Hepatitis C treatment outcomes among people who inject drugs co-infected with HIV in Manipur, India

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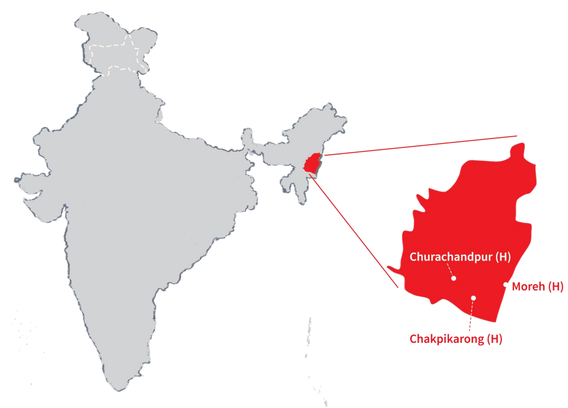


Figure 1. MSF operates three clinics in Manipur, a northeastern state of India

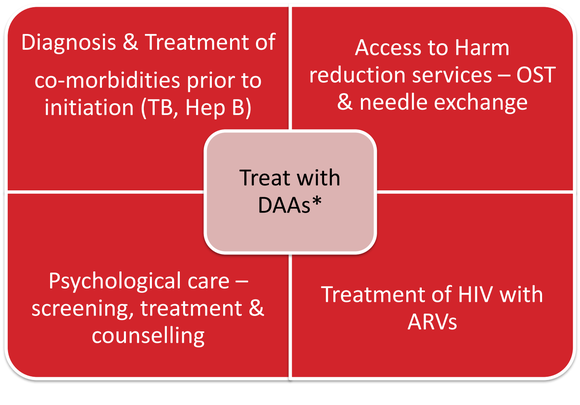
Introduction

- Up to 90% of People Living with HIV (PLHIV) who use drugs could be infected with Hepatitis C (HCV)(1, 2).
- Continued drug abuse alters HIV/HCV prognosis with higher mortality risk (2).
- People who inject drugs (PWID) have limited access to HCV care due to concerns over adherence, increased side effects and the risk of reinfection (3).
- Treatment outcome in PWID is infrequently reported from limited resource contexts.
- From 2014, MSF provides HCV care to co-infected PLHIV through three clinics in Manipur
- The context, has limited resources and is ridden with low-intensity conflict (Figure 1).
- Manipur has 12.1% prevalence of HIV among PWID (2017) (1). Small studies report up to 95% HCV prevalence in PWID and 29% in PLHIV (1).
- MSF adopted an integrated model of HCV care in Manipur (Figure 2).
- This study explored HCV treatment outcomes among active drug users in a HIV/HCV co-infected population

Methods

- *Study design*: Retrospective Cohort
- *Study cohort*: HIV/HCV co-infected patients treated for HCV in three MSF clinics of Manipur
- *Time period*: Oct 2014 to Oct 2019
- *Variables:* Demographic, biological, clinical characteristics, and treatment outcome
- *Analysis:* Risk of negative treatment outcomes (treatment failure, lost to follow up and death) in patients actively using drugs, tested using step-wise logistic regression
- *Ethics:* Cleared by Ethics Review Boards of MSF, Genève and Regional Institute of Medical Sciences, Imphal, Manipur

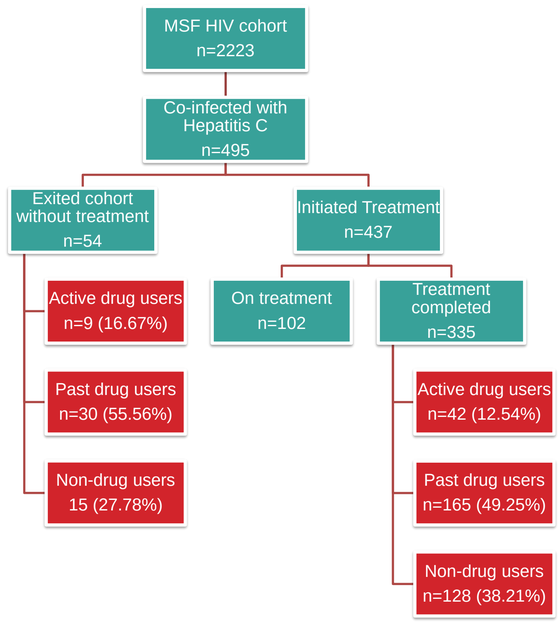
Figure 2. MSF – Integrated model of care for PLHIV co – infected with hepatitis C



