Crit Care Med. 2022 Nov 1;50(11):e794-e795. doi: 10.1097/CCM.0000000000005649. Epub 2022 Oct 13.

The authors reply

Free PMC article

*No abstract available*

Review World J Gastroenterol. 2022 Oct 7;28(37):5395-5402. doi: 10.3748/wjg.v28.i37.5395.

# Milestones in the discovery of hepatitis C

## Abstract

The discovery of hepatitis C has been a landmark in public health as it brought the opportunity to save millions of lives through the diagnosis, prevention and cure of the disease. The combined work of three researchers, Alter H, Houghton M and Rice C, which set the basis for the diagnosis, treatment and prevention of hepatitis C apart from laying the ground work for a new approach to study infections in general and developing new antiviral agents. This is a story of a transfusion-associated infection. A series of clinical studies demonstrated the existence of an infectious agent associated with hepatitis. That was followed by the identification of what was later known to be the hepatitis C virus (HCV) and the development of diagnostic tests. It all preceded the full molecular identification and demonstration of a causal effect. Finally it ended up with the development and discovery of a new class of therapeutic drugs, the direct acting antivirals, which are now used not only to cure the disease but most probably, to eliminate the problem. This work started with Dr Alter H who demonstrated that a new virus was responsible for the majority of post-transfusion hepatitis followed by Houghton M who cloned the virus and developed the blood test to identify those cases that carried the virus. Finally, the work of Rice C demonstrated that a cloned HCV produced after applying molecular biology techniques could cause long-standing infection and cause the same disease as the one observed in humans.

**Keywords:** Diagnosis; Discovery; Elimination; Hepatitis C; Nobel prize; Treatment; World Health Organization initiative.

Review Brain Sci. 2022 Oct 18;12(10):1405. doi: 10.3390/brainsci12101405.

# Alzheimer's Disease and SARS-CoV-2: Pathophysiological Analysis and Social Context

## Abstract

The COVID-19 pandemic has proven to be a challenge for healthcare systems, especially in terms of the care of patients with Alzheimer's disease (AD). Age is one of the major risk factors for severe forms of COVID-19, most probably due to the presence of comorbidities and inflammations. It is known that SARS-CoV-2 invades nerve endings and olfactory nerves through the binding of the spike protein to the angiotensin-converting enzyme 2 (ACE2) receptor. This interaction triggers an inflammatory cascade that results in cognitive impairment. In turn, the isoform of apolipoprotein-E4 (APOE-4ε) in AD is a risk factor for increased neuroinflammation through microglia activation, increased oxidative stress, and neurodegeneration. AD and SARS-CoV-2 are associated with increases in levels of inflammatory markers, as well as increases in levels of APOE-4ε, ACE2 and oxidative stress. Thus, there is a synergistic relationship between AD and SARS-CoV-2. In addition, the social isolation and other health measures resulting from the pandemic have led to a higher level of anxiety and depression among AD patients, a situation which may lead to a decline in cognitive function. Therefore, there is a need to develop strategies for keeping the patient calm but active.

**Keywords:** Alzheimer’s disease; COVID-19; SARS-CoV-2; inflammation; neurodegeneration; social behavior; social support.

Rev Invest Clin. 2022 Oct 25. doi: 10.24875/RIC.22000146. Online ahead of print.

# What did we learn about coronavirus disease-19-associated acute kidney injury during the pandemic?

## Abstract

Initial reports suggested that kidney involvement after coronavirus disease 19 (COVID-19) infection was uncommon, but this premise appears to be incorrect. Acute kidney injury can occur through various mechanisms and complicate the course of up to 25% of patients with COVID-19 hospitalized in our Institution, and of over 50% of those on invasive mechanical ventilation. Mechanisms of injury include direct kidney injury and predominantly tubular, although glomerular injury has been reported, and resulting from severe hypoxic respiratory failure, secondary infection, and exposure to nephrotoxic drugs. The mainstay of treatment remains the prevention of progressive kidney damage and, in some cases, the use of renal replacement therapy. Although the use of blood purification techniques has been proposed as a potential treatment, results to date have not been conclusive. In this manuscript, the mechanisms of kidney injury by COVID-19, risk factors, and the mainstays of treatment are reviewed.

Front Public Health. 2022 Oct 11;10:932010. doi: 10.3389/fpubh.2022.932010. eCollection 2022.

