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Introduction: Long-term administration of effective oral therapies improves liver parameters in CHB patients, but its effect on the esophageal varices (EV) status is unknown.

Aim: To evaluate EV development/progression/regression in compensated HBV monoinfected cirrhotics long-term treated with TDF/ETV in a real-life setting.

Materials and Methods: 186 Caucasian HBV monoinfected CPT-A HCC-free cirrhotics without high-risk varices (HRV), with at least one follow-up endoscopy, were enrolled in a longitudinal study from TDF/ETV start to June 2020 (or liver-transplantation). Blood exams and abdominal US were performed every six months, endoscopic surveillance according to Baveno recommendations.

Results: At TDF/ETV introduction: 61 (21–83) years-old, 80% males, 60% HBV-DNA undetectable, 63% NUCs previously-exposed, 73% normal ALT, platelets $154 (48-304) \times 10^9/L$, 25 (13%) with low risk varices (LRV). During 136 (26–170) months of TDF/ETV, 100% achieved virological response, 99% normalized ALT, 37 (20%) developed HCC, 4 (2%) non-neoplastic portal vein thrombosis (PVT). Overall, 666 endoscopies were performed, with a median of 3 [1–7] per patient. 25 patients had LRV at baseline: varices remained stable in 12 (48%), disappeared in 11 (44%) and progressed in 2 (8%) patients (one concomitant to HCC). The 10-year cumulative risk of EV progression was 9.3% (95%CI 2–33%), while the 10-year regression probability was 58.2% (95%CI 35–83%). Out of 161 patients without EV at baseline, only 7 (4%) developed EV (6 LRV, 1 HRV; in 3 cases concurrent to HCC), with a 10-year EV development risk of 4.5% (95%CI 2–9%), but only 0.6% (95%CI 0–4%) considering HRV. Overall, for the entire cohort, the 10-year risk of EV development/worsening was 5.1%. None bled from EV.

Conclusions: In compensated HBV cirrhotics treated with TDF/ETV, the 10-year risk of developing/progressing EV is negligible even in patients with LRV in the absence of HCC or PVT, thus challenging the Baveno recommendations.

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OC-3

A single center, large long-term cohort study of the relations between mutations in Basic-Core-Promoter and pre-C regions of Hepatitis B virus DNA and clinic-pathologic outcome of HBeAg-negative/anti-HBe-positive phase

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Introduction: The relation between Basic-Core-Promoter (BCP) and pre-Core (pC) mutations of hepatitis-B-virus (HBV) DNA and the clinic-pathologic outcome of HBeAg-negative/anti-HBe-positive HBV carriers remains unclear.

Materials and Methods: We directly sequenced BCP/pC HBV-DNA in 447 consecutive chronic HBeAg-negative/anti-HBe-positive, HBV-genotype-D carriers, followed prospectively for 93.4 (12.0/279.7) months: 144 HBeAg-negative infection (ENI, HBV-DNA \leq 2,000 IU/mL); 61 Grey-Zone (GZ; HBV-DNA \leq 20,000 IU/mL); 242 chronic hepatitis (CHB), 70 with cirrhosis (CHB+CI) (HBV-DNA $>$ 20,000 IU/mL).

Results: Overall BCP and pC mutants were found in 433/447 (96.8%) cases: A1762T: 51.7%; G1764A: 63.3%; pre-Core initiation codon (PIC: A1814, T1815, G1816) 10.7%; G1896A: 72.5%; G1899A: 55.5%. A1762T and G1764A prevalence was lower in ENI than CHB [35.6% vs 65.3%, $p < 0.001$ and 53.7% vs 71.5% $p < 0.001$, respectively]; PIC variants prevailed in ENI than CHB (15.1/70.0%, $p = 0.009$); G1896A and G1899A mutations were equally prevalent in ENI/CHB (73.2%/71.9% and 55.1/55.8%, respectively). The prevalence of different patterns [Wild type (a), BCP-mutation alone (b), pC-mutation alone (c) and BCP+pC mutations (d)] in carriers without liver-disease versus CHB was: a) 6/205 (2.9%) vs 8/242 (3.3%), $p = 0.818$; b) 13/205 (6.3%) vs 31/242 (12.8%) $p = 0.022$; c) 84/205 (41.0%) vs 58/242 (24%), $p < 0.001$; d) 102/205 (49.8%) vs 145/242 (59.9%), $p = 0.031$. Patients with CHB and BCP+pC mutations had a 10 years older median age [51.9 (4.9/80.8) vs 41.3 (16.8/86.6) years, $p < 0.001$], higher cirrhosis rate (40.0 vs 18.5%, $p < 0.001$) and liver stiffness values [7.7 (3.2/56.1) vs 6.8 (3.2/39.3) kPa, $p = 0.025$].

