

DIVERGENT PATTERNS OF HBV RNA AND HBcrAg LEVELS IN UNTREATED CHRONIC HEPATITIS DELTA: A LARGE EUROPEAN CROSS-SECTIONAL STUDY



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Introduction

Serum HBV RNA and HBcrAg levels have been proposed as useful biomarkers in the management of untreated and treated HBV patients.

However, the role of these biomarkers in the management of HDV infected patients is still unknown.

Results

Overall, 202 HDV patients were enrolled

Variables	Overall n=202
Age, years	46 (20-78)
Males	123 (61%)
European Union origin	138 (68%)
Cirrhosis	103 (51%)
Compensated cirrhosis	80%
Esophageal varices ^o	41%
Active HCC	11 (6%)
Fibroscan, kPa ^s	11 (1-75)
AST, U/L	64 (17-380)
ALT, U/L	76 (17-889)
ALT > ULN	169 (84%)
GGT, U/L	51 (12-491)
Platelets count, 10 ³ /mm ³	146 (30-369)
Platelets < 100x10 ³ /mm ³	53 (26%)
BMI, Kg/m ²	24 (17-44)
NA treatment	117 (58%)
qHBsAg, Log IU/mL	3.8 (0.3-4.6)
HBeAg positive	25 (13%)
Anti-HBe positive	162 (80%)
HBV DNA negative	139 (69%)
HDV genotype 1 [@]	67 (94%)
HDV RNA, Log IU/mL	4.9 (0.8-9.6)

Results are reported as number (percentage) or median (range). HCC: hepatocellular carcinoma; AST: aspartate aminotransferase; ALT: alanine aminotransferase; GGT: gamma-glutamyl-transferase; BMI: Body mass index; NA: Nucleos(t)ide analogues; ^o or previous endoscopic band-ligation; ^s 89 Fibroscan data available; [@]71 HDV gt available

Methods

Consecutive patients with untreated CHD were enrolled in this investigator driven cross-sectional study in two EU centers. All the standard clinical and virological characteristics were collected.

HDV RNA was quantified by sensitive and specific assays (Robogene or a local validated in-house assay). Serum HBV RNA was quantified by an automated real-time PCR based investigational assay (cobas® 6800, Roche Diagnostics, Pleasanton, Ca, USA, LLOQ 10 cp/mL) while serum HBcrAg levels were measured using LUMIPULSE® G HBcrAg assay (Fujirebio Europe, LLOQ 3 log₁₀ U/mL).

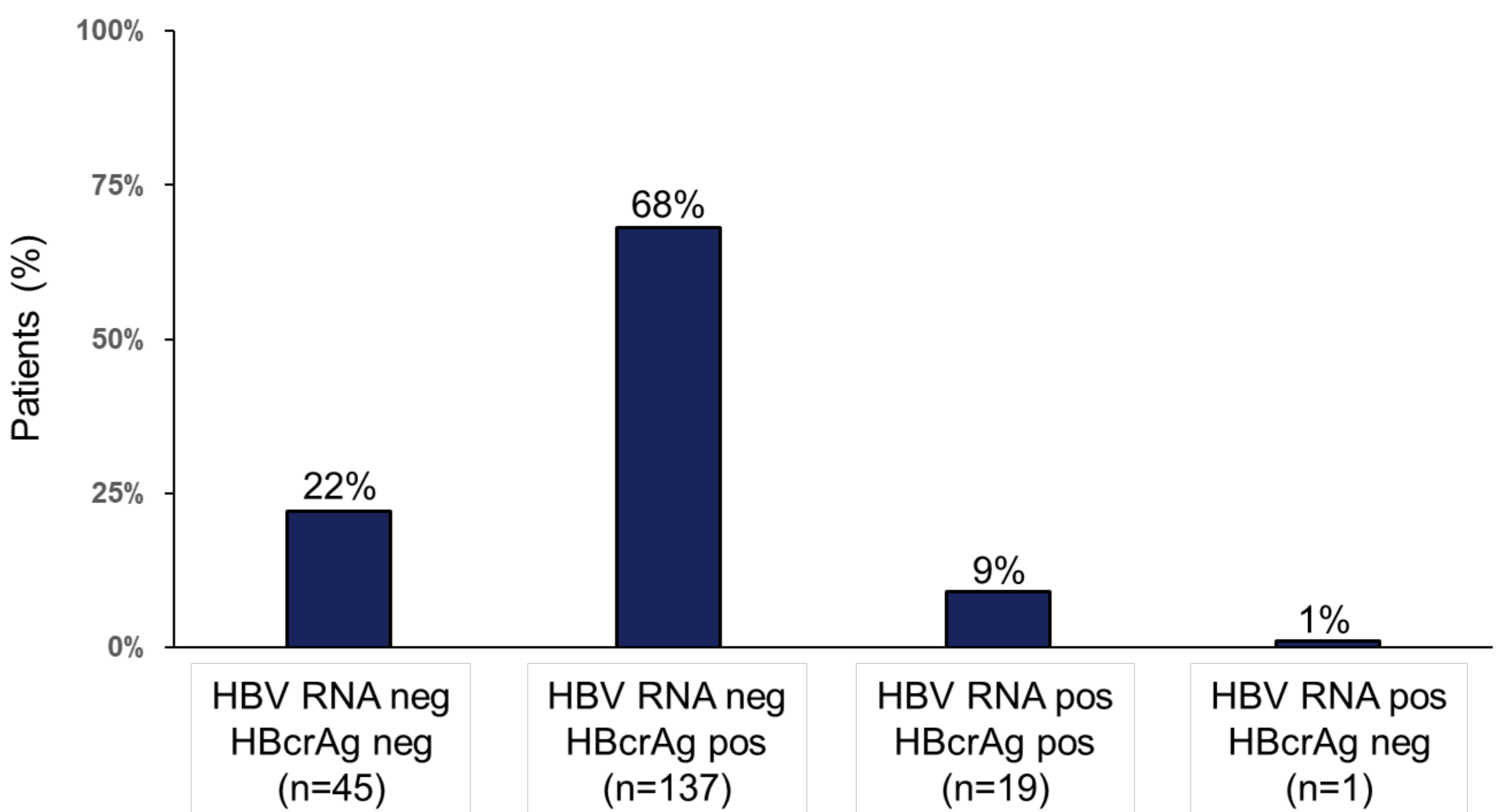
HBV RNA tested positive (>10 cp/ml) in only 10% of the patients: median 43 cp/ml (range 13-82,000). In contrast, most patients (77%) tested positive for HBcrAg (>3.0 Log IU/ml), median values being 4.2 Log (range 3-8) IU/ml.

Variables	Overall n=202
HBV RNA positive (>10 cp/mL)	20 (10%)
HBV RNA, cp/mL	43 (13-82,000)
HBcrAg positive (>3 Log IU/mL)	156 (77%)
HBcrAg, Log IU/mL	4.0 (3-8)
HBcrAg positive (>2 Log IU/mL)	183 (91%)

By combining these biomarkers, 3 categories were identified: 23% double negative, 9% double positive and 68% negative for HBV RNA but positive for HBcrAg.

HBV RNA levels were associated with younger age, higher HBV DNA, HDV RNA and HBcrAg, while HBcrAg positivity correlated with higher HBsAg and HDV RNA levels.

Double positive patients were younger, with higher HDV RNA levels and more likely of non-EU origin.



Conclusion

In untreated CHD patients, HBV RNA and HBcrAg show a divergent pattern: while HBV RNA was undetectable in most patients, the opposite was true for HBcrAg. Additional studies aimed to unravel the molecular mechanisms underlying these findings are warranted.