25-hydroxyvitamin D deficiency as a factor associated with the development of Hepatic Encephalopathy in the Mexican population.

Paloma Diego-Salazar¹, Diego Abendaño-Rivera¹, Daniel Santana-Vargas², Viridiana López-Ladrón-de-Guevara³, José Luis Perez-Hernández¹, Fátima Higuera-de-la-Tijera¹

¹ Department of Gastroenterology and Hepatology, General Hospital of México “Dr. Eduardo Liceaga”, Mexico City
² Research Department, General Hospital of México “Dr. Eduardo Liceaga”, Mexico City

Introduction and Objectives: Hepatic Encephalopathy (HE) is a common complication in patients with Chronic Liver Disease (CLD), and the development of this decomposition is multifactorial, including ammonia levels, inflammatory status, and sepsis, among others. A poorly studied factor in our population is the serum levels of 25-hydroxyvitamin D (25-OHD), which could act as a co-factor in the development of HE. To assess if serum 25-hydroxyvitamin D (25-OHD) deficiency acts as a cofactor in the development of HE.

Materials and Patients: Observational, retrospective, analytical, case-control study; included subjects of both sexes, 18 years old and over, diagnosed with Chronic Liver Disease of different etiologies. Complete blood count, liver and kidney function, serum electrolytes, coagulation profile, and serum levels of 25-hydroxyvitamin D were recorded. They were evaluated using the West-Haven Criteria (WH).

Results: Independent samples T-test was used to compare differences between 25-hydroxyvitamin D levels in patients with and without HE. The association between 25-OHD deficiency and HE was assessed using a chi-square test, with a significance level set at alpha=0.05. Out of a total of 96 patients, 36.5% had HE. The mean 25-OHD level in the HE group was 18.78 ± 8.56, compared to 22.77 ± 9.94 in the group without HE. The T-test was significant: T (1=2.072), p =0.041. Among patients with deficiency, 20/35 (57.1%) had EH, while 22/61 (36.1%) did not have HE. The chi-square test for the association between deficiency and HE was positive, with a value of (1) =4.015, p =0.045.

Conclusions: A causal relationship between 25-hydroxyvitamin D (25-OHD) deficiency and the development of HE cannot be attributed, as this is multifactorial. However, 25-OHD deficiency is common in patients with Chronic liver disease, and our study demonstrates that this deficiency acts as a co-factor, as there is a significant difference between the groups. It is necessary to validate these findings in the future through multivariate analysis to confirm our results.

Ethical statement
The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

Declaration of interests
None

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Incidence and Associated factors to development of hyponatremia in a cohort of ambulatory patients with compensated liver cirrhosis
Marlene López-Sánchez¹, Juan O. Talavera², Nayeli Ortíz-Olvera¹, Rosalba Moreno Alcántar³, Segundo Moran Villota³

¹ Laboratorio de Investigación en Gastro-Hepatología, Centro Médico Nacional Siglo XXI, IMSS, Ciudad de México
² Dirección de Enseñanza e Investigación, Centro Médico ABC, Ciudad de México
³ Servicio de Gastroenterología, Centro Médico Nacional Siglo XXI, IMSS, Ciudad de México

Introduction and Objectives: Hyponatremia is associated with ascites, hepatic encephalopathy, primary bacterial peritonitis, and increased mortality. However, the information about incidence and factors associated with hyponatremia in ambulatory patients with compensated cirrhosis is scarce. The aim of the study was to estimate the incidence and associated factors to the development of hypervolemic hyponatremia.

Materials and Patients: Ambulatory patients with compensated cirrhosis seen at Medical Center Siglo XXI were selected. All variables included in Child-Pugh Index and in the MELD Score and the types of treatment diet were analyzed. Hyponatremia was considered when
serum concentration of sodium was <135 mEq/L in hypotonic state and water retention.

**Results:** The incidence of hyponatremia was 9.6% (13/135). A prognostic risk index was identified based on fluid retention and the baseline MELD score (RH-MELD Index) (Table 1). A higher incidence of hyponatremia was observed in patients in category III [RR: 7.96 (95%CI: 3.50-89.52), p=0.001].

**Conclusions:** The results suggest that the incidence of dilutional hyponatremia in outpatients with cirrhosis is frequent; mild alterations in water retention and liver function in the compensated phase represent an early indicator of its development, which can be modified by the indicated diet.

**Ethical statement**

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

**Declaration of interests**

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**Table 1**

<table>
<thead>
<tr>
<th>RH-MELD Categories</th>
<th>N (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>I: No water retention, MELD ≤9</td>
<td>2/62 (3.2)</td>
<td>Reference</td>
</tr>
<tr>
<td>II: Water retention or MELD ≥10</td>
<td>6/55 (10.9)</td>
<td>0.201</td>
</tr>
<tr>
<td>III: Water retention + MELD ≥10</td>
<td>5/18 (27.8)</td>
<td>0.010*</td>
</tr>
</tbody>
</table>

* Fisher exact test.

