

## Dettaglio abstract

**N. pgm:** OC 150

**Title:** Prevalence and outcome of Hepatitis Delta virus (HDV) infection among Persons Living with HIV (PLWH) in Italy: the Delta-Icna study

**Presentation type:** Oral Communication

### Session/Topic

Novel clinical and epidemiological aspects of viral hepatitis

**Authors:** M. Puoti<sup>1,2</sup>, R. Salpini<sup>3</sup>, A. Tavelli<sup>4</sup>, L. Piermatteo<sup>3</sup>, S. D'Anna<sup>3</sup>, S. Carrara<sup>5</sup>, V. Malagnino<sup>6</sup>, V. Mazzotta<sup>7</sup>, G. Brancaccio<sup>8</sup>, G.B. Gaeta<sup>9</sup>, G. Marchetti<sup>10,11</sup>, E. Rosselli Del Turco<sup>12,13</sup>, C.F. Perno<sup>14</sup>, V. Svicher<sup>3</sup>, A. d'Arminio Monforte<sup>4</sup> for Icna Foundation Study Group

**Affiliation:** 1University of Milano Bicocca, School of Medicine, Milan, Italy, 2ASST GOM Niguarda, Infectious Diseases, Italy, 3University of Rome Tor Vergata, Department of Experimental Medicine, Italy, 4Icna Foundation, Milano, Italy, 5INMI, Unity of Microbiology and Biobank, Roma, Italy, 6University of Rome Tor Vergata, Department of Medicine of Systems, Clinical Infectious Diseases, Rome, Italy, 7INMI, Clinical and Research Infectious Diseases Department, Rome, Italy, 8University of Padua, Department of Molecular Medicine, Padua, Italy, 9University L. Vanvitelli, Infectious Diseases Unit, Naples, Italy, 10ASST Santi Paolo e Carlo, Clinic of Infectious Diseases, Milano, Italy, 11University of Milano, Department of Health Sciences, Milano, Italy, 12Alma Mater Studiorum Bologna University, Department of Medical and Surgical Sciences, Bologna, Italy, 13IRCCS Azienda Ospedaliero Universitaria S. Orsola- Malpighi, Infectious Diseases Unit, Bologna, Italy, 14Bambino Gesù Pediatric Hospital, Rome, Italy

### Abstract

**Background:** The prevalence and outcome of Delta infection among PLWH in different geographical and behavioral settings is poorly studied. Further, HDV-RNA pos PLWH may undergo clinical progression faster than HIV neg patients. We studied the prevalence and outcome of HDV infection with and without HDV viremia in HBsAg pos PLWH in the ICONA cohort.

**Methods:** All HBsAg-pos PLWH with a stored plasma sample were included. Anti-HDV was detected by Liaison XL Murex Anti-HDV assay; in case of anti-HDV positivity, HDV-RNA was quantified by Robogene v.2 assay. We compared demographic and clinical data between different groups:

- 1- HBsAg-pos /anti-HDV neg vs. HBsAg-pos/anti-HDV pos
- 2- anti-HDV pos/HDV-RNA neg vs. anti-HDV pos/HDV-RNA pos.

Baseline was the date of the first HDV serology/virology test. The time to and predictors of Liver Related Hard Outcome (LRHO; decompensated cirrhosis, HCC, liver transplantation, liver-related death) according to HDV status were identified. Chi-squared test and Wilcoxon rank sum test were used to compare clinical and demographical variables between groups. Cox multivariable analyses were fitted to identify the risk of LRHO according to 4 groups of HBsAg pos PLWH: anti-HDV neg vs. Anti-HDV pos/HDV-RNA pos vs. Anti-HDV pos/HDV-RNA neg vs. Anti-HDV pos/HDV-RNA unknown.

**Results:** A total of 1,028 out of 18,285 PLWH (5.6%) displayed at least 1 HBsAg-pos test. Among these, 809 were screened for anti-HDV: 152 (18.8%) showed anti-HDV reactivity. HDV viremia was detected in 63/95 (68%) tested anti-HDV pos PLWH.

Anti-HDV pos were less frequently female (7,9% vs 18,1%), more frequently IDU (67,1 vs 15,8%), more frequently anti HCV pos (66 vs 16%), less frequently HCV-RNA pos (11 vs 15%) and more frequently showed FIB-4 >3,25 (25 vs 11%) than HBsAg pos/anti-HDV neg PLWH (Table 1).

HDV-RNA pos were more frequently Italian (97% vs 72%) and more frequently with a FIB4 >3,25 (34 vs 9.7%) compared with HDV-RNA neg (Table 2).

Over a median follow-up of 5.1 (2.0-9.9) years, a total of 37 LRHO occurred in 736 HBsAg pos patients with >=1 follow-up after first HDV-screening.

By Kaplan-Meier curves, the 5- years overall cumulative probability of LRHO was 4.2% (95%CI 2.8-6.3); 2.0% (1.0-3.9) for anti-HDV neg, 11.0% (4.1-27.6) for anti-HDV pos / HDV-RNA missing, 12.0% (4.0-32.8)

for anti-HDV pos / HDV-RNA neg and 14.8% (7.3-28.7) for anti-HDV pos / HDV-RNA pos (log-rank  $p < 0.01$ ). Anti-HDV pos/HDV-RNA pos PLWH showed an unadjusted 6.60 (95%CI 3.08-14.14) fold higher risk than anti-HDV neg HBsAg pos PLWH.