Conclusions: The mutations in HBV-DNABCP/pC regions prevail in most (96.8%) of HBeAg-negative/anti-HBe positive carriers. The G1896A is the most prevalent (72.5%), independently from liver disease. HBeAg-negative infection is characterized by the absence of A1762T/G1764A and presence of PIC mutations whereas BCP/pC mutations prevail significantly in CHB and older patients with advanced liver disease. BCP/pC mutants might provide a selective viral fitness under the immune pressure in CHB patients.

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OC-4

Associated screening for HCV and SARS-Cov2 infection in an urban area of Southern Italy: the “Casola di Napoli” cohort study

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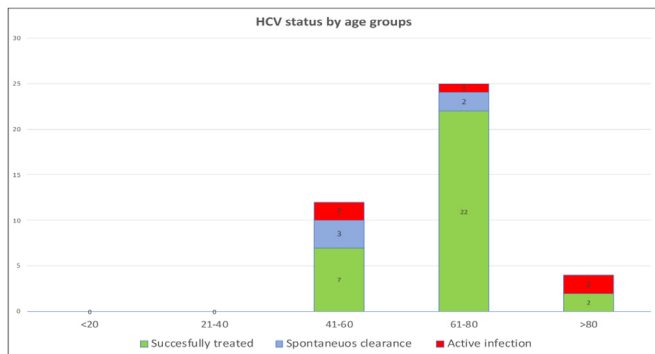
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Introduction: The spread of SARS-Cov2 pandemic led to a substantial reorganization of all the non-related and non-urgent clinical activities in Italy, with a subsequent reduction of the available resources for the management of other potentially curable diseases. This is the case of the HCV infection that, in Italy, had recently seen important milestones towards its elimination which, now, risk being nullified. On the other hand, one of the biggest questions regarding the epidemiology of COVID-19 is the real burden of the asymptomatic carriers. It would be very useful to associate the screening for both the diseases, in order to effectively respond to two important clinical needs.

Methods: A prospective observational cohort study was set-up in an urban area of the Naples province, in which a contemporary screening for HCVAb and for SARS-Cov-2 IgG/IgM rapid blood tests was performed. All the positive patients underwent RT-PCR for HCV RNA and/or SARS-Cov-2-RNA. The study was approved by our Ethical Committee.

Results: Of the 3845 people who live and work in the chosen area, 3556 were eligible for the screening and, of these, 2740 (77.05%) participated voluntarily from June 25 to July 12, 2020. Of them, 39 patients (1.4%) resulted SARS-Cov2-IgM- or -IgG-positive. None of these resulted subsequently positive for SARS-Cov2-RNA. Forty-one patients were HCVAb-positive (1.5%) and, of them, 5 (0.18%) resulted HCV RNA-positive. Of those HCVAb positive, 36/41 (87.8%) reported awareness of their positivity and, in 88.8% of cases (32/36), had already been subjected to antiviral therapy with a 96.87% (31/32) SVR. Of the other 4 patients aware of their positivity, 2 (50%) were HCV RNA-positive. Of the remaining 5 HCVAb-positive patients, that were unaware of their positivity, 2 were HCV RNA-positive. Of notice, HCVAb-positivity was detected in patients of >41 years with 82.0% (32/39) in the 61-80 years age-class.

