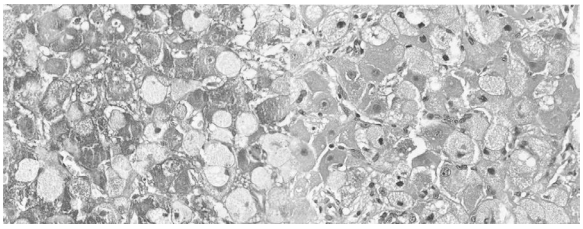

Figure 2. Microphotographs at 40X in H&E and PAS of lobular parenchyma with hepatocytes showing broad, granular cytoplasm, foamy appearance, standing out among normal hepatocytes.

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Clinical outcomes in patients with hepatitis A virus infection in a tertiary center: retrospective cohort 2022-2024.

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Introduction and Objectives: In Mexico, the incidence rate of hepatitis A virus (HAV) infection is 3.11/100,000 person/year. 70% of adults develop symptoms, representing 3% of cases of acute liver failure (ALF). This study aimed to evaluate the clinical outcomes obtained in our institution.

Materials and Patients: It is a retrospective, observational cohort study, which included all patients over 18 years of age hospitalized from March 2022 to April 2024. 16 patients with a confirmed diagnosis of HAV infection (IGM) who required hospital management in the Centro Medico Nacional 20 de Noviembre ISSSTE were included. All patients who did not have a confirmatory serological test were excluded. The SPSS v.24 program was used for statistical analysis, using frequencies and percentages for reporting the data.

Results: Of the total of 16 cases included, 31.3% (5) patients were women, and 68.8% (11) were men, with an average age of 35 years old (19-47). The comorbidities they presented were: type 2 diabetes in 18.8% (3), systemic arterial hypertension in 6.3% (1), rheumatoid arthritis in 6.3% (1). Among the clinical manifestations they presented during the evolution were the following: hepatic encephalopathy 31.3% (5), abdominal pain 62.5% (10), fever 3.1% (8), vomiting 3.5% (9), diarrhea 1.6% (4). Of our studied population, 25.0% (4) patients developed acute liver failure requiring attention in the intensive care unit, where they received adjuvant treatment based on n-acetylcysteine and renal replacement therapy. The remaining patients presented alarm symptoms 75.0% (12) without developing liver failure. The mortality reported in our population was 18.8% (3).

Conclusions: The observed mortality was 18.8% (3) of the total included, higher than that reported worldwide. In recent years, an epidemiological transition has been seen in patients with FHA. Among the factors that increased mortality were serious infections, hydroelectrolytic alterations, and limiting the transplant protocol.

Ethical statement: This study follows the ethical principles of clinical research; no intervention was performed on patients and the information is obtained from the clinical record.

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.

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Sarcopenia in patients with liver cirrhosis according to hepatic functional reserve

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Introduction and Objectives: Computed tomography (CT) is one of the most used and validated methods for the non-invasive diagnosis of sarcopenia; its measurement is not affected by the presence of obesity or ascites. The objective of the study was to know the frequency of sarcopenia in patients with liver cirrhosis with different degrees of liver reserve.

Materials and Patients: Patients who underwent liver function tests and an abdominal CT were included. The Child-Pugh index (CP) was obtained, and the skeletal muscle index (SMI) was calculated from the measurement of the cross-sectional area of the psoas muscle at the level of the third lumbar vertebra and normalized by the height of the patients (reference values for sarcopenia (Men <50cm2/m2; women <39cm2/m2).

Results: 110 patients were included (75 women and 35 men) with an average age of 54±11 years, in CP A (n=21), CP B (n=53), and CP C (n=36); with a history of non-alcoholic fatty liver disease (n=36), hepatitis C virus infection (n=19), primary biliary cholangitis (n=15), excessive alcohol consumption (n=10), and other etiologies (n=30). The SMI was significantly higher in Child-Pugh A patients (48.15±9 cm2/m2) compared to Child-Pugh B (44.19±9 cm2/m2) and Child-Pugh C (41.20±7 cm2/m2) patients. The frequency of sarcopenia was 59% (CP A: 33.3%; CP B: 43.4%; CB C: 66.6%).

Conclusions: The results of the study confirm that sarcopenia is common in patients with liver cirrhosis and increases as liver reserve deteriorates.

Ethical Statement: Approval for the study was obtained from the local ethics committee (R *2022-3601-239*).

Declaration of Interests: None.

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Metabolic reprogramming induced by fructose promotes therapy's failure in liver cancer cells *in vitro* and *in vivo*.

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Introduction and Objectives: Metabolic reprogramming is a hallmark of cancer cells. Fructose metabolism is decreased in liver cancer cells to counteract the oxidative environment induced by fructose. Ketohexokinase (KHK) A is overexpressed, and its switch confers advantages to cancer cells. The **objective** was to investigate the effect of fructose metabolism on the aggressiveness of liver cancer cells.

