Impact of COVID19 on Global Elimination of Viral Hepatitis: The US Perspective

Moderated By: John W. Ward, MD
Webinar Moderator

John Ward, MD

• Director, Coalition for Global Hepatitis Elimination
• Task Force for Global Health
• Rollins School of Public Health
• Emory University, Atlanta GA, USA
## Webinar Agenda

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Webinar Q&A

• Submit your questions anytime during the webinar in the Q&A box at the top or bottom of your screen.

• Questions will be answered at the end of the presentations.
Webinar Presenter

David L. Thomas, MD, MPH

• Director, Division of Infectious Diseases
• Professor of Medicine
• Johns Hopkins Medicine
Webinar Presenter

Don C Des Jarlais, PhD

- Professor of Epidemiology
- New York University School of Global Public Health
- CDUHR - Associate Director, Infectious Disease Epidemiology and Theory Core
Webinar Presenter

Natasha Martin, DPhil

• Associate Professor in the Department of Medicine, Division of Infectious Diseases and Global Public Health – University of California, San Diego

• Co-Director of the Biostatistics and Modeling Core of the University of California San Diego Center for AIDS Research (UCSD CFAR)
AASLD’s COVID-19 Clinical Oversight Subcommittee

- Co-chair, Oren K. Fix, MD, MSc, FAASLD, Swedish Medical Center (Washington)
- Co-chair, Elizabeth C. Verna, MD, MS, Columbia University (New York)
- Kimberly Brown, MD, Henry Ford Health System (Michigan)
- Jaime Chu, MD, Icahn School of Medicine at Mount Sinai (New York)
- Bilal Hameed, MD, University of California (California)
- Laura M. Kulik, MD, Northwestern Medical Faculty Foundation (Illinois)
- Ryan M. Kwok, MD, Uniformed Services University (Maryland)
- Brendan M. McGuire, MD, University of Alabama (Alabama)
- Jennifer C. Price, MD, PhD, University of California, San Francisco (California)
- Daniel S. Pratt, MD, FAASLD, Massachusetts General Hospital (Massachusetts)
- Nancy S. Reau, MD, Rush University (Illinois)
- Mark W. Russo, MD, MPH, FAASLD, Carolinas Medical Center (North Carolina)
- Michael Schilsky, MD, FAASLD, Yale University (Connecticut)
- Norah Terrault, MD, MPH, FAASLD, Keck Medicine of USC (California)
- Andrew Reynolds, (Patient Advocate)
- Raymond Chung, Massachusetts General Hospital (Massachusetts) (ex-officio)
- K. Rajender Reddy, University of Pennsylvania Medical Center (Pennsylvania) (ex-officio)
"Impact of COVID-19 on Global Elimination of Viral Hepatitis: The US Perspective“

Introduction

John W Ward, MD

jward@taskforce.org
I have no financial conflicts of interest to disclose

• John W Ward, MD
Impact of COVID-19 Response

- Vaccination
- Testing and treatment
- Syringe Service Programs
Declines in Child Vaccination Coverage during the COVID-19 Pandemic - United States May 2020

- Vaccination coverage declined in all milestone age cohorts
- Declines in up-to-date status for all vaccines to < 50%
  - Michigan 49.7%
  - New York City: 63%
  - Washington, D.C: 44.9%
  - Texas: 48%
  - Pennsylvania: 48%
  - Montana: 47%
  - Maryland: 42%

- Globally, 85% of countries report declines in vaccination
  - Potential 5.3M new chronic HBV infections
  - One million future HBV-related deaths

Bramer CA, MMWR 2020 [https://www.cdc.gov/mmwr/volumes/69/wr/mm6920e1.htm](https://www.cdc.gov/mmwr/volumes/69/wr/mm6920e1.htm)
Meg Doherty, oral remarks, WHO webinar, World Hepatitis Day
Global Assessment of the Impact of the COVID-19 Response on Hepatitis Prevention and Care Services