DAA – Directly Acting Antivirals

> **"In an integrated care program, two-thirds of people who inject drugs, co-infected with HIV cured hepatitis C infection"**

Figure 3. Flow of MSF's HIV/HCV co-infected cohort in Manipur; Oct 2014 – Oct 2019

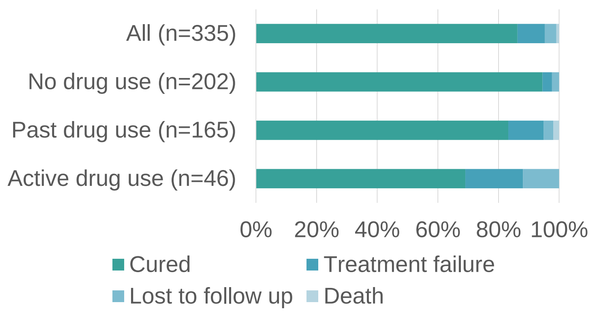


Proportion of active drug users was similar between groups completing treatment and exiting cohort without treatment

Results

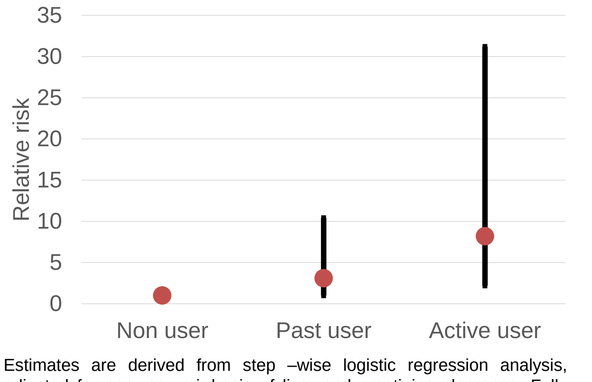
- 22.2% (495/2223) of HIV cohort had positive HCV viral load (Figure 3)
- 12.54% (42/335) and 49.2% (247/335) patients reported active and past use of drugs respectively during HCV treatment
- In a bivarate analysis, younger age, active drug use, higher creatinine clearance and cirrhosis of liver were associated with negative treatment outcomes (Table 1).
- In a fully adjusted model of step wise logistic regression, active drug use younger and presence of were associated with negative outcomes. (Table 2).

Figure 4. Distribution of drug use history and treatment outcome



Proportion of treatment failure and lost to follow up were significantly higher in active drug use group than that of past drug use (chi^2 = 12.2; p=0.002) and no drug use (Chi^2 = 6.1; p=0.01) groups. The three deaths were not related to HIV or HCV infections.

Figure 5. Drug use history and relative risk of Hepatitis C treatment failure



Estimates are derived from step –wise logistic regression analysis, adjusted for age, sex, cirrhosis of liver and creatinine clearance. Fully adjusted model was significant (p=0.001) with R^2 = 0.15.

Table 1. Demographic and Clinical Characteristics of patients and association with treatment outcome

