Background

Hepatitis D virus (HDV) or delta hepatitis is a defective single-stranded RNA virus that requires hepatitis B surface antigen (HBsAg) for replication and transmission. HDV infection has been mainly studied in HIV negative patients, while data on HDV+ positive patients are limited.

We investigated the clinical pattern as well as virological and clinical features of liver disease and immune status in HDV+ positive patients with delta hepatitis. Their clinical characteristics were compared with those of anti-HDV negative, hepatitis B surface antigen (HBsAg) negative patients.

Methods

Patients

This retrospective observational study examined demographic, clinical, therapeutic information and laboratory data retrieved from the database of the Division of Infectious Diseases of the San Raffaele hospital (Gianluca Celletti), Milan, Italy.

Data were collected for each HDV+ infected/HBV positive patient at least visit available in 2017. The CS-HIV cohort was approximately the ethics committee of the San Raffaele hospital.

At their first visit the patients provide written informed consent for scientific analyses of their data.

Statistical analysis

Results for continuous variables were reported as median (interquartile range (IQR)).

Characteristics of HDV+ positive patients were compared using the Pearson’s chi-square test or Fisher’s exact test for categorical variables and the Mann-Whitney test for continuous variables. Potential denominators for HDV positivity were examined by applying multivariate regression model.

All statistical tests were two-sided at the 5% level (p < 0.05).

Results

Detection of anti-HDV

Among 110 HDV+ infected patients treated for anti-HDV for whom were available clinical data, 31 were anti-HDV negative (HDV-), 76% and 31 were anti-HDV positive (HDV+), 24.4%.

Clinical characteristics of HDV+ patients and HDV− patients are depicted in Table 1

Univariate analysis

1. Male gender predominating in these two groups.
2. HDV frequency extremely high in extra-serious drug users (ESDU) respect to patients usually exposed to viral risk (P=0.001).
3. HDV+ patients had higher alveolar anti-particle transaminase levels (ALT) than HDV− patients (P=0.021).
4. Liver stiffness measured by transient elastography and expressed by a palpable (NAS), resulted higher in anti-HDV subjects respect to HDV− ones (P=0.001).
5. Higher degree of fibrosis assessed by transient elastography according to presence conditions found in HDV+ patients (P=0.011).
6. HDV+ patients were two times higher than HDV− patients (50% and 22.0%, respectively, P=0.001).

Virologic Characteristics

No difference in HCV RNA and anti-HDV (measured by qualitative and quantitave assays) was found between these two groups.

HCV RNA was more frequently found positive in HDV− than in HDV+ patients (47.6% vs 76.4%; P=0.001).

HCV RNA+ patients were found to be HCV+ in 76.4% of anti-HDV+ and 62% of anti-HDV− subjects, P=0.011.

HCV RNA+ qualitative assays were available in 71% of anti-HDV+ patients and was found positive in 77.3% of HDV+ patients. In 5 patients found HDV RNA+ positive, the only were reported a subclinical serum complex with a persistence of anti-HDV positivity or negativity.

Comparison of Fibrosis Degree between HDV+ and HDV− Common HDV+ and HDV− patients had higher degree of fibrosis and were more frequently anti-HCV positive respect to HDV− patients. We compared fibrosis degree between HDV+ and HDV− patients, and anti-HCV+ and anti-HCV− subjects, showing no difference in the fibrosis score between individuals with or without positivity for anti-HCV.

Conclusions

Our study was limited by the nature of cross-sectional investigation and small sample size. So, it is possible that a number of HDV+ patients were not tested for anti-HDV or their data were not reported in the database. In addition, HCV-RNA assay was not performed in all anti-HDV positive patients. Therefore, we considered anti-HDV infected those patients with anti-HDV positivity.

We confirmed the severity of liver disease by a non invasive method (transient elastography) for assessing liver fibrosis and added information on demographics, immunological and clinical features of HIV-1/HDV+ patients, that could be taken in consideration for the management of this difficult to treat group.