Gastroenterological Aspects of COVID-19 Infection: A Review Article

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ABSTRACT

The coronavirus outbreak has shifted the medical community's focus. A novel coronoviridae variant (COVID-19) was found in Wuhan, China, in December 2019. Initially, an infection causes a wide range of symptoms, including muscle aches, fever, dry cough, and shortness of breath. COVID-19 infection affects all gastrointestinal system organs because it aims to hit the ACE2 receptor (angiotensin-converting enzyme 2), which is located in intestinal epithelial cells in the human body and liver cells. Coronavirus-caused liver damage often causes decreased albumin and increased aminotransferase and bilirubin. Pathophysiological hypotheses include direct damage, immune-mediated injury, ischemia and hypoxia, thrombosis, and medication hepatotoxicity. The harm is most likely multifactorial, and infected patients with preexisting liver illnesses should be managed accordingly. A vaccine will be required to help reduce COVID-19 cases and provide immunity to the public. However, safety considerations, particularly for RNA- or DNA-based vaccines, must be addressed when assessing the types of vaccines accessible. The effects of severe COVID-19 infection on gastrointestinal symptoms and liver damage in patients with chronic gastrointestinal disease are discussed in this study.

Keywords: COVID-19, Gastrointestinal Manifestation, Angiotensin-converting enzyme 2, Liver Injury, Viral damage

INTRODUCTION

World health organization has named this virus as COVID-19 after the pandemic[1]. Following that, a cascade of knowledge on this novel virus hit gastroenterologists, much of it relevant and clinically useful. COVID-19 was assumed to be a respiratory disease, but new research shows it can affect the stomach function. This review compiles the essential material about the digestive system and will be published until May 2022. Moreover, 521 million patients of COVID-19 were documented worldwide by the time of acceptance (October 2020), with over 6.26 million deaths[2]. The COVID-19 virus is a member of the coronavirus (SARS) family. It is a single-stranded RNA virus that was initially characterized as a fatal acute respiratory virus[3]. It is similar to the viruses that caused the SARS epidemic in China in 2002–2004 and the MERS epidemics in the Middle East from 2012–to 2020. COVID-19 shares a close relationship with bat coronaviruses, implying a zoonotic origin. The virus spreads through droplets and aerosols. COVID-19 was isolated from feces, although fecal-oral transmission is undetermined. This article examines the current COVID-19 features of gastroenterology, pathogenesis, Symptoms of Covid-19, and liver injury. Because knowledge about this virus is continually evolving, readers are recommended to frequently keep up updated.

ORIGIN OF COVID-19

Wuhan, China, reported a cluster of pneumonia cases to the Chinese CDC on December 31, 2019. The cause was COVID-19 (previously 2019-nCoV)[4]. The infection initiated in the Huanan seafood and animal market in Wuhan, Hubei Province, giving evidence of animal-to-human transmission through the sale of seafood and live animals[5,6]. After that, the virus was found in a rising number of Wuhan residents who had not been to animal markets, indicating person-to-person transmission[5,6]. The novel coronavirus was highly contagious, spreading around the globe in just 2-3 months. Since March 2020, the number of COVID-19-related cases and deaths has surged exponentially outside of China[7,8]. To this point, new COVID cases have been documented in 213 countries and territories[8]. The Worldwide Health Regulations Emergency Committee declared a public health emergency of international concern (PHEIC) on January 30, 2020[9]. In addition, the World Health Organization (WHO) designated this coronavirus illness as a pandemic on March 11, 2020, and they gave it the name COVID-19 on February 19, 2020[4,10]. As of June 8, 2020, 7 million cases and 400 thousand deaths have been reported globally. COVID-19 has produced catastrophic human and health disasters and a global financial crisis.

VIRAL STRUCTURE AND CELLULAR ENTRY

Corona-viruses are larger, enclosed, single-stranded, positive-sense RNA viruses[9]. In addition to spike (S), envelope (E), membrane (M), and nucleocapsid (N) proteins, they contain four structural proteins[11]. The S protein is a crucial determinant of pathogenicity and host specificity and a target for neutralizing antibodies. As a result, scientists working on potential vaccines are pretty interested in it. Random homologous and non-homologous mutations and recombination allow the virus to effortlessly transcend the species barrier and cause cross-species infection. Coronaviruses are extremely infective across significant taxonomic distances due to a large pool of animal reservoirs, particularly bats, genetic recombination, and the capacity to exploit numerous receptors[12].