# Preventive measures against the COVID-19 pandemic in Mexico: A cross-sectional study

## Abstract

**Introduction:** Understanding how Mexicans behave during the pandemic could present a complete picture of the phenomenon in our country and provide better management of it.

**Objective:** This study aimed to analyze the Mexican population's behavior and preventive measures.

**Methods:** This was a cross-sectional study in which a total of 4,004 participants from the general population responded to the survey.

**Results:** Almost 99% of the participants mentioned knowing the symptoms of COVID-19. Although 77.5% of participants considered that they followed proper social distancing measures, 60% of them mentioned that they knew at least six individuals who did not follow social distancing measures. Furthermore, 96.2% of participants reported using preventive measures at least 50% of the time. Only 51.3% used a certified mask.

**Conclusion:** The COVID-19 pandemic outcomes in Mexico are the result of multiple negative factors, such as high rates of comorbidities, high number of people living together at home, many people breaking social isolation, and most of the population using non-certified preventive measures that may not be effective enough.

**Keywords:** COVID-19; Mexico; health behavior; pandemic; risk-taking.

Eur Respir J. 2022 Oct 13;2101870. doi: 10.1183/13993003.01870-2021. Online ahead of print.

# A Randomised trial of anti-GM-CSF Otilimab in severe COVID-19 pneumonia (OSCAR)

**Abstract** BACKGROUND: Granulocyte-macrophage colony-stimulating factor (GM-CSF) and dysregulated myeloid cell responses are implicated in the pathophysiology and severity of coronavirus disease 2019 (COVID-19).

**Methods:** In this randomised, sequential, multicentre, placebo-controlled, double-blind study, adults aged 18-79 years (Part 1) or ≥70 years (Part 2) with severe COVID-19, respiratory failure, and systemic inflammation (elevated C-reactive protein/ferritin) received a single intravenous infusion of otilimab 90 mg (human anti-GM-CSF monoclonal antibody) plus standard care. The primary outcome was the proportion of patients alive and free of respiratory failure at Day 28.

**Results:** In Part 1 (N=806 randomised 1:1 otilimab:placebo), 71% of otilimab-treated patients were alive and free of respiratory failure at Day 28 *versus* 67% who received placebo; the model-adjusted difference of 5.3% was not statistically significant (95% CI -0.8, 11.4; p=0.09). A nominally significant model-adjusted difference of 19.1% (95% CI 5.2, 33.1; p=0.009) was observed in the predefined 70-79 years subgroup, but this was not confirmed in Part 2 (N=350 randomised) where the model-adjusted difference was 0.9% (95% CI -9.3, 11.2; p=0.86). Compared with placebo, otilimab resulted in lower serum concentrations of key inflammatory markers, including the putative pharmacodynamic biomarker CCL17, indicative of GM-CSF pathway blockade. Adverse events were comparable between groups and consistent with severe COVID-19.

**Conclusions:** There was no significant difference in the proportion of patients alive and free of respiratory failure at Day 28. However, despite the lack of clinical benefit, a reduction in inflammatory markers was observed with otilimab, in addition to an acceptable safety profile.

Enferm Infecc Microbiol Clin (Engl Ed). 2022 Oct;40(8):445-448. doi: 10.1016/j.eimce.2021.01.008.

# Analysis of biofilm production and expression of adhesion structures of circulating Clostridioides difficile strains from Mexico

## Abstract

**Introduction:** Clostridioides difficile biofilms are believed to protect the pathogen from antibiotics, in addition to potentially contributing to recurrent infections.

**Methodology:** Biofilm production of 102 C. difficile isolates was determined using the crystal violet staining technique, and detachment assays were performed. The expression levels of cwp84 and slpA genes were evaluated by real-time PCR on selected isolates.

**Results:** More than 70% of isolates (75/102) were strong biofilm producers, and the highest detachment of biofilm was achieved with the proteinase K treatment (>90%). The overall mean expression of cwp84 was higher in RT027 than in RT001 (p=0.003); among strong biofilm-producing strains, the slpA expression was lower in RT027 than in RT001 (p<0.000).

**Conclusions:** Proteins seem to have an important role in the biofilm's initial adherence and maturation. slpA and cwp84 are differentially expressed by C. difficile ribotype and biofilm production level.

Review Int J Mol Sci. 2022 Oct 14;23(20):12324. doi: 10.3390/ijms232012324.