After controlling for baseline factors at time-fixed covariates, alcohol consumption, baseline CD4 count, anti-HCV status, this association was attenuated but the effect size was still remarkable: aHR = 4.08 (95%CI 1.69-9.86) (Table 3).

**Conclusions:** Even if HDV circulation among PLWH is not so extended, HDV screening is mandatory, as its presence is associated with severe liver outcomes, and new therapies are approaching.

This publication is supported by a grant from Gilead Sciences

Table 1: Demographic and clinical characteristics of HBsAg+ participants by anti HDV status

	HDV-negative	HDV-positive	p-value
<b>N (%)</b>	<b>657 (81.2)</b>	<b>152 (18.8)</b>	
Age, median (IQR)	39 (33-47)	37 (33-43)	0.025
Female, n (%)	119 (18.1)	12 (7.9)	0.002
HIV transmission group, n (%)			
MSM	244 (37.1)	20 (13.2)	<0.001
PWID	104 (15.8)	102 (67.1)	
HET	262 (39.9)	21 (13.8)	
Other/missing	42 (6.4)	9 (5.9)	
Italian (%)	500 (76.1)	137 (90.1)	<0.001
Alcohol use, n (%)			
Yes	144 (21.9)	23 (38.8)	0.944
No	230 (35.0)	36 (23.7)	
Unknown	283 (43.1)	93 (61.2)	
Months between inclusion in the cohort and anti HDV measurement, median (IQR)	0.92 (0-20.6)	0 (0-10.6)	0.001
Months follow up, median (IQR)	51.8 (16.5-107.0)	63.2 (19.2-140.6)	0.100
CD4 count, cells/μl, median (IQR) at inclusion in the cohort	367 (156-561)	389 (188-604)	0.309
CD4 count, cells/μl, median (IQR) at anti HDV measurement	368 (166-564)	371 (192-603)	0.540
FIB-4 > 3.25 at anti HDV measurement, n (%)	69 (11.0)	36 (25.2)	<0.001
Death for any cause, n (%)	59 (8.9)	30 (19.7)	<0.001
Liver related death, n (%)	11 (1.67)	16 (10.5)	<0.001
Anti-HCV Ab at anti HDV measurement, n (%)			
Positive	108 (16.4)	100 (65.8)	<0.001
HCV-RNA at anti HDV Measurement among HCVAb pos, n (%)			
Positive	20 (18.5)	11 (11.0)	0.256
Negative	10 (9.3)	13 (13.0)	
Missing	78 (72.2)	76 (76.0)	

Table 2: Demographic and clinical characteristics of anti HDV positive participants by HDV-RNA status

	HDV-RNA negative	HDV-RNA positive	p-value
<b>N (%)</b>	<b>32 (32.3%)</b>	<b>63 (67.7%)</b>	
Age, median (IQR)	45 (37-48)	43 (37-49)	0.921
Female, n (%)	4 (12.5)	4 (6.3)	0.308
HIV transmission group, n (%)			
MSM	4 (12.5)	7 (11.1)	0.226
PWID	18 (56.2)	44 (69.8)	
HET	8 (25.0)	6 (9.5)	
Other/missing	2 (6.2)	6 (9.5)	
Italian (%)	23 (71.9)	61 (96.8)	<0.001
Alcohol use, n (%)			
Yes	8 (25.0)	20 (31.7)	0.578
No	13 (40.6)	19 (30.2)	
Unknown	11 (34.4)	24 (38.1)	
Months between inclusion in the cohort and anti HDV measurement, median (IQR)	10.3 (0.0-89.3)	40.9 (10.2-87.6)	0.069
CD4 count, cells/μl, median (IQR) at inclusion in the cohort	297 (68-579)	396 (206-602)	0.164
CD4 count, cells/μl, median (IQR) at anti HDV measurement	292 (61-612)	349 (214-575)	0.363
FIB-4 > 3.25 at anti HDV measurement, n (%)	3 (9.7)	21 (34.4)	0.038
Death for any cause, n (%)	7 (21.9)	14 (22.2)	0.969
Liver related death, n (%)	4 (12.5)	8 (12.7)	0.978
Anti-HCV Ab at anti HDV measurement, n (%)			
Positive	19 (59.4)	45 (71.4)	0.346
HCV-RNA at anti HDV Measurement among HCVAb pos, n (%)			
Positive	6 (31.6)	4 (8.9)	0.065
Negative	4 (21.0)	16 (35.6)	
Missing	9 (47.4)	25 (55.5)	

Table 3- Hazard Ratio (HR) and Adjusted HR (AHR) of developing liver failure (ESLD, HCC or Liver related death) after first HDV screening from fitting a Cox Regression model

HDV Status	HR	95%CI	P	AHR*	95%CI	P
HDVAb neg	1			1		
HDVAb pos / HDV-RNA miss	4.68	1.81 12.09	0.001	2.05	0.68 6.15	0.200
HDVAb pos / HDV-RNA neg	3.87	1.28 11.75	0.017	1.53	0.42 5.60	0.523
HDVAb pos / HDV-RNA pos	6.60	3.08 14.14	<0.001	4.08	1.69 9.86	0.002

\*Adjusted for alcohol use, anti-HCV status (HCVAb and HCVRNA), CD4 at baseline