- Global Survey
  - Assess changes in HepB vaccination, HBV and HCV testing and treatment
  - From the COVID-19 response, identify opportunities for improving hepatitis prevention and care
- Methods
  - Developed by CGHE staff with input from CHAI, clinicians, civil society and WHO staff
  - Released on August 12, 2020 and opened till October 30, 2020.
  - Distributed by
    - AASLD
    - Hepatitis ECHO network USA
    - Hepatitis ECHO network Africa
    - Canadian Association for the study of the Liver (CASL)
    - EASL
    - CHAI

Please complete the survey at https://app.smartsheet.com/b/form/d487cee5adee40df8e5527e5a146469c
57 respondents were physicians or nurses
Infection Control Procedures for Hepatitis Care During the Covid-19 Response

N=65

- Staff Masks: 54
- Cleaning: 38
- Patient Masks: 36
- Staff Gowns or Gloves: 44
- Spacing: 33
- Patient Screening: 33
- Patient Screening via Phone: 21

Frequency
Declines in Hepatitis C screening (N=55)

Declines in Hepatitis C treatment (N=48)

N = Among respondents who indicated baseline HCV screening and treatment volumes
Changes in Hepatitis Clinical Services to Decrease COVID-19 Exposures

- Deferred laboratory testing: 39 (67%)
- Deferred imaging: 44 (79%)
- Increase pill count per prescription: 38 (66%)
Among respondents who indicated baseline OST volumes.
Potential Benefits to Hepatitis Prevention, Care and Treatment
Medical impact of COVID-19 on persons living with liver disease

David L Thomas, MD
Johns Hopkins Medicine
Medical impact of COVID-19 on persons living with liver disease

David L Thomas, MD
Johns Hopkins Medicine

Scientific advisory and/or data safety monitoring for Merck & Co and Excision Bio Therapeutics.
Medical impact of COVID-19 in persons living with liver disease

• Transaminitis is common in hospitalized COVID-19
• Impact of COVID-19 most severe in decompensated cirrhosis
• Special challenge for liver transplant patients
• Possible management implications
• Pathophysiology unclear
Liver related blood tests abnormalities are common in those hospitalized with COVID-19

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n = 1,827)</th>
<th>Nonsevere COVID-19 (n = 1,175)</th>
<th>Severe COVID-19 (n = 652)</th>
<th>PValue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), years</td>
<td>64.6 (18.2)</td>
<td>63.4 (18.5)</td>
<td>66.7 (17.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>969 (53.0)</td>
<td>574 (48.9)</td>
<td>395 (60.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI, mean (SD)</td>
<td>29.8 (7.8)</td>
<td>29.2 (7.3)</td>
<td>30.7 (8.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DM, n (%)</td>
<td>712 (39.0)</td>
<td>412 (35.1)</td>
<td>300 (46.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Obesity, n (%)</td>
<td>748 (42.5%)</td>
<td>455 (40.4%)</td>
<td>293 (46.1%)</td>
<td>0.019</td>
</tr>
<tr>
<td>AST, median (range), U/L</td>
<td>42 (8-3,054)</td>
<td>38 (8-1,399)</td>
<td>51 (12.3,054)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AST abnormal (&gt;33 U/L)</td>
<td>1,158 (66.9%)</td>
<td>667 (60.7%)</td>
<td>491 (77.8%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ALT, median (IQR), U/L</td>
<td>29 (5-1,831)</td>
<td>28 (5-1,831)</td>
<td>31 (6-1,441)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ALT, abnormal (&gt;34 U/L)</td>
<td>726 (41.6%)</td>
<td>440 (39.7%)</td>
<td>286 (44.8%)</td>
<td>0.035</td>
</tr>
<tr>
<td>ALP, median (IQR), U/L</td>
<td>76 (20-919)</td>
<td>76 (20-903)</td>
<td>76 (28-919)</td>
<td>0.79</td>
</tr>
<tr>
<td>ALP abnormal (&gt;122 U/L)</td>
<td>237 (13.5%)</td>
<td>140 (12.6%)</td>
<td>97 (15.2%)</td>
<td>0.13</td>
</tr>
<tr>
<td>TBIL, median (IQR), mg/dL</td>
<td>0.5 (0.1-8.9)</td>
<td>0.4 (0.1-8.0)</td>
<td>0.5 (0.1-8.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TBIL, abnormal (&gt;1.2 mg/dL)</td>
<td>4 (4.3%)</td>
<td>33 (3.0%)</td>
<td>41 (6.5%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Albumin, median (IQR) mg/dl</td>
<td>3.5 (1.2-5.4)</td>
<td>3.5 (1.3-5.4)</td>
<td>3.3 (1.2-4.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Albumin, abnormal (&lt;3.5 mg/dL)</td>
<td>990 (56.7%)</td>
<td>584 (52.6%)</td>
<td>406 (63.8%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
SARS-CoV-2 infection increases liver enzymes compared to pre-admission

