Long Covid and Liver Injury AKA PASC: Post Acute Sequelae of SARS-CoV-2 (COVID-19) Infection

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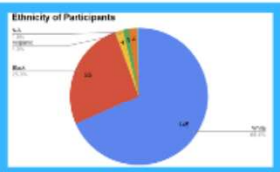
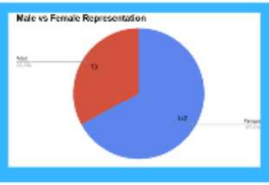
Introduction

Long Covid is a complex, multi-organ illness that occurs in individuals with a history of SARS-CoV-2 infection, with onset and persistence occurring usually 3 months from the onset of COVID-19 with symptoms that last for months or years and cannot be explained by an alternative diagnosis (WHO), It is believed that long Covid typically results from ongoing inflammatory changes in multiple tissues1. The Long Covid patients require need for multiple specialists. Long Covid is likely to impact 80% of those infected with h/o Sars Cov 19 infection with at least one symptom and can linger on. Fatigue is the most reported symptom of long COVID2. More severe cases involve damage to a variety of organ systems primarily from ongoing inflammatory processes in the lungs, heart, nervous system, kidneys, and liver, thrombotic and cerebrovascular disease, type 2 diabetes, myalgic encepha- lomyelitis/chronic fatigue syndrome dysautonomia, postural orthostatic tachycardia syndrome (POTS) as well as along with mental health impairment3-4. The pathophysiological pathways may involve direct consequences of the post infectious inflammatory or autoimmune responses5. More than 200 symptoms have been identified to be associated with long COVID. It is also believed that Long Covid triggers 25% increase in prevalence of anxiety and depression worldwide6.

Tissue injury from SARS-CoV-2 results from interaction with the primary host receptor through attaching to the angiotensin-converting enzyme 2 (ACE2) receptor.8 Cells that express more ACE2 receptors are more vulnerable to SARS-CoV-27.ACE2 is expressed in various organ systems, including lung tissue (specifically type II alveolar cells), the nervous, cardiovascular and gastrointestinal system, kidneys, endothelium, and the liver.8Because of the wide range of organ systems that express ACE2, research has been carried to investigate the potential health effects that SARS-CoV-2 might have on the liver, 9-10 gastrointestinal tract,16 cardiovascular and nervous system, kidneys and the respiratory system11.

COVID-19-associated liver injury can be defined as any liver damage that occurs during the course and treatment of COVID-19, with or without pre-existing liver disease12, and it might be either reversible or irreversible with prolonged deficits. In the liver, ACE2 is highly expressed in the endothelial layer of small blood vessels and in cholangiocytes, with a less significant amount expressed in hepatocytes.13Due to different liver cell types expressing ACE2 in varying quantities and the liver being highly influenced by other organ systems and medications, the spectrum of potential pathological mechanisms of liver injury is broad. It includes direct cytotoxicity from active viral replication of SARS-CoV-2 in the liver,14 immunemediated liver damage, vascular impairment due to coagulopathy, endothelitis or cardiac congestion, respiratory failure induced hypoxic changes, drug induced liver injury and exacerbation of an underlying chronic liver disease.14 On the cellular level COVID-19 associated liver injury is two-fold. Firstly, it is caused by hepatocellular damage, mainly characterized by moderate steatosis, lobular and portal inflammation, and zones of apoptosis/necrosis, which causes elevation of plasma alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Secondly, it causes cholangiocellular damage that affects the bile ducts and results in a rise of gamma-glutamyl transferase (GGT) and bilirubin fractions among others.
We at the CBCCA and NOLA (no one left alone) team decided to carry out a retrospective analysis of liver scans performed over a period of six months in 2024 to identify liver abnormalities and correlate them to the SDoH (Social Determinants of Health).