# Role of Micronutrients and Gut Microbiota-Derived Metabolites in COVID-19 Recovery

## Abstract

A balanced and varied diet provides diverse beneficial effects on health, such as adequate micronutrient availability and a gut microbiome in homeostasis. Besides their participation in biochemical processes as cofactors and coenzymes, vitamins and minerals have an immunoregulatory function; meanwhile, gut microbiota and its metabolites coordinate directly and indirectly the cell response through the interaction with the host receptors. Malnourishment is a crucial risk factor for several pathologies, and its involvement during the Coronavirus Disease 2019 pandemic has been reported. This pandemic has caused a significant decline in the worldwide population, especially those with chronic diseases, reduced physical activity, and elder age. Diet and gut microbiota composition are probable causes for this susceptibility, and its supplementation can play a role in reestablishing microbial homeostasis and improving immunity response against Coronavirus Disease 2019 infection and recovery. This study reviews the role of micronutrients and microbiomes in the risk of infection, the severity of disease, and the Coronavirus Disease 2019 sequelae.

Int J Vitam Nutr Res. 2022 Oct 24. doi: 10.1024/0300-9831/a000771. Online ahead of print.

# CD36 polymorphism, sugary drinks, and sedentarism are associated with hypertriglyceridemic waist phenotype

## Abstract

*Background:* The hypertriglyceridemic waist (HTGW) phenotype is characterized by concomitant increases in waist circumference (WC) and blood triglyceride levels (TG), which has been identified as a predictor of metabolic disorders. This study aimed to analyze associations between food consumption, exercise, and the *CD36* gene rs1761667 G>A polymorphism with the HTGW phenotype in adult Mexicans. *Methods:* This cross-sectional study included a total of 255 participants (both genders, between 18-64 years of age). The HTGW phenotype was defined as WC >88 cm in women, WC >102 cm in men, and TG >150 mg/dL. Body composition was analyzed by electrical bioimpedance. Dietary intakes (macro and micronutrients) were evaluated through a validated 64-item food frequency questionnaire and a 24-h recall. Physical exercise was subjectively recorded asking the participants if they regularly performed some systematic exercise or sport of moderate intensity at least 150-300 minutes a week. Biochemical tests were determined by an automated system. A Taqman real-time assay was used to detect the rs1761667 (G>A) polymorphism of the *CD36* gene. A multivariate logistic regression model was performed to analyze the variables potentially associated with the HTGW phenotype (adjusted for age, energy intake, and total fat mass). *Results:* Overall, 21.6% of the population presented the HTGW phenotype; compared to the HTGW-, also, they were older, had more body fat, higher glucose, cholesterol and insulin levels, and high blood pressure. Female sex (OR=2.92, 95% CI: 1.12-7.60, p=0.028), body mass index (OR=1.19, 95% CI: 1.07-1.32, p=0.001), total cholesterol (OR=1.01, 95% CI:1.00-1.02, p=0.039), daily consumption of sugary drinks (OR=6.94, 95% CI: 1.80-26.8, p=0.005), and the *CD36* AG genotype (OR=3.81, 95% CI: 1.08-13.4, p=0.037) were positively associated with the HTGW phenotype, while performing exercise played a protective role (OR=0.23, 95% CI: 0.08-0.62, p=0.004). Overall, the model predicted HTGW phenotype in 47% (R2=0.47, p≤0.001). *Conclusion:* The *CD36* AG genotype, daily consumption of sugary drinks and sedentarism are risk factors for HTGW phenotype in Mexicans.

J Viral Hepat. 2022 Oct 5. doi: 10.1111/jvh.13758. Online ahead of print.

# Implementation of a re-linkage to care strategy in patients with chronic hepatitis C who were lost to follow-up in Latin America