Hundt Hepatol 2020, Fu Hepatol 2020, Lim Hepatol 2020
SARS-CoV-2 infection increases liver enzymes compared to others hospitalized

<table>
<thead>
<tr>
<th></th>
<th>Overall (n = 3,381)</th>
<th>Positive (n = 2,273)</th>
<th>Negative (n = 1,108)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial ALT, median (IQR)</strong></td>
<td>26 (17, 46)</td>
<td>28 (18, 49)</td>
<td>21 (14, 37)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Initial ALT (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;ULN</td>
<td>736 (22)</td>
<td>537 (24)</td>
<td>199 (18)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;2×ULN</td>
<td>209 (6.2)</td>
<td>134 (5.9)</td>
<td>75 (6.8)</td>
<td>0.4</td>
</tr>
<tr>
<td>&gt;5×ULN</td>
<td>58 (1.7)</td>
<td>29 (1.3)</td>
<td>29 (2.6)</td>
<td>0.007</td>
</tr>
<tr>
<td><strong>Peak ALT, median (IQR)</strong></td>
<td>37 (21, 76)</td>
<td>45 (25, 89)</td>
<td>25 (17, 52)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Peak ALT (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALT peak &gt;ULN</td>
<td>1,303 (39)</td>
<td>1,015 (45)</td>
<td>288 (26)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ALT peak &gt;2×ULN</td>
<td>624 (18)</td>
<td>489 (21)</td>
<td>135 (12)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ALT peak &gt;5×ULN</td>
<td>200 (5.9)</td>
<td>145 (6.4)</td>
<td>55 (5.0)</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Lim+Verna Hepatol 2020
5x increased ALT associated with cytokine storm

<table>
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<tr>
<th>Covariate</th>
<th>Univariate Analysis</th>
<th>Multivariate Analysis</th>
</tr>
</thead>
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<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Age</td>
<td>0.99</td>
<td>0.97, 1.00</td>
</tr>
<tr>
<td>Female sex</td>
<td>0.48</td>
<td>0.30, 0.74</td>
</tr>
<tr>
<td>BMI &gt;35</td>
<td>0.75</td>
<td>0.47, 1.23</td>
</tr>
<tr>
<td>Liver disease</td>
<td>1.33</td>
<td>0.54, 2.81</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.87</td>
<td>0.58, 1.30</td>
</tr>
<tr>
<td>HTN</td>
<td>0.95</td>
<td>0.64, 1.42</td>
</tr>
<tr>
<td>Peak IL-6</td>
<td>2.16</td>
<td>1.77, 2.69</td>
</tr>
<tr>
<td>Peak ferritin</td>
<td>3.01</td>
<td>2.47, 3.72</td>
</tr>
<tr>
<td>Peak D-Dimer</td>
<td>1.57</td>
<td>1.37, 1.82</td>
</tr>
<tr>
<td>Peak CRP</td>
<td>2.55</td>
<td>1.76, 3.94</td>
</tr>
<tr>
<td>Peak procalcitonin</td>
<td>1.48</td>
<td>1.35, 1.63</td>
</tr>
<tr>
<td>Peak CK</td>
<td>1.52</td>
<td>1.33, 1.73</td>
</tr>
<tr>
<td>Peak HS troponin</td>
<td>1.53</td>
<td>1.35, 1.75</td>
</tr>
</tbody>
</table>
The outcome SARS-CoV-2 is worse with cirrhosis