The S protein must attach to the transmembrane ACE2 host receptor for viral cell entrance (Figure 1). Almost every cell in the body expresses the ACE2 receptor. The S protein comprises two different subunits: S1, which is responsible for recognizing the ACE2 protein, and S2, which is responsible for fixing the protein to the host cell membrane and facilitating viral fusion[13-15]. The ACE2 receptor has a high binding affinity for COVID-19, and activation of ACE is not required for virus binding and endocytosis. After endocytosis, the virus takes over the cellular machinery to create viral RNA and viral-specific proteins. The virus is built inside the cells before being secreted. Viral secretion in the GI tract is accompanied by the production of cytokines, which causes symptoms.

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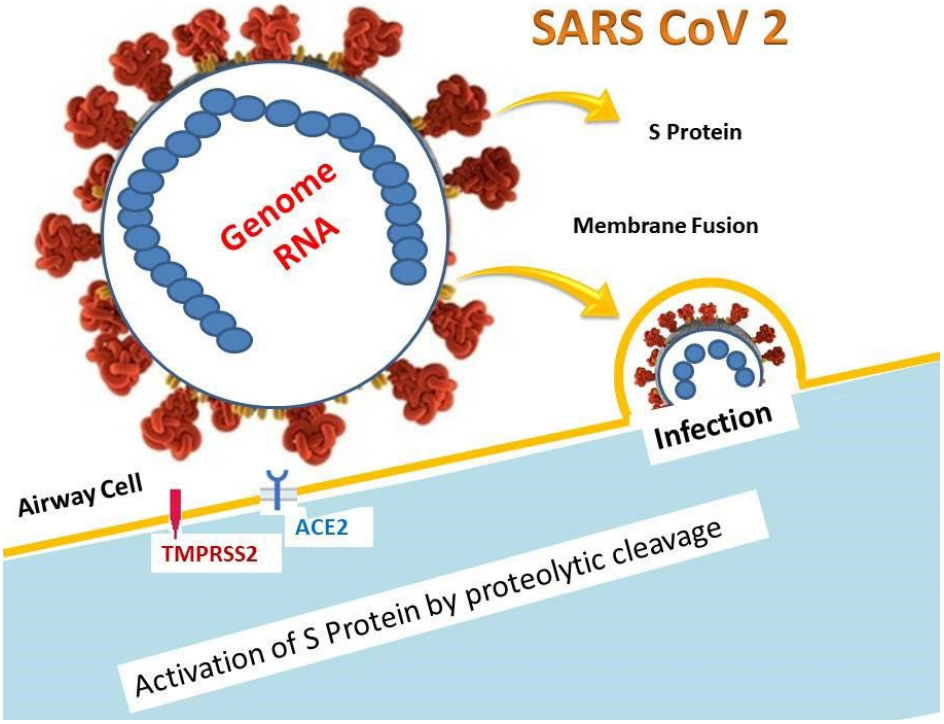

Figure 1: Viral invasion into human cells. SARS-CoV-2 spike proteins attach to ACE 2 proteins on the target cell, while TMPRSS2 binds to and cleaves the ACE 2 receptor. The spike protein is triggered during this process. Infection is facilitated by cleaved ACE 2 and activated spike protein.