To achieve WHO's goal of eliminating hepatitis C virus (HCV), innovative strategies must be designed to diagnose and treat more patients. Therefore, we aimed to describe an implementation strategy to identify patients with HCV who were lost to follow-up (LTFU) and offer them re-linkage to HCV care. We conducted an implementation study utilizing a strategy to contact patients with HCV who were not under regular follow-up in 13 countries from Latin America. Patients with HCV were identified by the international classification of diseases (ICD-9/10) or equivalent. Medical records were then reviewed to confirm the diagnosis of chronic HCV infection defined by anti-HCV+ and detectable HCV-RNA. Identified patients who were not under follow-up by a liver specialist were contacted by telephone or email, and offered a medical reevaluation. A total of 10,364 patients were classified to have HCV. After reviewing their medical charts, 1349 (13%) had undetectable HCV-RNA or were wrongly coded. Overall, 9015 (86.9%) individuals were identified with chronic HCV infection. A total of 5096 (56.5%) patients were under routine HCV care and 3919 (43.5%) had been LTFU. We were able to contact 1617 (41.3%) of the 3919 patients who were LTFU at the primary medical institution, of which 427 (26.4%) were cured at a different institutions or were dead. Of the remaining patients, 906 (76.1%) were candidates for retrieval. In our cohort, about one out of four patients with chronic HCV who were LTFU were candidates to receive treatment. This strategy has the potential to be effective, accessible and significantly impacts on the HCV care cascade.

J Epidemiol Glob Health. 2022 Oct 5. doi: 10.1007/s44197-022-00069-x. Online ahead of print.

# Multinational Prospective Cohort Study of Mortality Risk Factors in 198 ICUs of 12 Latin American Countries over 24 Years: The Effects of Healthcare-Associated Infections

## Background: The International Nosocomial Infection Control Consortium (INICC) has found a high ICU mortality rate in Latin America.

**Methods:** A prospective cohort study in 198 ICUs of 96 hospitals in 46 cities in 12 Latin American countries to identify mortality risk factors (RF), and data were analyzed using multiple logistic regression.

**Results:** Between 07/01/1998 and 02/12/2022, 71,685 patients, followed during 652,167 patient-days, acquired 4700 HAIs, and 10,890 died. We prospectively collected data of 16 variables. Following 11 independent mortality RFs were identified in multiple logistic regression: ventilator-associated pneumonia (VAP) acquisition (adjusted odds ratio [aOR] = 1.17; 95% CI: 1.06-1.30; p < 0.0001); catheter-associated urinary tract infection (CAUTI) acquisition (aOR = 1.34; 95% CI: 1.15-1.56; p < 0.0001); older age, rising risk 2% yearly (aOR = 1.02; 95% CI: 1.01-1.02; p < 0.0001); longer indwelling central line(CL)-days, rising risk 3% daily (aOR = 1.03; 95% CI: 1.02-1.03; p < 0.0001); longer indwelling urinary catheter(UC)-days, rising risk 1% daily (aOR = 1.01; 95% CI: 1.01-1.26; p < 0.0001); higher mechanical ventilation (MV) (aOR = 6.47; 95% CI: 5.96-7.03; p < 0.0001) and urinary catheter-utilization ratio (aOR = 1.19; 95% CI: 1.11-1.27; p < 0.0001); lower-middle level income country (aOR = 2.94; 95% CI: 2.10-4.12; p < 0.0001); private (aOR = 1.50; 95% CI: 1.27-1.77; p < 0.0001) or public hospital (aOR = 1.47; 95% CI: 1.24-1.74; p < 0.0001) compared with university hospitals; medical hospitalization instead of surgical (aOR = 1.67; 95% CI: 1.59-1.75; p < 0.0001); neurologic ICU (aOR = 4.48; 95% CI: 2.68-7.50; p < 0.0001); adult oncology ICU (aOR = 3.48; 95% CI: 2.14-5.65; p < 0.0001); and others.

**Conclusion:** Some of the identified mortality RFs are unlikely to change, such as the income level of the country, facility ownership, hospitalization type, ICU type, and age. But some of the mortality RFs we found can be changed, and efforts should be made to reduce CL-days, UC-days, MV-utilization ratio, UC-utilization ratio, and lower VAPs and CAUTI rates.

Ann Hepatol. 2022 Nov-Dec;27(6):100767. doi: 10.1016/j.aohep.2022.100767. Epub 2022 Oct 9.

# Whole-Exome Sequencing identified Olfactory Receptor genes as a key contributor to extreme obesity with progression to nonalcoholic steatohepatitis in Mexican patients: Olfactory receptor genes in obese NASH patients

## Abstract

**Introduction and objectives:** Obesity is a global health problem that triggers fat liver accumulation. The prevalence of obesity and the risk of non-alcoholic steatohepatitis (NASH) among young obese Mexican is high. Furthermore, genetic predisposition is a key factor in weight gain and disrupts metabolism. Herein, we used Whole-Exome Sequencing to identify potential causal variants and the biological processes that lead to obesity with progression to NASH among Mexican patients.

