

# MASLD AND CHRONIC VIRAL HEPATITIS: BASELINE RESULTS FROM PATIENTS ENROLLED IN THE PITER HCV AND HBV AND HDV ITALIAN COHORTS

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## INTRODUCTION

Metabolic dysfunction-associated steatotic liver disease (MASLD) encompasses patients who have hepatic steatosis and at least one of five cardiometabolic risk factors. The coexistence of other forms of liver disease as MASLD with viral hepatitis is also recognized. There are no accurate data neither on the prevalence of MASLD in HCV or HBV induced chronic liver disease nor on the liver disease progression due to MASLD in patients who achieved viral HCV elimination/or HBV disease control.

## AIM

We evaluated the prevalence and clinical characteristics of MASLD in the large PITER HCV and HBV (HDV coinfecting or not) Italian cohorts.

## METHOD

**Patients:** The study population consisted of patients with chronic HCV or HBV (with or without HDV coinfection) consecutively enrolled in the ongoing, prospective PITER-HCV and PITER HBV/HDV cohorts (the Italian Platform for the study of Viral Hepatitis Therapy) from about 60 centers specialized in liver and infectious diseases distributed throughout Italy (1). For the purpose of the present study, patients with HIV co-infection were excluded. Potential MASLD was defined taking into account the presence of steatosis and at least one of the metabolic dysfunctions included in the New Nonalcoholic fatty Liver Disease (NAFLD) Nomenclature (2).

**Statistical analysis:** Patients' main characteristics were reported as the median and interquartile range (IQR) for continuous or as proportions for categorical variables. The Mann-Whitney rank-sum test and the Chi-squared test were used as appropriate. A p-value of <0.05 was considered statistically significant. Adjusted odds ratios for potential confounding variables were calculated by multiple logistic regression analyses.

## RESULTS

### Patients' main baseline characteristics

Data from 3571 HBV monoinfected patients (62.3% males), 372 HBV/HDV coinfecting patients (54.8% males) and 11.619 HCV monoinfected patients (53.4% males), were included.

The baseline demographic, clinical and biochemical characteristics of the study population are shown in **Table 1**. The median age of HBV, HDV/HDV and HCV infected patients was 59 years (IQR 47-68), 55 years (IQR 45-62) and 63 years (IQR 52-71), respectively ( $p < 0.001$ ).

The prevalence of steatosis was 27.4%, 21.2% and 27.4% in HBV, HBV/HDV and HCV infected patients' cohort  $p = 0.029$ . Cardiovascular diseases and diabetes were significantly more prevalent ( $p < 0.001$ ) in HCV versus HBV and HBV/HDV patients' cohort (37.9%, 25.6% and 20.2% respectively; 14.1%, 10.1% and 5.7%, respectively) whereas cirrhosis was significantly higher ( $p < 0.001$ ) in HBV/HDV versus HBV and HCV patients' cohort (70.2%, 23.5% and 49.7%, respectively). Current alcohol use was more frequently present in HBV versus HBD/HDV and HCV patients' cohort (22.4%, 18.2% and 15.6% respectively,  $p < 0.001$ ). These results were confirmed after adjusting for potential confounders (data not shown).

### Prevalence of MASLD in patients' cohorts

The prevalence of MASLD was 21.2% (756/3571), 12.6% (47/372) and 22.7% (2640/11619) in the HBV, HBV/HDV and HCV cohorts, respectively ( $p < 0.001$ ) (**Table 1**). In the HCV cohort, the prevalence of MASLD remained 23.0% also excluding 1077 patients with genotype 3 (data not shown). In patients with liver cirrhosis, the prevalence of MASLD was significantly higher in the HBV versus the HBV/HDV and HCV cohorts: 24.7% (207/838), 12.6% (33/261) and 20.0% (958/4787) respectively ( $p < 0.001$ ) (**Table 2**). In patients with F0-F3 fibrosis stage the prevalence of MASLD was significantly higher in HCV chronic infected patients compared with HBV and HBV/HDV chronic infected patients, specifically: 23.7% (1148/4854) in HCV vs 20.1% (549/2733) in HBV and 12.6% (14/111) in HBV/HDV cohorts ( $p < 0.001$ ) (**Table 2**).