Conclusions: The screening of an entire cohort of an urban area of Southern Italy showed a seroprevalence of anti-SARS-Cov2-Ab and HCV-Ab of 1.4% and 1.5%, respectively, whereas only 0.18% had an active HCV infection. This study shows how the pandemic can be an opportunity to promote prevention activities for HCV.



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OC-5

SIRT5 rs12216101 T>G variant is associated with fibrosis severity in patients with non-alcoholic fatty liver disease

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Introduction: Sirtuin 5 (SIRT5) is a NAD⁺-dependent deacetylase that modulates the antioxidant defense through post-translational modifications of target proteins.

Aim: In this study we assessed the expression of SIRT5 in patients with non-alcoholic fatty liver disease (NAFLD) and the effect of the rs12216101 T>G non-coding SNP at the SIRT5 gene locus.

Materials and Methods: The rs12216101 genotypes were evaluated in 2606 patients with biopsy-proven NAFLD consecutively recruited at three European centers and transcriptomic analysis was carried out in a sub-cohort of 112 Italian bariatric patients. Genotyping of SIRT5 rs12216101 variants was performed by TaqMan assays. LX-2 cells were treated with 100 ng/mL LPS to assess changes in SIRT5 expression upon stress conditions.

Results: In the whole cohort the frequency distribution of SIRT5 rs12216101 TT, TG and GG genotypes was 47.0%, 42.3% and 10.7% respectively. At multivariate logistic regression analysis adjusted for gender, age >50 years, diabetes, and PNPLA3 rs738409 status, SIRT5 rs12216101 T>G variant was associated with presence of ballooning (OR 1.20, 95% C.I. 1.04-1.39), NASH (OR 1.20, 95% C.I. 1.03-1.40) and F2-F4 fibrosis (OR 1.18, 95% C.I. 1.00-1.37). At transcriptomic analysis, rs12216101 G variant was associated with upregulation of several metabolic pathways in the liver (adjusted p<0.05), including oxidative phosphorylation and fatty acid metabolism, which were also co-regulated with hepatic SIRT5 transcript levels (adjusted p<0.05). In agreement with a higher expression of SIRT5 in liver samples of patients with advanced fibrosis, treatment of LX-2 with LPS induced a time-dependent up-regulation of SIRT5 in vitro.

Conclusions: SIRT5 is up-regulated in patients with NAFLD and rs12216101 T>G variant of SIRT5 is independently associated with disease severity.

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OC-6

GEMS, a Genetic and Metabolic Staging predicting the outcome of non-alcoholic fatty liver disease

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Background and Aim: Non-alcoholic fatty liver disease (NAFLD) is an emergent cause of liver-related events (LRE). We have assessed the ability of a composite score based on clinical features, metabolic comorbidities and genetic background, to predict LRE.

Methods: 546 consecutive patients with NAFLD were recruited and stratified according to FIB-4 (low risk <1.3; intermedium-high risk ≥1.3). LRE were defined as occurrence of HCC or hepatic decompensation. Cox regression multivariate analysis was used to identify baseline variables associated with LRE.

Results: Over a median follow-up of 73.8 months, 58 patients experienced LRE (only 1 in the cohort of patients with FIB-4 <1.3). At multivariate Cox Regression analysis performed in 229 patients with FIB-4 ≥1.3, clinical variables like age between 55 and 65 years (HR 13.96), age >65 years (HR 17.96), platelets between 110,000 and 150,000/mm³ (HR 6.89), platelets < 110,000/mm³ (HR 13.54) and albumin < 4 g/L (HR 1.5), metabolic variables like low HDL Cholesterol (HR 1.88), genetic variables such as TM6SF2 rs58542926 CT/TT (HR 1.94) and HSD17B13 rs72613567 T/TA (HR 1.83), and the interactions between PNPLA3 rs738409 and both male gender (HR 0.32) and diabetes (HR 5.16) were independently associated with the development of LRE. The AUC of the