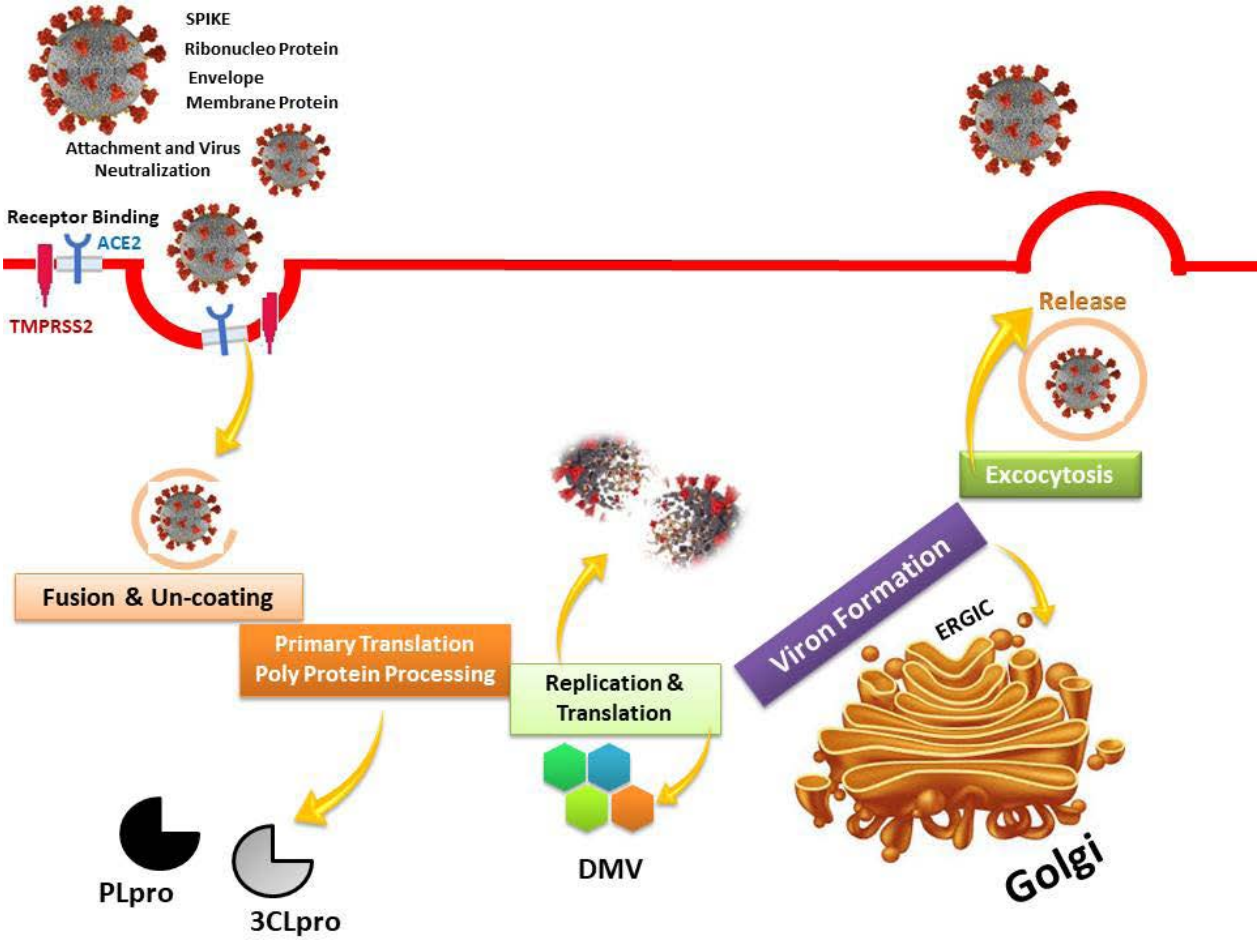

Figure 2: Pathogenesis of COVID-19 Liver

In ciliated goblet and surfactant-producing type 2 alveolar cells, high ACE2 receptor expression is found, allowing the virus to enter the body[16,17] The intestinal epithelium[18] and the cardiac and vascular endothelium have high ACE2 expression, which may explain why COVID-19 causes complications in these organ systems[19].

PATHOGENESIS

It is becoming more evident that the viruses' ability to connect with ACE 2 receptor, that allows entrance into the epithelial cells, is crucial for significant disease outcomes. This can lead to a severe hyperimmune response in the lungs, which can cause a cytokine storm and systemic inflammatory response syndrome, both of which are life-threatening[20,21]. The coat of spike protein is activated by the cellular transmembrane serine protease 2 (TMPRSS-2)[22] allows the virus to enter epithelial cells. The mechanism is the same in the gastrointestinal system, and hospitalized patients with COVID-19 illness had a virus in their stool. GI epithelial cells had the ACE 2 receptor identified in their cytoplasm. The nucleocapsid protein of the virus was detected in the cytoplasm of stomach, duodenal, and rectal glandular epithelial cells but not in the oesophageal epithelial cells[23]. Age, inflammation, and disease location influence ACE 2 expression in inflammatory bowel disease (IBD). The terminal ileum expressed more ACE 2 than the colon, whereas the colon expressed more ACE 2 than the terminal ileum[24]. The Mechanism of Pathogenesis with COVID-19 is shown in (Figure 2).