International registry study

29 countries
130 centres
over 105 days

1365 patients included
745 chronic liver disease
- 359 without cirrhosis
- 386 with cirrhosis
620 without liver disease

Marjot J Hepatol In Press 2020 (with permission); EASL 2020
COVID-19 is challenging for liver transplant recipients

- 112 LT recipients with COVID-19
- 22.3% died; 72.3% hospitalized
- ALT: 2-5X 22.2%; >5X 12.3%
- ALT elevation assoc with younger, Hispanic, metabolic syndrome, vaso-pressors, antibx
There could be therapeutic implications

*Clinical Best Practice Advice for Hepatology and Liver Transplant Providers During the COVID-19 Pandemic: AASLD Expert Panel Consensus Statement*


*Care of patients with liver disease during the COVID-19 pandemic: EASL-ESCMID position paper*

Tobias Boettler, Philip N. Newsome, Mario U. Mondelli, Mojca Maticic, Elisa Cordero, Markus Cornberg, Thomas Berg
Hepatic pathophysiology of COVID-19 is multifactorial

- Little evidence of SARS-CoV-2 in hepatocytes
- Cirrhosis diminishes anti-microbial immunity
- Cytokine source and target
- Coagulopathy/endothelial damage
- ARDS alone sufficient
Medical impact of COVID-19 in persons living with liver disease

- Transaminitis is common in hospitalized COVID-19
- Impact of COVID-19 most severe in decompensated cirrhosis
- Special challenge for liver transplant patients
- Possible management implications
- Pathophysiology unclear
No Conflicts of Interest
HISTORICAL RECONSTRUCTION OF HIV-1 SEROPREVALENCE AMONG ACTIVE PERSONS WHO INJECT DRUGS IN NEW YORK CITY

- Rapid transmission, estimated Incidence 13/100 PY
- Stabilization, risk reduction & loss of HIV seropositives to death & disability, estimated incidence 4-6/100 PY
- Expansion of syringe exchange programs, continued loss of seropositives, estimated incidence 1/100 PY
- Increasing provision of ART, reduction in AIDS deaths, estimated incidence >0.5/100 PY, most transmission sexual
COMBINED PREVENTION

- Combined prevention for PWID, including needle/syringe exchange programs, medically assisted treatment and antiretroviral therapy can significantly reduce overall HIV prevalence and new HIV infections among PWID.

- Several locations have documented reductions in HIV incidence among PWID as a result of implementing combined prevention, including Vancouver, France, Australia, New York City and the United Kingdom.
CURRENT SITUATION IN NEW YORK CITY

- HIV prevalence: 7% among PWID
- HIV incidence: 0.04/100 person-years at risk
- HCV prevalence stable at approximately 70%, down from 90%
- HCV incidence: 50% HCV seropositive by 5 years of injecting
HIV OUTBREAKS AMONG PWID

- Scott County, US; Athens, Greece; Dublin, Ireland; Luxembourg; Glasgow, Scotland; Saskatchewan, Canada; Tel Aviv, Israel

- **Precipitating Factors**: Community economic problems; Reductions in HIV prevention services; New drugs to be injected; Homelessness PWID as a highly vulnerable subgroup