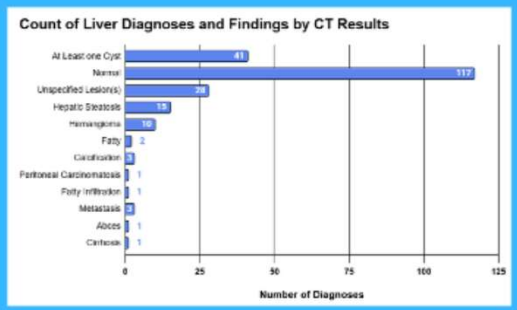


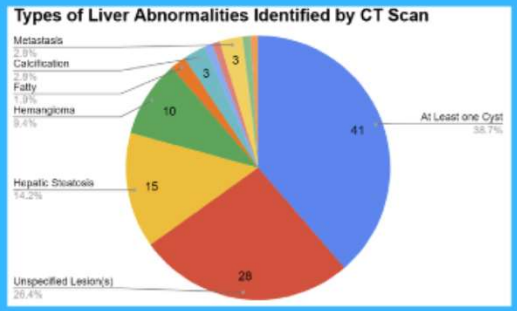
Objectives

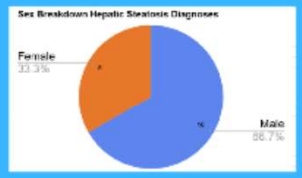
This study aimed to define patterns of liver injury after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection using Computed tomography (CT scans) with intravenous contrast in a variable patient population with differing severities of COVID-19.
Type: Retrospective observational

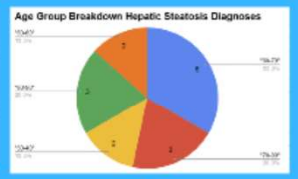
Methods

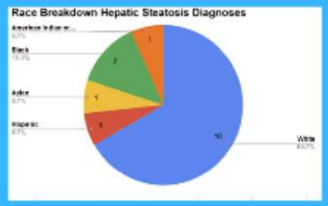
213 were enrolled into the study: All patients underwent CT evaluation of the liver All patients were screened for biochemical markers of liver injury. Here are detailed analysis of findings
This study had appropriate representation of ethnic population. Surprisingly, there were more than half of the female representation.











Summary of results and future implications:

Close to half of the patients (48%) were identified to have hepatic abnormalities in this retrospective observational study. We also noticed that higher number of women had Liver steatosis. Surprisingly there was no correlation with Increased biochemical markers of liver injury with findings on CT. Patients with more severe forms of COVID-19 and patient obesity had increased values of liver damage observed. We did not find any difference in the pattern of liver injury based on racial or ethnic origin. However, our finding may be limited and in conclusive due to small number of patients. Further research is warranted to establish this promising method for evaluating post-COVID-19 liver involvement in the aftermath of the pandemic.
Due to the main pathogenic mechanism of cell invasion of SARS-CoV-2, which is through binding to ACE2 receptors, the liver is among the first-line targets of cell injury in COVID-19 by its high expression of ACE2.The potential mechanisms of liver injury in COVID-19 are multifaceted, including inflammation, steatosis, and biliary duct damage. Liver injury caused by COVID-19 can be assessed by using biochemical markers as well as imaging modalities such as US, MR and CT.

Population Health Impact with Long Covid29-31

With more than 600 million individuals infected with Covid-19 it is estimated that least 65 million individuals around the world have long COVID, based on a conservative estimated incidence of 10% of infected people. In the USA over 100 million COVID infections are have occurred by the fall and winter of 2022-23 in the USA. With estimated 15-30% of those infected will develop Long COVID, it is postulated that 7% or close to 15 millio million Americans have been impacted by long COVID. Long COVID outpaces Diabetes in terms of cost per member for a given health plan (Beckers Payer). Long COVID is associated with all ages and acute phase disease severities, with the highest percentage of diagnoses between the ages of 36 and 50 years, and most long COVID cases are in non-hospitalized patients with a mild acute illness.

Summary:

This study presents a compelling case for the urgent need to investigate the intricate relationship between Long COVID, inflammation, and liver injury. We recognize the potential implications of this emerging health crisis and the impact it may have on patients' long-term well-being. By analyzing various aspects such as cardiovascular disease, neurological complications, health care disparities, and the impact of long COVID on chronic comorbidities, we aim to shed light on the broader population health impact of this condition. Additionally, we explore the role of COVID-19, mitochondria, miRNA, methylation, and viruses in the context of chronic liver injuries and well as potential of inflammation associated newer hepatobiliary neoplasms and the associated healthcare costs. Finally, we examine the trends in new cancer patients among community cancer patients before and after the COVID-19 pandemic. By shedding light on these interconnected areas, we aim to encourage oncologists and pharmaceutical companies to support research efforts and collaborate in seeking effective treatments for this complex condition.

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