SYMPTOMS OF COVID-19

COVID-19 affected persons may experience symptoms between 2 to 14 days. However, this disease can also manifest after 27 days. However, according to Chinese experts, the average incubation time is 5.2 days[25]. PBL and lymphocytes in the peripheral blood did not change significantly. Viruses typically spread through the lungs, heart, gastrointestinal tract, and bloodstream. Primary lesions grow noticeably worse around 7-14 days, and PBL, comprising both T and B cells, decreases significantly[26]. The time it takes for COVID-19 patients to die ranges from 6 to 41 days, with the median being 14 days[27]. However, the length of time relies on two essential factors: the patient's age and immunological health. It is worth noting that the number of instances in adults over 70 years old is higher than in people under 70 years old[27]. Hemoptysis (bloody diarrhea), dyspnea (breathing difficulties), lymphopenia (swollen lymph nodes), and sputum production are all signs of COVID-19 (Figure 3)[28-30]. Fever, dry cough, and tiredness are the most common symptoms, followed by aches and pain, conjunctivitis, sore throat, diarrhea, headache, loss of taste or smell, skin rash, and finger and toe discolouration (i.e., difficulty during breathing or shortness of breath, chest pain or pressure, and loss of speech or movement). COVID-19 infects children, the elderly, and some individuals with diabetes, cancer, heart problems, or lung disease[31]. COVID-19 individuals had gastrointestinal symptoms, mainly diarrhea, while SARS-CoV and MERS-CoV patients did not. It is vital to evaluate urine and feces symptoms to rule out a transmission pathway via doctors, nurses, and patients[32]. Respiratory distress syndrome patients are very unwell and have respiratory failure, septic shock, and organ failure[29,32,33].

GI MANIFESTATION

In more than half of the reported patients, at least one person has symptoms of hunger, nausea, vomiting, diarrhea, or abdominal discomfort, which affects 11 percent to 53 percent of patients[34]. In an extensive study of 60 studies and 4243 individuals, the rate of GI symptoms was reported to be 17.6%[35]. In a meta-analysis of 47 trials and 10890 participants, nausea/vomiting, diarrhea, and stomach discomfort were the most prevalent GI symptoms[36]. Many common GI conditions included diarrhea (11.5 percent), vomiting, diarrhea, and gastrointestinal problems (6.3 percent) in a meta-analysis of 43 studies including 18246 people (2.3 percent)[37]. Ferm et al., discovered that gastrointestinal disorders such as diarrhea (19.8%), nausea (16.6%), vomiting (10.2%), lack of appetite (11.8%), stomach discomfort (7.8%), and loss of taste (7.8%) were among the most prevalent complaints in their research of 892 participants (2.4 percent). *COVID-19 patients suffered diarrhea, nausea, vomiting, or stomach pain. GI discomfort averaged 3-7 days*[8]. The prevalence of GI symptoms was 19.8% in our research of 430 cases, with nausea/vomiting, stomach discomfort, and diarrhea being the most common (10.4 percent, 6.1 percent, and 2.9 percent, respectively)[38]. Table 1 shows the frequencies of GI symptoms in COVID-19 transmission

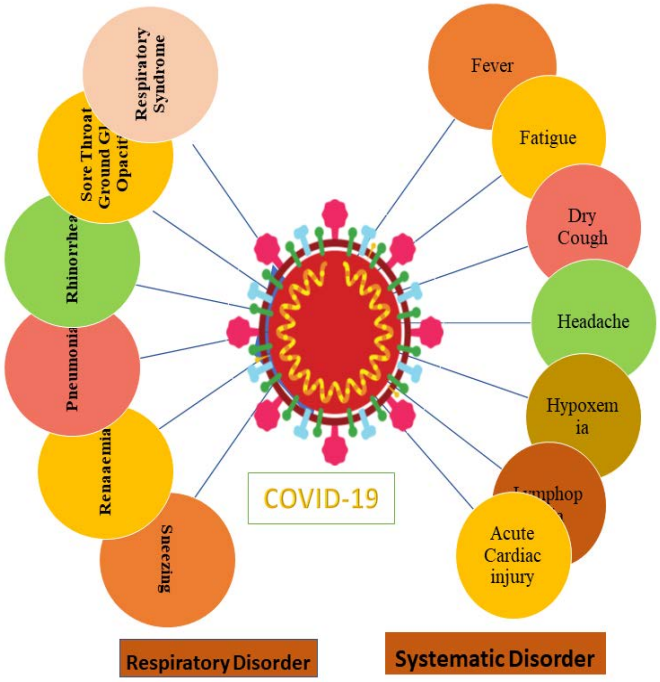

Figure 3: Systematics and Respiratory Symptoms of COVID-19

Table 1: Gastrointestinal manifestations (GI) of COVID-19

GI manifestations	Frequency %
Overall involvement	11 - 79%
Loss of appetite	34 - 67%
Diarrhea	2 - 49.5%
Vomiting	1 – 16%
Nausea	1 – 16%
Abdominal pain	2.7 - 9.2%