- HCV outbreaks as warning
SARS-COV-2/COVID-19

1. Community economic stress
2. Reduction in HIV and HCV prevention services
3. Disruption of drug markets, with new drugs, especially novel psychoactive substances
4. Increased homelessness among PWID
SARS-COV-2/COVID-19 AND PWID

- Replicates the conditions for community outbreaks of HIV
- Many PWID have “underlying conditions” for severe disease
US SYRINGE SERVICE PROGRAMS

- 300 – 400 in US
- Provided HIV and HCV as standard service
- Referrals to evaluation and treatment

- Glick, et al., Des Jarlais. AIDS and Behavior 2020
- COVID-19 lockdowns in spring 2020
- Almost all ceased HIV and HCV testing-- social distancing, limited interaction time
ORAL FLUID HCV TESTING

- Approved in Europe but not in the US
- Recent study in Estonia comparing HCV oral fluid testing to ELISA (reference)
- Sensitivity = 100%
- Specificity = 56%
SUMMARY

- SARS-CoV-2/COVID-19 replicates conditions that facilitated HIV outbreaks among PWID
- Need to detect and limit HCV and HIV outbreaks
- Flying blind: greatly reduced HIV and HCV testing in the community
- Possibility of oral HCV testing?
HCV elimination in the COVID-19 era in the U.S.: Data and Modeling

Natasha Martin, DPhil
Associate Professor
Division of Infectious Diseases and Global Public Health, University of California San Diego
Disclosures

I have received unrestricted research grants from Gilead and Merck unrelated to the work presented.
HCV elimination projects in the U.S. - March 2020
Important program gaps remain


Hepvu.org
HCV elimination program disruption in Louisiana

Number of Persons Who Started Treatment for HCV Through Medicaid/Corrections by Year/Month Treatment First Started - January 2019 to present

No. of Persons Who Started HCV Treatment

Year/Month HCV Treatment First Started

Alexander Billioux. Impact of the COVID-19 Epidemic on Viral Hepatitis Webinar 2020
Global impact of a 1-year delay in HCV programming (relative to no delay)

- New diagnoses, 2020–2030: -906,000
- Treatment starts, 2020–2030: -746,000
- Incident HCV, 2020–2030: +121,000
- Liver-related deaths, 2020–2030: +72,300
- Incident HCC, 2020–2030: +44,800
- Viraemic infections, 2030: +623,000

*no region achieving target
*only HIC achieving target

Disproportionate impact on liver related deaths in the U.S.

Even 1 year of harm reduction disruption can stall progress towards HCV incidence elimination target

HCV incidence (per 100py) among PWID in Tijuana, Mexico

- No scale-up
- HCV treat + harm reduction **disrupted**
- HCV treat + harm reduction **sustained**

Marquez and Martin NK et al. Int J Drug Policy 2020
Drug overdoses and overdose mortality increasing during COVID-19 era

ODMAP weekly suspected overdose submissions before and during COVID in the U.S.

Provisional U.S. drug overdose deaths (12 month ending)
Key challenges

- Drops in HCV testing and treatment initiations
- Disruption in syringe service programs
- Continued gaps in surveillance
- Anticipated budget constraints
- Ongoing syndemics of opioid misuse, overdose, HCV, HIV
Opportunities

- **Innovation and decentralization** of services:
  - Telemedicine
  - Mobile outreach
  - Home testing

- **Integration** of viral hepatitis and COVID-19 services

- Enhanced public health **surveillance** infrastructure
Acknowledgements

- **UC San Diego**: Steffanie Strathdee, Lara Marquez, Annick Borquez, Richard Garfein, Patricia Zuniga
- **Johns Hopkins University**: Javier Cepeda
- **National Institute of Psychiatry Mexico**: Clara Fleiz
- **Universidad Nacional Autonoma de Mexico**: Claudia Rafful
- **San Diego State University**: Susan Keine, Stephanie Brodine
- **Funders**: NIDA, NIAID
Panel Discussion

Please submit your questions to the Q&A Chat now.