Characteristics	Failure (%) [1]	Success (%)	RR of failure[2] (95%CI)
Patients with outcome (n=335)	46 (13.73)	289 (86.27)	NA
Age in years			
Mean (95 % CI)	35.0 (1.39)	40.06 (0.46)	0.92 (0.89 – 0.96) [4]
Sex (n=335)			
Male (n=249, 74.33%)	39 (84.78)	210 (72.66)	1.0
Female (n=86, 25.67%)	7 (15.22)	79 (27.34)	0.47 (0.20 – 1.11)
Drug use status			
Non user (n=128, 38.21%)	7 (15.22)	121 (41.87)	1.0
Active user (n=42, 12.54%)	13 (28.26)	29 (10.03)	7.74 (2.83 – 21.15) [5]
Past user (n=165, 49.25)	26 (56.52)	139 (48.10)	3.23 (1.35 – 7.71)
Imprisonment history			
No (n= 289, 86.27%)	41 (89.13)	248 (85.81)	1
Yes (n= 46, 13.73%)	5 (10.87)	41 (14.19)	0.72 (0.27 – 1.9)
BMI mean (95% CI) Kg/m²	20.89 (0.32)	20.91(0.16)	0.99 (0.88 – 1.11)
HCV Genotype distribution			
Indeterminate (n= 3, 0.95%)	1 (2.17)	2 (0.74)	1.0
1 (n= 85, 26.81%)	12 (26.09)	73 (26.94)	0.32 (0.02 – 3.91)
3 (n= 113, 35.65%)	15 (32.61)	98 (36.16)	0.30 (0.02 – 3.58)
4 (n= 0)	0	0	0.36 (0.03 – 4.26)
6 (n= 116, 36.59%)	18 (39.13)	98 (36.16)	
HIV staging (n=329)			
1 (n= 231, 70.21%)	31 (68.89)	200 (70.42)	1.0
2 (n= 6, 1.82%)	0	6 (2.11)	NA
3 (n= 65, 19.76%)	12 (26.67)	53 (18.66)	1.46 (0.70 – 3.03)
4 (n= 25, 7.60%)	2 (4.44)	23 (8.10)	0.56 (0.12 – 2.49)
Cirrhosis of liver			
No (n= 192, 57.31%)	17 (36.96)	175 (60.55)	1.0
Yes (n= 34, 10.15%)	6 (13.04)	28 (9.69)	2.20 (0.80 – 6.07) [4]
Missing (n= 109, 32.54%)	23 (50.00)	86 (29.76)	2.75 (1.39 – 5.42)
Treated with interferons			
No[3] (n= 287, 85.67%)	43 (93.48)	244 (84.43)	1.0
Yes (n= 48, 14.33%)	3 (6.52)	45 (15.57)	0.37 (0.11 – 1.27)

1–Includes Lost to follow up and death; 2– Estimate of logistic regression; 3 – Treated with directly acting antiviral drugs. 4 – Significant difference between treatment failure and success groups. Men having sex with men and female sex workers were three and six respectively. One from each group failed treatment. Employment and marital status did not differ between treatment failure and success groups

Table 2. Factors associated with negative treatment outcome of hepatitis C infection (n=318)

Variable	Relative risk (95%CI)	p value
Active drug user (n=42)	8.2 (2.19–31.2)	0.002
Age (n=335)	0.94 (0.89– 0.98)	0.012
Presence of liver cirrhosis (n=34)	1.64 (1.13–2.36)	0.010
Past drug use (n=165)	3.16 (1.0 – 3.2)	0.058
Female Sex (n=165)	0.95 (0.28 – 3.2)	0.947
Creatinine clearance (n=335)	1.05 (0.99 – 1.01)	0.248

Estimates are derived from step –wise logistic regression analysis. Fully adjusted model was significant (p=0.001) with R^2 = 0.15. MSF clinic site, BMI, genotype distribution, viral load at initiation and treatment with interferons did not change the model.

> Active drug use, younger age and liver cirrhosis were independently associated with negative treatment outcomes. Access to integrated HCV care is essential for PWID to break HCV transmission in local populations.

Discussion

- MSF follows patient-centered model of HCV care addressing influencers of treatment outcome (Figure 2).
- In HIV/HCV co-infected patients, Non-drug users had highest probability of treatment success
- Active drug users had higher risk of negative outcome relative to non-drug users (Figure 4,5).
- Younger age and cirrhosis of liver were independently associated with risk of negative outcome
- Higher relative risk of negative outcome among active drug users could be partly attributed to higher probability of lost to follow up.
- A recent cohort from USA reported 94% treatment success in drug users (5), indicating possibility of comparable outcomes with non-drug users.
- As over two-thirds of active drug users cure HCV, access to integrated HCV care could break transmission cycle in local populations and contributes to micro-elimination of HCV (6)

Conclusion

- When integrated with care for HIV, treatment for co-morbidities, psychosocial support and link to harm reduction services, DAAs treatment cured HCV in over two-thirds of patients who injected drugs
- HIV/HCV co-infected patients actively using drugs had highest risk of negative outcomes relative to patients who previously used or who never used drugs
- Negative treatment outcome was associated with younger age and liver cirrhosis; characteristics not linked to active drug use.
- Providing integrated HCV care to people who inject drugs is essential to achieve micro-elimination of HCV in local populations

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