LIVER MANIFESTATION

In COVID-19 infections, liver involvement is expected even though COVID-19 is a respiratory virus. By connecting to ACE2 receptors, SARS-CoV-2 penetrates the cell. Many physiological systems, including the lungs, liver, heart, kidney, and blood arteries, contain ACE2 receptors[39,40]. Cholangiocytes (57.7%) express ACE2 receptors more than liver cells (hepatocytes 2.6%)[41]. ACE2 receptor overexpression in cholangiocytes induces liver damage. Bile duct cell injury is thought to cause liver damage[42].

In COVID-19 infection, cholestatic hepatitis is not the typical liver involvement pattern[40,41]. Females had greater levels of hepatic ACE2 receptor expression. This could explain why females have a better

clinical result from COVID-19 infection[41,43]. During infection with COVID-19, liver damage can be caused by several causes, including the direct cytopathic effect of the virus, inflammatory, intrahepatic immune activation, microvascular thrombosis, hepatic congestion, and alteration of the gut liver axis, medication toxicity, and multidrug interactions[43,45]. The causes of liver damage are listed below (Figure 4).

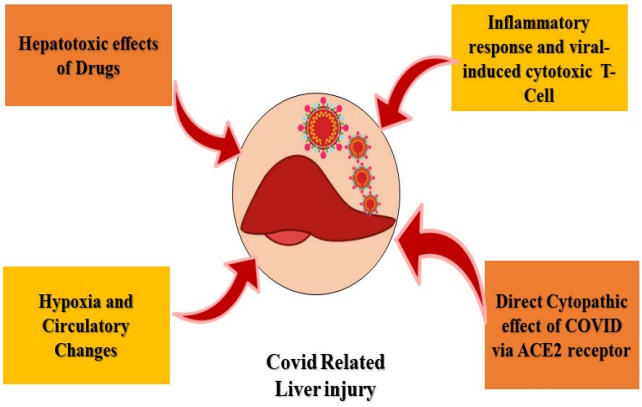

Figure 4: COVID-19 has adverse effects on human organs

Liver harm can be caused by a virus's direct cytopathic action, such as lysis or induction of apoptosis[46-48]. Virus-specific protein 7a activates caspase-dependent apoptosis in lung, kidney, and liver cell lines. The virus was found in liver tissue with a low viral load[49]. It was also discovered that the virus can replicate in hepatocytes and that spike proteins can be identified in the cytoplasm.
These data imply that SARS-CoV-2 may cause hepatocyte cytopathy by directly affecting liver tissue[50]. Wang et al., found that SARS-CoV-2 enlarged mitochondria, dilated the endoplasmic reticulum, reduced glycogen granules, and damaged hepatocyte membranes[51]. The investigation found massive liver apoptosis and binuclear hepatocytes. The ultrastructure and histology revealed a viral infection lesion. Immunohistochemistry detected a few CD4+ and CD8+ lymphocytes. Hepatitis B virus (HBV) infection was not present[51].

Second, proinflammatory cytokines (IL-1, IL-6, TNF) and inflammatory cells generated in response to SARS-CoV-2 infection cause immune-mediated liver damage[34,50,52]. Liver damage is also caused by cytokine storm and mass syndrome. All inflammatory and coagulopathy markers were linked to sickness severity and poor outcome, including IL-2, IL6, chemokines, CRP, ferritin, D-dimer, and lactate dehydrogenase (LDH)[34,52].

Another key pathophysiology of viral infections is virally-induced cytotoxic T cells (CD8)[53]. The leading reason of liver harm in COVID-19 infection is revealed to be coagulation disruption and endothelial damage. In liver biopsy samples from 40 COVID-19 patient autopsies, Lagana et al.,[54] demonstrate mitochondrial expansion, ER dilation, and cell membrane failure. 55% of patients had PCR-positive liver tissue[54]. Histological findings and liver enzymes were associated with PCR positivity and viral load[54]. Post-mortem liver autopsy specimen investigations revealed mild lobular and portal activity[55].

