

OP-1 FEATURES OF IDIOSYNCRATIC DRUG-INDUCED LIVER INJURY (DILI) IN LATIN AMERICA: LONG-TERM EXPERIENCE OF THE LATINDILI NETWORK

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Introduction and Objectives: The Latin American DILI (LATINDILI) Network is an international registry of prospectively identified drug-induced liver injury (DILI) cases to enhance case characterization. We aimed to analyze features and outcomes of DILI in Latin America.

Materials and Methods: Information of DILI cases included in the LATINDILI database between 2011 and July 2022 was collected and analyzed.

Results: Of 468 patients included, 13 had positive rechallenge and 5 recurrent DILI (different drugs). Mean age was 49 years (range 14–89), 62% women. The most common type of injury was hepatocellular (62%). Overall, 42% of patients were hospitalized. Most cases were mild/moderate, but 6.2% were considered severe, and 4.1% resulted in death/liver transplantation. Overall, eleven cases (2.4%) developed chronic DILI (no biochemical resolution within one year), and nine had drug-induced autoimmune-like hepatitis (1.9%).

Histological information was available for 80 patients (17%), of whom 5 had chronic cholestasis with ductopenia. The most frequent drugs were amoxicillin-clavulanate (12%), herbal and dietary supplements (HDS, 9%), anabolic androgenic steroids (4.9%), anti-tuberculosis medications (anti-TB) and nitrofurantoin (4.3% each). Among the 15 most common causative agents, all but azathioprine, were

associated with cases fulfilling nR-based Hy's law. However, only anti-TB, nimesulide and HDS were associated with worst outcome cases, while many were not, such as amoxicillin-clavulanate, nitrofurantoin and diclofenac. Causative agents more common in women included methyldopa (100%) nitrofurantoin (95%) and nimesulide (86%), while cyproterone (100%) and phenytoin (67%) were more common in men.

Conclusions: The increasing number of liver injuries associated with HDS is a major concern in Latin America. The predictive value of the nR-based Hy's law is drug-specific. These findings have regulatory implications for the promotion of public health, as common DILI-causing drugs in Latin America are either second-line drugs, no longer in use, or have been withdrawn from other markets due to liver toxicity. Funding: AEMPS, CIBERehd, ISCIII-FEDER (PI21/01248, PI-0310-2018).

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OP-2 ANALYSIS OF THE GENETIC DIVERSITY OF HEPATITIS DELTA VIRUS CIRCULATING IN BRAZIL BETWEEN 2013 AND 2021 AND ITS RELATIONSHIP WITH HEPATITIS B VIRUS

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Introduction and Objectives: Hepatitis D virus (HDV) is a defective virus dependent on the hepatitis B virus (HBV) to replicate. Currently, HDV is divided into 8 genotypes and several subgenotypes, HDV-1 and 3 being predominant in Brazil. Although crucial to understanding the evolution and spread of the virus worldwide, few studies address the genetic variability of the complete HDV genome. This study aimed to investigate the genetic variability of HDV in Brazil.

Materials and Methods: From 41 anti-HDV positive sera collected between 2013 and 2021 in distinct Brazilian regions, 12 HDV genomes were obtained by RT-PCR. Additionally, a fragment of ~900 base of S/POL regions of HBV genome was PCR amplified. The amplicons were sequenced using the Sanger method and phylogenetically analyzed.

Results: The phylogeny showed the circulation of HDV-3 (10/12; 83.3%), HDV-5 (1/12; 8.3%) and HDV-8 (1/12; 8.3%). Most HDV-3 samples (8/10; 80%) were found in the endemic North Brazilian region, while two were found in Brazilian non-endemic areas. HDV-5 and 8, whose circulation is usually restricted to African countries, were found in São Paulo, a cosmopolitan city from Southeast Brazil. Phylogenetic analysis of HDV-8 strains indicated that the sample in our study, along with previously reported sequences from Brazil, formed a highly supported monophyletic clade, probably representing a new HDV-8 subgenotype. Among HBV sequences, the association between HDV/HBV genotypes was: HDV-3/HBV-F2 (5/11; 41.7%), HDV-3/HBV-A1 (2/11; 18.2%), HDV-3/HBV-D3 (1/11; 9.1%), HDV-3/HBV-D4 (1/11; 9.1%), HDV-5/HBV-E (1/11; 9.1%) and HDV-8/HBV-E (1/11; 9.1%). The HBV genotypes commonly found in Brazil, HBV-A, HBV-D and HBV-F, were detected in coinfection with HDV-3, endemic in the country. However, HBV-E, native from Africa, was found in coinfection with HDV-5 and HDV-8, suggesting allochthonous infection.

Conclusions: This study emphasizes the importance of epidemiological surveillance in mapping HDV transmission pathways and imported variants.

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