**Materials and methods:** Whole-Exome Sequencing was performed in nine obese patients with NASH diagnosis with a BMI ≥30 kg/m2 and one control (BMI=24.2 kg/m2) by using the Ion S5TM platform. Genetic variants were determined by Ion Reporter software. Enriched GO biological set genes were identified by the WebGestalt tool. Genetic variants within ≥2 obese NASH patients and having scores of SIFT 0.0-0.05 and Polyphen 0.85-1.0 were categorized as pathogenic.

**Results:** A total of 1359 variants with a probable pathogenic effect were determined in obese patients with NASH diagnosis. After several filtering steps, the most frequent pathogenic variants found were rs25640-HSD17B4, rs8105737-OR1I1, rs998544-OR5R1, and rs4916685, rs10037067, and rs2366926 in ADGRV1. Notably, the primary biological processes affected by these pathogenic variants were the sensory perception and detection of chemical stimulus pathways in which the olfactory receptor gene family was the most enriched.

**Conclusions:** Variants in the olfactory receptor genes were highly enriched in Mexican obese patients that progress to NASH and could be potential targets of association studies.

Molecules. 2022 Oct 10;27(19):6741. doi: 10.3390/molecules27196741.

# Steroid Resistance Associated with High MIF and P-gp Serum Levels in SLE Patients

Approximately 30% of patients with systemic lupus erythematosus (SLE) present steroid resistance (SR). Macrophage migration inhibition factor (MIF) and P-glycoprotein (P-gp) could be related to SR. This work aims to evaluate the relationship between MIF and P-pg serum levels in SR in SLE.

**Methods:** Case-control study including 188 SLE patients who were divided into two groups (90 in the steroid-resistant group and 98 in the steroid-sensitive (SS) group) and 35 healthy controls. MIF and P-gp serum levels were determined by ELISA. Multivariable logistic regression and chi-squared automatic interaction detection (CHAID) were used to explore risk factors for SR.

**Results:** The steroid-resistant group presented higher MIF and P-gp serum levels in comparison with the SS (*p* &lt; 0.001) and reference (*p* &lt; 0.001) groups. MIF correlated positively with P-gp (rho = 0.41, *p* &lt; 0.001). MIF (≥15.75 ng/mL) and P-gp (≥15.22 ng/mL) were a risk factor for SR (OR = 2.29, OR = 5.27). CHAID identified high P-gp as the main risk factor for SR and high MIF as the second risk factor in those patients with low P-gp.

**Conclusions:** An association between MIF and P-gp serum levels was observed in SR. CHAID identified P-gp ≥ 15.22 ng/mL as the main risk factor for SR. More studies are needed to validate these results.

Gastroenterol Hepatol. 2022 Oct 12;S0210-5705(22)00233-3. doi: 10.1016/j.gastrohep.2022.10.007. Online ahead of print.

# Gastrointestinal symptoms and complications in patients hospitalized due to COVID-19, an international multicentre prospective cohort study (TIVURON project)

**Background:** retrospective studies suggest that coronavirus disease (COVID-19) commonly involves gastrointestinal (GI) symptoms and complications. Our aims was to prospectively evaluate GI manifestations in patients hospitalized for COVID-19.

**Methods:** this international multicentre prospective cohort study recruited COVID-19 patients hospitalized at 31 centres in Spain, Mexico, Chile, and Poland, between May-September 2020. Patients were followed-up until 15 days post-discharge and completed comprehensive questionnaires assessing GI symptoms and complications. A descriptive analysis as well as a bivariate and multivariate analysis were performer using binary logistic regression. P<0.05 was considered significant.

**Results:** eight hundred twenty-nine patients were enrolled; 129 (15.6%) had severe COVID-19, 113 (13.7%) required ICU admission, and 43 (5.2%) died. Upon admission, the most prevalent GI symptoms were anorexia (n=413; 49.8%), diarrhoea (n=327; 39.4%), nausea/vomiting (n=227; 27.4%), and abdominal pain (n=172; 20.7%), which were mild/moderate throughout the disease and resolved during follow-up. One-third of patients exhibited liver injury. Non-severe COVID-19 was associated with ≥2 GI symptoms upon admission (OR 0.679; 95% CI 0.464-0.995; p=0.046) or diarrhoea during hospitalization (OR 0.531; 95% CI 0.328-0.860; p=0.009). Multivariate analysis revealed that worse hospital outcomes were not independently associated with liver injury or GI symptoms