Areas with a high concentration of neutrophils (neutrophils, Kupffer cells, and plasmocytes) degraded water[56,57]. A postmortem assessment of 48 COVID-19 positive patients revealed acute vascular abnormalities like terminal arterial dilatation, thrombosis, luminal ectasia, and chronic alterations like fibrous thickening of the portal sinusoidal vein walls[57]. COVID-19 patients had intranuclear or intracytoplasmic viral inclusions. There was no evidence of bile duct injury or liver failure in liver samples from severe COVID-19 individuals[58].

Direct viral impact, hypoxia, or medications can all cause histopathological alterations. Antivirals, anti-inflammatory drugs, anticoagulants, antibiotics, and other medications needed to address underlying chronic illnesses and those used meanwhile in COVID-19 condition will play a role in liver damage[42,50]. Hepatotoxicity has been linked to the use of multiple drugs and their combinations.

Hypoxia caused by pneumonia is another prominent cause of liver damage. Hypoxic liver damage can occur even with oxygen therapy. Gut vascular barrier and dysbiosis also contribute to liver injury from opportunistic microorganisms' toxic chemicals (microbiota changes). Chronic liver illness may increase liver damage (CLD). CLD increased the probability of hospitalization and COVID-19 pandemic[34].

As for CLD, moderate hepatitis has been seen with COVID-19 infection. Nearly half of COVID-19 patients' pathologic liver function test values increased[14,42]. In difficult situations, liver damage can occur[42,58]. Elevated liver enzymes and reduced albumin indicate hepatic involvement and sometimes elevated bilirubin. Tests for liver injury include elevated levels of AST, ALT, ALP, gamma-glutamyl transferase (GGT), LDH, hyperbilirubinemia, prolonged prothrombin time, and hypoalbuminemia. Parenchymal, cholestatic, and mixed types of changes in liver function tests exist. ALT and AST readings in the parenchymal form are 3-fold higher than the upper limit of normal (ULN); ALP or GGT values are 2-fold higher than in the cholestatic form ULN; and in the mixed type, both parenchymal and cholestatic diseases are present. In COVID-19 infection, the incidences of parenchymal, cholestatic, and mixed form liver damage were 75 percent, 29.2 percent, and 43.4 percent, respectively. The hepatocellular pattern was identified in most cases, and ALT-AST values rarely exceeded 5 ULN[45]. Elevations of ALT and AST were 15.0 percent and 20 percent in countries other than China in a meta-analysis involving 47 studies and 10890 patients[59].

Raises in ALT and AST occurred at rates ranging from 2.5 percent -50.0 percent to 2.5 percent -61.1 percent[22]. In a case series of 1100 patients with COVID-19 infection, severe cases had higher AST and ALT values (56 percent and 28 percent, respectively) than mild-moderate cases (18 percent and 29 percent)[51]. The AST level has been linked to mortality[52]. Another study discovered that AST/ALT, LDH, and bilirubin levels increased by 25%, 20%, and 3%, respectively. However, in the same study, ALP was reported as normal in virtually all individuals. COVID-19 did not show a significant increase in bilirubin or ALP levels. Bilirubin elevation rates have ranged from 0% to 35.3%[50]. Total bilirubin levels were elevated in 16.7% of COVID-19 patients from China[59]. Increased bilirubin levels peaked 5 days (4 to 12 days) following discharge. Male patients were more likely to have hyperbilirubinemia and high ALT, ALP, and GGT levels, although males were also more likely to have hypoalbuminemia[57]. ALP and GGT tests are standard, although 37.6% of NAFLD patients had elevated GGT[42], in another study, 41% of patients had increased GGT levels, but severe cases often do[41]. Even though a study found higher GGT levels in 41% of patients, GGT levels normally rise in severe illness[42,48]. GGT elevation is frequently unrelated to ALP elevation and results from drug toxicity rather than blockage. GGT, a cholangiocyte damage marker, was not elevated in all COVID-19 patients. Only severe patients have high levels[37]. Hypoalbuminemia has been linked to illness severity and catastrophic outcomes[42].