Materials and Patients: KHK isoform expression was measured by qRT-PCR in Huh-7 and HepG2 cells. Metabolic characteristics of liver cancer cells (Huh-7 and HepG2) treated with a fructose (1mM) for 48h in a high glucose DMEM media (11mM) was developed using Mito Fuel Flex assay and Glycolysis Rate Assay using SeaHorse technology. To prove the hypothesis that fructose metabolism enhances aggressiveness, we performed proliferation and enzymatic assays. Chemoresistance assays (*in vitro* and *in vivo*) was developed using Huh-7 cells previously treated with Fructose (1mM) for 72h. Then, we applied Fructose (1mM), Cisplatin (CDDP, 22,11μM for in vitro assays or 100μM for in vivo assays) or Fructose (1mM) + CDDP (22,11μM for in vitro or 100μM for in vivo) for 48h.

Results: ***Huh-7 cells expressed higher levels of khk-a compared to HepG2 cells. The isoform switch was*** associated with improved fructose uptake and higher proliferation in Huh-7 cells. We did not detect differences in mitochondrial glucose or fatty acid oxidation capacity, but glutamine oxidation capacity was lower in Huh-7, indicating the overall dependence of this cell line on the glutamine pathway. However, we only detected differences with fructose-treated (Fru-treated) cells with less dependence on fatty acid oxidation in hepatoma cells, suggesting that fructose metabolism has a different effect with respect to the differentiation level of the cells. Next, we evaluated the glycolytic pathway in the aggressive cell line (Huh-7), and the analysis showed that Fru-treated cells contributed less to media acidification, suggesting the activation of alternative pathways by fructose. The pentose phosphate pathway was affected by fructose and inhibition of glutathione reductase abolished the benefits gained. We then assessed survival to CDDP treatment, and found that both, in vitro and in vivo, fructose treatment improved survival and resistance to CDDP therapy.

Conclusions: Fructose promotes a metabolic remodeling leading to the sustained proliferation of liver cancer cells. Specifically, fructose metabolism promotes alternative metabolic pathways that contribute to the aggressiveness of HCC cells. In addition, fructose may increase cancer cell survival and the treatment failure.

Ethics statement: All the cell lines were obtained from the American Type Culture Collection (ATCC). The material was obtained legally, ethically, and with due consideration for the well-being, privacy, and dignity of the donor.

Declaration of interests: None.

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Neutrophil-lymphocyte ratio as a prognostic factor in patients with alcoholic hepatitis.

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Introduction and Objectives: The neutrophil-lymphocyte ratio (NLR) has been used as a predictor of survival in critically ill patients. However, there are scarce studies that evaluate the relationship between NLR and alcoholic hepatitis. Thus, we aimed to determine the association between NLR with mortality and the degree of acute-on-chronic liver failure (ACLF).

Materials and Patients: Longitudinal, retrospective, observational and descriptive cohort study of a hospital center. Patients who attended from March 1, 2022, to April 30, 2024, to Gastroenterology service were included. The subjects met criteria for alcohol hepatitis established by the National Institute on Alcohol Abuse and Alcoholism: alcohol consumption >40 g/day (women) or >60 g/day (men) for six or more months, jaundice during the previous eight weeks, AST > 50 IU/L, AST/ALT ratio > 1.5, and both values < 400 IU/L, BT > 3.0 mg/dL. Patients with concomitant infections or conditions that could alter the NLR (steroid use, pancreatitis, hemorrhage, neoplasms) were excluded. Statistical analysis was performed with the SPSS version 26 program. To compare clinical values, Student's T-test or Mann Whitney U test were performed according to the distribution of the data. The association analysis between NLR and 30-day mortality, as well as the association between NLR and ACLF degrees, were carried out using a point-biserial correlation. Cohen's d test was performed to determine the effect size.

Results: This study included 58 patients with alcoholic hepatis (98% men). The mean of the INL was 24.3. There was significant difference between patients who died within 28 days compared with those who survived (Table 1). The main differences were observed in the following data: leukocytes ($p < 0.001$), creatinine levels ($p = 0.007$), BT ($p < 0.001$); as well as, in the indexes: INL ($p < 0.001$), CLIF SCORE ($p < 0.001$), MELD ($p = 0.02$) and MELD Na ($p = 0.01$). (Table 1). The mean NLR value in patients who survived was approximately three times the value presented in patients who died within 28 days [23.0 (19.1, 28.6) vs. 8.0 (5.0, 11.0); ($p < 0.001$)]. A gradual increase in severity-dependent NLR was identified based on the CLIF SCORE scale (significant difference among the three groups considering CLIF SCORE 0). In addition, significant associations between NLR and 28-day mortality ($p < 0.001$), and between NLR and the degree of ACLF ($p < 0.001$) were found. According to Cohen's test, the effect size of the NLR was moderate (0.678).

Conclusions: The association between high NLR levels and mortality within 28 days is confirmed. Furthermore, there is an association between NLR and the severity of ACLF. Therefore, the NLR could be a useful prognostic factor in the clinical practice for alcoholic hepatitis. However, more studies with larger sample sizes are required.

Ethical statement: The protocol was registered and approved by the Ethics Committee. Patient confidentiality was maintained, and informed consent 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.