were composed of nearly 2000 male prisoners. Most of the prisoners in these 2 sectors were drug offenders. Universal HIV and HCV screening and posttest counseling were offered to all prisoners using an opt-in approach with written informed consents.

A total of 1028 prisoners participated in the evaluation and testing of blood-borne viral (BBV) infections conducted by prison health care workers. The prevalence of HCV and other BBV infections such as HIV, hepatitis B virus (HBV), and syphilis infections was previously reported. Prisoners with positive HCV RNA were then linked to the prison health care center (Central Correctional Hospital) for 400/100 mg of sofosbuvir/velpatasvir under the routine prison standard of care, regardless of their HCV genotypes and duration of prison sentences. All screening/evaluation processes and treatment procedures were conducted by prison health care workers.

Study Outcomes and Assessments
The primary objective was to investigate the effectiveness of HCV universal test-and-treat approach by evaluating SVR rates at 12 weeks after completing a course of DAA treatment. Demographic and clinical characteristics were collected before and after HCV treatment (a 3-month window period). Pretreatment and posttreatment HCV RNA and liver fibrosis markers were also collected. HCV RNA was evaluated using RealTime PCR test (m2000 system, Abbott Molecular, Inc., Des Plaines, IL). HCV genotypes were determined by Abbott RealTime HCV Genotype assay. The AST to platelet ratio index (APRI) score was calculated using the Wai formula: (AST in IU/L)/(AST upper limit of normal in IU/L)/(platelets in 10⁹/L) × 100.

HCV Treatment in Prison Health Center (Central Correctional Hospital)
Counseling pertaining to the transmission of HCV and other blood-borne infections was provided by health care workers to all participants after testing, regardless of their test results. DAA therapy was provided as directly observed therapy by prison health care workers (1 general practitioner and 2 nurses) who are not specialized in hepatology or infectious diseases in the prison hospitals. DAA therapy was provided according to the Thailand practice guideline for HCV management. Training for HCV treatment and care including drug–drug interaction management was obtained. Owing to limitation of Internet access inside the prison and Correctional Hospital, telemedicine among physician and specialists were routinely conducted after the physician’s working hour. For prisoners with HIV coinfection, ART regimen was also switched from efavirenz or nevirapine to rilpivirine for 1–3 months before HCV therapy to avoid potential drug–drug interactions with DAA.

Statistical Analysis
Demographic and clinical characteristics were presented as frequencies (percentages) or median [interquartile range (IQR)]. Genotype distribution was presented for all prisoners, stratified by injection drug use status. Pretreatment and posttreatment liver biomarkers (ALT and APRI) were compared using the Wilcoxon test. The treatment outcomes were reported using intention-to-treat analysis, which included all prisoners who started DAA treatment, and per-protocol analysis, which included only prisoners with an available posttreatment SVR. All analyses were conducted using Stata 16.1 (StataCorp, College Station, TX), and the graphs were generated using GraphPad Prism 8.0 (GraphPad Software, Inc., CA).

Ethical Considerations
All the participants provided informed consent to participate in the study. The study was approved by the Department of Corrections, Ministry of Justice, Thailand, and by the ethics committee of the Faculty of Medicine, Chulalongkorn University.

RESULTS
Of 1028 male prisoners who agreed to participate in the screening, 61 (6%) had positive HCV antibodies. Of them, 43 (71%) prisoners had detectable HCV RNA. All prisoners with positive HCV RNA received treatment, regardless of their prison sentence duration, drug use status, or fibrosis stage. Twenty-five prisoners with HCV infection were referred from other sectors (Fig. 1A).

A total of 68 prisoners received DAA treatment. Baseline characteristics of 68 prisoners with positive HCV RNA are summarized in Table 1. Overall, the median age and median duration of prison sentences were 44 years (IQR, 41–53) and 25 (IQR, 19–33) years, respectively. The median time served in the prison was 5.9 (IQR, 6.7–8.9) years. Sixty percentage of the participants had a history of previous incarceration, and 72% of the participants reported previous
injection drug use, of which 35.3% had reported sharing syringes for drug use. There were 14 prisoners (20.1%) who identified themselves as men who have sex with men. The median pretreatment HCV RNA was 7.1 (IQR, 6.3–8.4) log_{10} IU/mL. The median pretreatment ALT and APRI score were 56 (IQR, 30–91) IU/mL and 0.52 (0.27–0.87), respectively. Five prisoners (7.5%) met cirrhosis definition by APRI >1.5, none of them experienced decompensated cirrhosis. Twenty-five percentage of the participants were coinfected with HIV, and 6% was coinfected with HBV. The distribution of HCV genotype (GT) was as follows: 20 (29.4%) had GT-1a, 3 (4.4%) had GT-1b, 22 (32.3%) had GT-3a, 3 (4.4%) had GT-3b, and 7 (10.3%) had GT-6. The genotypes for 13 (19.1%) participants were unknown or could not be determined from genotyping (Fig. 1B).

