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Surge In Hepatitis C Incidence Associated with Syphilis Infection among Thai MSM

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BACKGROUND

- Sexual transmission of hepatitis C viral infections (HCV) has been reported among men who have sex with men (MSM) living with HIV from major cities of the world, although less frequently from the Asia-Pacific region.
- We investigated the incidence of HCV among HIV-positive MSM taking long-term antiretroviral therapy (ART) in Bangkok, Thailand.

METHODS

- A prospective cohort analysis was done among MSM with negative baseline anti-HCV antibody tests in a long-term follow-up Thai HIV-NAT 006 cohort from October 1996 to July 2018.
- HCV incidence among MSM was defined by two positive anti-HCV antibody tests and confirmed by a positive HCV RNA level.
- HCV genotyping was determined by nucleotide sequencing of the core and NS5B regions followed by phylogenetic analysis
- Recent syphilis infection was defined as a reactive RPR within 6 months of HCV seroconversion.
- Kaplan-Meier estimate methods were used for the probabilities of anti-HCV seroconversion among those with or without recent syphilis infections during the follow-up years.

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RESULTS

TABLE 1. Participants Characteristics

Characteristics	All MSM participants (n=464)	MSM with HCV incidence (n=29)	MSM without HCV (n=435)	P-value
Age, median IQR	38.8 (32.3-46.9)	36.7 (31.3-43.9)	38.9 (32.7-47.5)	0.18
CD4 cell count (cells/mm³), median IQR	303(180-466)	368 (227-535)	298 (175-460)	0.14
HIV-RNA level (log_{10} copies/mL), median IQR	4.60 (4.09-5.09)	4.99 (4.37-5.36)	4.59 (4.07-5.04)	**0.012**
HBsAg positive, n (%)	76/460 (16.52)	8/29 (27.59)	68/431(15.78)	0.12
Alcohol drinking, n (%)	21/393 (5.34)	0/27 (0.00)	21/366 (5.74)	0.38
Current smoking, n (%)	90/400 (22.50)	5/27 (18.52)	85/373 (22.79)	0.81
Follow-up years, median (IQR)	7.5 (5.7-12.5)	7.6 (6.2-8.7)	7.4 (5.7-12.7)	0.94
Number of anti-HCV tests, median (IQR)	2 (1-3)	2 (2-3)	2 (1-3)	0.75
Number of anti-HCV tests per year$, median (IQR)	0.5 (0.3- 0.7)	0.6 (0.3-0.7)	0.5 (0.3-0.7)	0.25
HCV genotype, n (%)		N=29		
1		23 (79.31)	N/A	
3		5 (17.24)	N/A	
4		1 (0.03)	N/A	
Syphilis infection at first anti-HCV test¶, n (%)	N=172	N=15	N=157	**<0.001**
No	139 (80.81)	7 (46.67)	132 (84.08)	
Yes	33 (19.19)	8 (53.33)	25 (15.92)	
Recent Syphilis infection at HCV diagnosis¶, n (%)		N=16		
No		3 (18.75)	N/A	
Yes		12(75.00)	N/A	
CD4 count at time of HCV diagnosis¶ median (IQR)		581 (506-782)		
HIV-RNA (log) at time of HCV diagnosis¶				
≤50 copies/mL		24 (82.76)		
>50 copies/mL		5 (17.24)		

$ number of HCV tests per year was calculated as the number of anti HCV tests divided by total of duration of follow-up from the baseline to latest test in years
¶ Recent syphilis acquisition, CD4 cell count, HIV-RNA level, syphilis infection at the time of HCV diagnosis were evaluated within +/- 6 months of HCV diagnosis

TABLE 2. Incidence of HCV infection among MSM stratified by calendar years of follow-up

	Number of events	Person year of follow-up	Incidence rate, per 100 PY (95%CI)
Total	29	2885.87	1.00 (0.70 to 1.45)
	Number of events		
Before 2007	3	314.79	0.95 (0.31 to 2.95)
2007-2014	4	1577.39	0.25 (0.10 to 0.68)
2014-2018	22	993.69	2.21 (1.46 to 3.36)
Before 2014	7	1892.18	0.37 (0.18 to 0.78)
2014-2018	22	993.69	2.21 (1.46 to 3.36)

- A total of 464 MSM with median (IQR) baseline age of 38 (32-46) years and median CD4 count of 303 (180-466) cells/mm3 were included in the study.
- Participants had been treated with ART for a median of 7.5 (5.7-12.5) years. Of 464 MSM, 29 incident cases were identified during 2885 person-years (PYS) of follow-up.
- **The crude incidence rate of HCV surged from 0.37 per 100 person-years of follow-up (PYS) before 2014 to 2.21 per 100 PYFU in 2014-2018.**
- At the time of HCV seroconversion, most participants (82%) had suppressed HIV viremia and the median CD4 count was 581 (479-792) cells/mm3.
- Of the HCV incident cases, 79.3% had genotype 1a and 27.6% had hepatitis B co-infection (defined by HBsAg positivity).
- In multivariate analysis, age < 35 years (HR, 3.31, 95% CI, 1.42-7.71, p=0.005) and recent syphilis infection (HR, 3.84, 95% CI, 1.78-8.26, p=0.001) were strongly associated with incident HCV among Thai MSM living with HIV.
- Among 29 incident cases, 3 participants reported injecting methamphetamine use from collected behavioral risk assessment questionnaire and only one case was spontaneously cured.

FIGURE. Proportion of MSM with HCV incidence without or without syphilis infection at first anti-HCV test

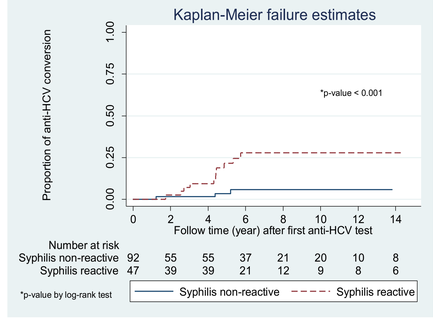


TABLE 3. Univariate and multivariate time-to-event analysis for HCV incidence cases among MSM participants

		Univariate			Multivariate		
	N	HR	95% CI	P	aHR	95% CI	P
Age at HCV diagnosis	464						
< 35		4.12	1.82-9.34	0.001	3.19	1.38 -7.36	**0.007**
≥ 35		Ref			Ref		
CD4 cell count (cells/mm³) (time update)	460						
< 200		5.19	1.22-22.12	0.026	3.23	0.74-14.09	0.118
≥ 200		Ref					
HBsAg positive	460						
No		Ref			Ref		
Yes		2.12	0.94-4.80	0.071	1.66	0.73-3.80	0.228
Recent syphilis infection at HCV diagnosis	464						
No/Not done		Ref			Ref		
Yes		5.13	2.44-10.80	<0.001	3.84	1.78-8.26	**<0.001**
Current smoking (time update)							
No		Ref					
Ever smoked		0.48	0.06-3.81	0.49			
HIV-RNA level (time update)	459						
≤ 50 copies/mL		Ref					
> 50 copies/mL		1.89	0.72-4.99	0.196			

CONCLUSION

- In a Bangkok cohort with MSM living with HIV attending chronic HIV care, we found a surge of HCV incidence in the recent years.
- In the era of effective direct acting agents (DAAs) and "Undetectable=Untransmissible", sexually transmitted diseases such as hepatitis C and syphilis infections among MSM living with HIV receiving chronic HIV care need to be routinely screened and treated effectively to prevent further transmission to both HIV-positive and HIV-negative partners.

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