Unadjusted risk: RH-MELD I (reference), II (RR:3.67, CI 95%:0.71-19.01, p=0.121), III (RR:11.53, CI 95%: 2.01-66.13, p=0.006).

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**“Explosive” worsening of chronic hepatitis C-associated cryoglobulinemia vasculitis, as unmasking of lymphoma a case report.**

Mara S. Olivo-Saldana, Jimena Sánchez-Zumaya, Clara C. Sánchez-Rodríguez

*Department of Internal Medicine, Regional General Hospital 6, Instituto Mexicano del Seguro Social (IMSS), Madero City, Tamaulipas, México*

**Introduction and Objectives:** Hepatitis C virus (HCV)-related lymphoproliferative disease from cryoglobulinemia to B-cell non-Hodgkin lymphoma (B-NHL) through cryoglobulinemic vasculitis (CryoVas). The CryoVas is difficult to diagnose; once diagnosed, we must rule out the HCV infection. We presented a patient with HCV and CryoVas, which presented a sudden “explosive” worsening, warning about the development of a B-NHL.

**Materials and Patients:** 55-year-old male with HCV and CryoVas; what was the trigger for the diagnosis of HCV twenty years before? He received pegylated interferon and ribavirin without response. The virological, biochemical, and immunological characteristics are shown in Table 1. The flare of CryoVas appeared twice a year at most, limited to purpuric lesions on the legs, below the knees, arthralgia, and fatigue; was often triggered by infections, self-limiting throughout 2 to 3 weeks. The last flare started as usual but getting worse rapidly, spreading to the thighs, abdomen, chest, and upper extremities, plus fever, nocturnal diaphoresis, severe wasting, and inguinal, axillary lymph nodes. Lymph node biopsy shows diffuse large B-cell lymphoma (DLBCL).

**Results:** He received chemotherapy (CT), previously was retreated with sofosbuvir/velpatasvir for 12 weeks. Five months after first-line treatment for DLBCL he presented an early relapse and received a second line of CT; at 3-year follow-up is in remission with no relapse of CryoVas, waiting for a bone marrow transplant.

**Conclusions:** Clinicians treating hepatitis C should be aware of the need to carry out immunological parameters at the basal evaluation, such as cryoglobulins, rheumatoid factor, C4 fraction, and even a flow cytometry in specific patients to the detection of leukemias and/or related lymphomas.

**Ethical statement**

The identity of the patients is protected. Consentment was obtained.

**Declaration of interests**

None

**Funding**

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Table 1**

<table>
<thead>
<tr>
<th>Variable</th>
<th>2006 Viral load, UI/mL (log)</th>
<th>Basal 2019 y</th>
<th>SVR12 Last follow up 2022y</th>
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</thead>
<tbody>
<tr>
<td>Genotype</td>
<td>1b 1b</td>
<td>NR NR</td>
<td></td>
</tr>
<tr>
<td>Hemoglobin g/dL</td>
<td>9.9 10.6</td>
<td>12.8 13</td>
<td></td>
</tr>
<tr>
<td>Total lymphocytes K/µL</td>
<td>NR 8.6</td>
<td>7.6 9</td>
<td></td>
</tr>
<tr>
<td>Total lymphocytes K/µL</td>
<td>NR 2.3</td>
<td>1.5 1.9</td>
<td></td>
</tr>
<tr>
<td>Platelets</td>
<td>152 88</td>
<td>80 122</td>
<td></td>
</tr>
<tr>
<td>AST</td>
<td>40 79</td>
<td>20 21</td>
<td></td>
</tr>
<tr>
<td>ALT</td>
<td>83 108</td>
<td>20 29</td>
<td></td>
</tr>
<tr>
<td>GGT</td>
<td>38 66</td>
<td>33 NR</td>
<td></td>
</tr>
<tr>
<td>LDH</td>
<td>130 370</td>
<td>180 100</td>
<td></td>
</tr>
<tr>
<td>AFP</td>
<td>1 2</td>
<td>3 2</td>
<td></td>
</tr>
<tr>
<td>FIB4</td>
<td>1.16 4.76</td>
<td>3 0.49</td>
<td></td>
</tr>
<tr>
<td>APRI</td>
<td>0.75 2.57</td>
<td>0.71 1.86</td>
<td></td>
</tr>
<tr>
<td>Cryoglobulins</td>
<td>NR Positive</td>
<td>NR Negative</td>
<td></td>
</tr>
</tbody>
</table>

SVR12: Sustained viral response at 12 weeks after treatment, AST, Aspartate aminotransferase ALT, Alanine aminotransferase; GGT, gamma glutamyl transpeptidase; LDH, lactate dehydrogenase; AFP, alpha-fetoprotein; ND, No detected.

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**Intrahepatic Cholestasis Induced by Leflunomide: An Unusual Presentation of DILI**

Genesis P. Martínez-Pérez, Pamela Duran-Azamar, Ana D. Cano-Contreras, Peter Grube-Pagola, José M. Remes-Troche

*Institute of Medical-Biological Research, Veracruziana University, Mexico*