In liver disorders and other viral infections, AST levels typically rise faster than AST, but in COVID-19 infection, AST levels are higher

than ATL[60]. Hepatocyte cell zone 3 damage could cause elevated AST. Zone 3 has the most AST and is the most sensitive to hypoxia. The cytosol and mitochondria both contain AST. Due to the virus's mitochondrial damage, AST production increases. An increase in AST could have been caused by the connection between SARS-CoV-2 and proteins found in the mitochondria. Skeletal muscle, heart, renal, and lung tissues produce AST. As a result, a high AST indicates liver impairment and multiorgan damage. In severe cases of pneumonia, a condition known as hypoxia can cause damage to the liver. An infection with COVID-19 causes damage to multiple organs, including the liver, as a result of a cytokine storm and endothelial stimulation.

In patients with ICU and severe pneumonia, an AST/ALT ratio > 1 was observed to forecast death, critical pneumonia, and the need for intensive care unit (ICU) care[61]. In cirrhotic COVID-19 patients, the AST/ALT ratio, total bilirubin, and ALT/ALP ratio may be used to predict prognosis. The prevalence of liver damage varies between 15% and 53%. Changes in liver function tests have been found in 19 percent to 76 percent of COVID-19 cases[45]. Hepatic injury developed in 23.70 percent of COVID-19 infected patients, 31.66 percent of non-severe patients, and 44.63 percent of severe patients. The severe disease had 39.58 percent and 49.68 percent ALT and AST increases, while non severe disease had 24.15 percent and 19.40 percent. In severe COVID disease, AST levels were higher than ALT levels. The elevated ALP and GGT percentages were 7.48 percent and 27.94 percent, respectively. Elevations of ALP (11.33 percent vs. 4 percent) and GGT (46.90 percent vs. 18.66 percent) were observed to be related to illness severity. Hyperbilirubinemia (31.04 percent vs. 9.24 percent) and hypoalbuminemia (61.27 percent vs. 18.80 percent) were also linked to disease severity. Hypoalbuminemia, according to the investigators, was the most common anomaly. Other liver tests, aside from ALP, were considered abnormal in severe patients[62]. Another meta-analysis showed that patients affected with COVID-19 found that 23.1 percent had liver impairment early on, while 24.4 percent had liver injury later[63]. Liver injury was identified in 48.5 percent of patients within the first two weeks of hospitalization, and it peaked 10 days (7-12) after discharge[64]. In patients with severe pneumonia, liver injury occurs in 26.7 percent of cases[34,65].

A meta-analysis indicated that increased ALT, AST, and bilirubin levels were related to illness severity[66]. A 9-fold greater potential for serious disease, increased critical care requirements, intubation, and mortality is associated with liver injury. It has been suggested that the presence of liver injury at the entrance can serve as an independent prognostic feature for COVID-19[67]. Patients with liver dysfunction died at a higher rate (28.9 % vs. 9.0 %), were male (65.1 % vs. 40.8 %), and had systemic inflammatory response syndrome (28.9 percent vs. 9.0 percent). (53.5 % vs. 41.3%). Males were found to have greater grade-2 liver damage than females. The severity of liver damage was also a predictor of death (hazard ratio: 1.377). ICU patients had a greater rate of liver injury (61.5 percent) than non-ICU patients (25.0 percent)[67]. The fatal cases with altered liver function ranged from 58.06 percent to 78 percent[42].

More extensive hospitalization, illness severity, GGT, ferritin, decreased albumin, CD4+ T cells, and B lymphocytes were linked to liver injury. Patients who died from the infection had considerably lower serum albumin levels. CRP, procalcitonin, IL-6, and ferritin levels have all been linked to liver injury and albumin and platelet levels. Reduced lymphocyte count and male gender were linked to liver damage and deprived outcomes. CT imaging may be used to predict liver damage and a bad result. Acute liver failure caused by COVID-19 infection is relatively uncommon[68]. As a result, SARS-CoV-2 cannot be classified as a hepatotropic virus. In the intensive care unit (ICU), acquiring a subsequent nosocomial infection could fail several organs and have severe systemic implications. Albumin and AST concentrations were associated with the severity of illness, the presence of pneumonia, the requirement for intensive care, and lengthy stays in the hospital in our research. In 9.6% of individuals with liver injury, intensive care was required.