### Variables associated with MASLD

Further analysis showed that MASLD was independently associated with older age (OR 1.02, 95% CI 1.01 - 1.02), male gender (OR 1.39, 95% CI 1.28 - 1.51), HCV infection (OR 1.10, 95% CI 1.00 - 1.21) and a fibrosis stage different from cirrhosis (OR 1.30, 95% CI 1.19 - 1.42) (**Table 3**).

**Table 1** - Baseline characteristics of the study populations.

	HBV (N=3571*)		HBV/HDV (N=372*)		HCV (N=11619*)		P**
	N.	%	N.	%	N.	%	
Median age years (IQR)	59 (47 - 68)		55 (45 - 62)		63 (52 - 71)		<0.001***
Sex	Male	2223 62.3	204 54.8	6199 53.4			<0.001
	Female	1348 37.8	168 45.2	5420 46.7			
BMI	Underweight-Normal	1260 45.9	131 50.6	5724 49.3			0.005
	Overweight-Obese	1488 54.2	128 49.4	5894 50.7			
Alcohol use	Never	2159 65.7	215 69.8	7548 66.6			<0.001
	Current	735 22.4	56 18.2	1764 15.6			
	Past	394 12.0	37 12.0	2022 17.8			
Country of birth	Italian natives	2744 76.8	234 62.9	10058 95.6			<0.001
	Non-Italian natives	827 23.2	138 37.1	464 4.4			
Cirrhosis	Yes	838 23.5	261 70.2	4787 49.7			<0.001
	No	2733 76.5	111 29.8	4854 50.3			
Cirrhosis with complications	Yes	348 53.4	169 71.0	2984 62.3			<0.001
	No	304 46.6	69 29.0	1803 37.7			
Liver Stiffness Measurement	≥ 20 kPa	57 3.0	33 17.7	1399 17.3			<0.001
	< 20 kPa	1827 97.0	154 82.4	6700 82.7			
Diabetes	Yes	359 10.1	21 5.7	1633 14.1			<0.001
	No	3212 90.0	351 94.4	9986 86.0			
Cardiovascular disease	Yes	915 25.6	75 20.2	4400 37.9			<0.001
	No	2656 74.4	297 79.8	7219 62.1			
Steatosis	Yes	980 27.4	79 21.2	3189 27.4			0.029
	No	2591 72.6	293 78.8	8430 72.6			
MASLD	Yes	756 21.2	47 12.6	2640 22.7			<0.001
	No	2815 78.8	325 87.4	8979 77.3			
Previous Interferon use	Yes	560 15.7	122 32.8	4314 37.1			<0.001
	No	3011 84.3	250 67.2	7305 62.9			
History of previous HCC	Yes	96 2.8	32 8.8	512 4.4			<0.001
	No	3378 97.2	332 91.2	11107 95.6			
Child	A	744 88.8	219 83.9	3520 84.3			0.002
	B	92 11.0	36 13.8	599 14.3			
	C	2 0.2	6 2.3	58 1.4			

**Table 2** - Prevalence of MASLD by cirrhosis.

	HBV (N=3571*)		HBV/HDV (N=372*)		HCV (N=11619*)		P**
	N.	%	N.	%	N.	%	
MASLD in F4 cirrhosis	Yes	207 24.7	33 12.6	958 20.0			<0.001
	No	631 75.3	228 87.4	3829 80.0			
MASLD in F0 - F3 fibrosis stage	Yes	549 20.1	14 12.6	1148 23.7			<0.001
	No	2184 79.9	97 87.4	3706 76.3			

\* For some variables inconsistencies are due to missing values

\*\* p value Chi-square test

\*\*\* p value Mann-Whitney rank-sum test

**Table 3** - Variables associates with MASLD.

	Adjusted OR * (95% CI)	
Age (years)	1.02 (1.01 - 1.02)	
Sex	Female	1.00
	Male	1.39 (1.28 - 1.51)
Cirrhosis	Yes	1.00
	No	1.30 (1.19 - 1.42)
Hepatitis	B mono + Delta	1.00
	HCV	1.10 (1.00 - 1.21)

\* Adjusted for all variable listed in table

## CONCLUSIONS

Different prevalence of MASLD was observed in patients with HBV, HBV/HDV and HCV, chronic infection and in those with different stages of liver disease due to viral hepatitis. Prospective evaluations are necessary to evaluate if MASLD is a cofactor or bystander on HBV, HBV/HDV and HCV disease progression.

## REFERENCES

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