Among 68 prisoners who received DAAAs, 67 completed treatments. SVR data were not available for 4 prisoners who were unexpectedly released from prison but completed the 12-week treatment course of DAAAs. One prisoner was transferred to a psychiatric hospital without completing the treatment course. Five prisoners did not have posttreatment HCV RNA data; 1 had HCV genotype (GT)-1, 3 had GT-3, and the genotype of 1 individual was unknown.

Data from 63 prisoners were included in the per-protocol analysis; 2 treatment failures were observed. HCV treatment outcomes using per-protocol analysis (N = 63) were as follows: overall (96.8%, 61/63), GT-1 (95.5%, 21/22), GT-3 (100%, 22/22), GT-6 (85.7%, 6/7), and unknown GT (100%, 12/12). The treatment outcomes using intention-to-treat analysis (N = 68) were as follows: overall (89.7%, 61/68), GT-1 (91.3%, 21/23), GT-3 (84.6%, 22/26), GT-6 (85.7%, 6/7), and unknown GT (92.3%, 12/13) (Fig. 1E).

No serious adverse events or laboratory abnormalities were reported during the treatment. Two prisoners (3%) reported fatigue. Of the 2 prisoners with treatment failure, 1 had GT-1b and the other had GT-6. None of them had advanced liver disease or were coinfected with HIV and HBV. The median posttreatment ALT was reduced to 17 IU/mL (IQR, 11–25), with a median difference of −35 IU/mL (95% CI: −24 to −49, P < 0.001) (Fig. 1C). A reduction in the median APRI score was also seen [0.23 (IQR, 0.17–0.31)] with a median difference of −0.21 (95% CI: −0.13 to −0.36, P < 0.001) (Fig. 1D).

**DISCUSSION**

This is the first report to present the DAA outcomes among prisoners using universal test-and-treat approach led by prison health care workers in Thailand. Overall, DAA was
highly effective (97% SVR, PP analysis) and safe for prisoners with chronic HCV infection. Universal screening approach and linkage to prison health care center for DAA treatment can provide a model for other prison settings to facilitate HCV microelimination in the country, where the burden of injection drug use is still high.

The prevalence of HCV in this study was low (6%), probably due to its low proportion of prisoners with injection drug use (7%) from the 2 prison sectors. However, the genotype distribution showed that most of the prisoners with HCV infection had GT-3a (32%), followed by GT-1a (29%). This is consistent with the genotype distribution among PWID of the general population in Thailand, where GT-1 and GT-3 were the most prevalent types.12 The overall SVR was 97% (PP analysis) among those who received DAA, and SVR rate was high across all HCV genotypes. The overall SVR rate according to intention-to-treat (ITT) analysis was 90%. Missing SVR data in the ITT analysis were mainly due to the release of prisoners after treatment completion.

Previous models have also shown that the successful treatment was achievable by using either nurse-led programs or linkage to prison clinic for HCV treatment.8,13 Recent development of DAAs have further provided more effective HCV treatment options than previous interferon-based therapy in the prison settings.14 The use of pangenotypic or shorter duration of DAA therapy has also been shown to be feasible and effective for HCV-positive prisoners.8,15,16 However, there is a concern for reinfection among those who have been cured of the infection successfully. Prisoners with long sentences have increased risk for reinfection because there are potential exposures to new comers who may have HCV infection and have opted out for HCV screening. In this study, the median duration of prison sentence was 25 years. Along with HCV “test and treat” for all prisoners and newcomers, providing health education including risks and access to harm reduction services are critical for preventing HCV reinfection after HCV cure in these settings. Moreover, postrelease linkage to public health services in the community should also be provided to facilitate HCV elimination among this marginalized and vulnerable population.

This study has several limitations to be acknowledged. First, opt out screening approach was adopted (nearly 50% refused); therefore, the prevalence of BBV infections, including HCV, was unknown in those who did not consent for screening. The high refusal rate of testing could be due to the fear of stigmatization and discrimination and due to the concerns over disclosure of their status to staff or other fellow prisoners.17,18 Second, we were unable to evaluate for NS5A resistance–associated substitution for 2 prisoners who had treatment failure although the treatment adherence was reported as optimal. In addition, further work in investigating HCV reinfection is needed. The care cascade of screening and treatment procedures led by prison health care workers with minimal specialist involvement seems highly feasible. However, more work needs to be conducted to facilitate HCV microelimination in the country. For example, harm reduction services such as needle syringe exchange programs and opiate substitution therapy together with improved public health services, including wider treatment accessibility for PWID in the community, are critical for this marginalized population.

In conclusion, HCV treatment using DAA through a universal test-and-treat approach led by prison health care workers is highly effective and well tolerated among prisoners, and such model can potentially help to facilitate HCV microelimination in Thailand.

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