DRUG HEPATOTOXICITY

Although various therapeutic drugs have been tested for COVID-19 therapy, only a handful may be effective. Antiviral medicines that supplement basic supportive care are eagerly sought by researchers around the world. In clinical trials, Remdesivir, an experimental medication, showed in vitro antiviral efficacy against COVID-19 and a faster recovery time[69]. However, due to the lack of experience with remdesivir for COVID-19 treatment, its side effects and potential medication interactions are unknown. After taking remdesivir for five days, a 64-year-old man with COVID-19 saw an abrupt rise in ALT and AST levels[70]. The quick withdrawal of remdesivir led to a rapid return of ALT and AST to normal levels, indicating that remdesivir was the most likely source of hepatic damage. In previous cases of remdesivir use, elevated liver enzymes have been described as a severe adverse medication reaction[69,71]. Some investigations relate this unexpected increase to the effects of infection rather than the drug's side effects, given SARS-hepatotoxicity. CoV-2's[71]. Whether or whether it was impacted by COVID-19, Montastruc et al., hypothesized that remdesivir increased the risk of liver injury when compared to other drugs[71]. We should be aware of this probable relationship and conduct liver monitoring in the time since the FDA and EMA have advised the use of remdesivir for COVID-19. Other medicines routinely used to treat COVID-19 patients, in addition to remdesivir, have been linked to liver damage due to drug hepatotoxicity, which may explain the differences in symptoms observed in various cohorts to some extent the use of lopinavir/ritonavir may cause liver damage in COVID-19 patients, according to Fan Z and colleagues[72]. In COVID-19 patients, targeted medications including ACE inhibitors and angiotensin II receptor blockers were observed to cause higher liver enzyme values, indicating the presence of liver damage[73,74]. As previously stated, the modest micro vesicular steatosis and mild lobular and portal activity found in COVID-19 autopsy are likely due to drug-induced liver injury[55]. Treatment with macrolides and quinolones, antivirals, steroids, and other drugs may cause liver damage in SARS patients[75]. All these medications have the potential to cause liver damage during infection. However, there is currently no convincing evidence[60]. The importance of drug use optimization in COVID-19 management cannot be overstated despite the lack of data.

VACCINES OF CORONAVIRUSES

A vaccine against COVID-19 will be critical in reducing virus spread and loosening social limitations. Still, several elements must be considered in vaccine development to avoid increasing innate immune response, autoimmune disease risk, or Drug-induced liver injury (DILI). Vaccines are expensive and require years to undergo rigorous animal and human studies before becoming available to the public. In a pandemic, scientists are under pressure to develop a vaccine quickly. Before and after the pandemic stopped, monies were diverted to other projects[76].

In this review, it its crucial to note that one possible adverse effect of vaccines is liver damage. In pandemic conditions, RNA- or DNA-based vaccinations have the highest promise[76]. These vaccines do not need to be cultured or fermented, they do not involve working with live pathogens, and they can encode important antigens without coding for other toxins. Still, they're not without risk[77].

Yet, no RNA vaccines have been licensed since toxicity cannot always be forecast from animal research due to species variances[76]. Early studies of RNA-based vaccines documented cases of pancreatitis, metabolic acidosis, hepatic steatosis, nerve damage, and even deaths[76]. Liver damage was documented in preclinical investigations using RNA therapy for Crigler-Nayjor syndrome. An RNA-based rabies vaccine study was terminated due to an elevated and harmful inflammatory response. This could be because RNA induces type 1 interferon, which is known to cause autoimmune disorders. Toll-like receptor (TLR) 9 and non-TLR activation have also been linked to DNA-based vaccinations generating an innate immune response[77].

CONCLUSION

COVID-19 is a newly discovered coronavirus that can cause severe respiratory infections, with symptoms similar to the common cold and flu with fatal pneumonia. Severe cases might affect other organs like the kidneys and liver. COVID-19 patients usually have liver damage from inflammation, infection, hypoxia, micro thrombotic events, Drug-induced liver injury, and viral damage. In conclusion, COVID-19's potential significance in the gastrointestinal system and liver should not be neglected. It may enter cells directly via the ACE2 receptor, affecting the normal function of the gastrointestinal tract and liver. Different routes, such as cytokine storm and the gut-lung axis, are also possible. Meanwhile, COVID-19 and digestive system illnesses are frequently linked, which may affect patient prognosis and increase the chance of mortality. The essential mechanisms behind COVID-19's link to digestive system disorders are unclear. As a result, we expect future research to focus on this area and deliver more effective preventative measures, pharmaceutical treatments, and therapeutic procedures.

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