Coronavirus disease (COVID-19) and acute nonicteric hepatitis: A case report from Asokoro, Nigeria

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Abstract:
We report our first case of Coronavirus disease (COVID-19) infection with hepatitis B co-infection who presented with fever, catarrh, headaches, fatigue, and loss of smell. He had a history of chronic hepatitis B infection which appeared to be inactive given a history of normal outpatient liver tests prior to admission for COVID-19. Following the positive nasopharyngeal polymerase chain reaction diagnosis with COVID-19, liver function tests revealed evidence of hepatitis with elevated bilirubin and liver enzymes and deranged full blood count findings.

Keywords:
Co-infection, coronavirus, COVID-19, hepatitis, liver

Introduction
Coronavirus disease (COVID-19) is caused by infection with the novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), an enveloped ribonucleic acid (RNA) virus, which was first reported from Wuhan, China, in December 2019. The virus since then has spread rapidly, infecting millions across the world, resulting in the death of approximately 1.38% of infected cases at the time of writing.[1] In symptomatic cases, the disease is known to progress rapidly, resulting in an acute respiratory distress syndrome in about 14% of confirmed cases.[2]

The most common clinical presentation is respiratory symptoms such as fever, cough, catarrh, shortness of breath, and occasionally radiographical features consistent with pneumonia.[3] What has not yet been clearly established is the presence of abnormal liver enzymes in COVID-19 infection, and if viral hepatitis is a feature in infected patients with or without any prior co-infection with hepatitis viruses.[4]

Currently, the management of COVID-19 relies on supportive treatment and the use of therapies such as Vitamin C, Vitamin D, hydroxychloroquine or chloroquine, anticoagulants, immunosuppressants, anti-inflammatory drugs, ivermectin with its antiviral properties and antibiotics for any opportunistic bacterial infections. Clinical trials are currently ongoing to determine the efficacy of treatment regimens such as hydroxychloroquine or chloroquine, lopinavir/ritonavir, and remdesivir in the preexposure or postexposure prophylaxis of COVID-19 infection and treatment of patients with mild, moderate, and severe COVID-19 infection.[5] We thus report our first case of COVID-19 with hepatitis B virus co-infection presenting as acute, nonicteric hepatitis.

Case Report
A 53-year-old man presented at our facility with a 5-day history of fever, catarrh,
headache, fatigue, and loss of smell and a positive nasopharyngeal polymerase chain reaction (PCR) test for SARS-CoV-2. He was immediately isolated, and a surgical facemask placed on him according to our facility protocol. He denied any history of cough, chest pain, sore throat, or shortness of breath. He lived with his family; his wife and teenage son, who later reported ill, were screened, also confirmed PCR positive for SARS-CoV-2 and were admitted to the same ward to provide them the opportunity of bonding, allay fears and provide emotional support. He had a positive history of contact with a SARS-CoV-2 infected colleague. He also had a medical history of hepatitis B infection and no other comorbidities. There was a 5-day history of intake of acetaminophen, but no recent intake of any antibiotics. His outpatient (pre-admission) medications included routine hematinics and multivitamins. Recent outpatient liver chemistries were normal and viral load results were suggestive of an inactive disease, but on admission, increased bilirubin and liver enzymes were observed. On presentation, his temperature was 36.7°C. There were no cutaneous manifestations, his respiratory examination was normal (SPO₂ 97% on room air), and there was no jaundice, right upper quadrant tenderness, hepatomegaly, or splenomegaly. Admission blood pressure was 129/87 mmHg.

Laboratory tests revealed microcytosis (+) (mean corpuscular volume 74fL), leucocytopaenia (white blood cell 3.1 × 10⁹/L), lymphocytosis (54%), monocytopaenia (15%) and thrombocytopenia (140 × 10⁹/L), direct bilirubin 7.3 µmol/L, aspartate aminotransferase (AST) 127 IU/L, alanine aminotransferase (ALT) 130 IU/L, alkaline phosphatase 324 IU/L [Tables 1 and 2]. Abdominal ultrasonography done 4 days prior to admission was essentially normal.

The patient was commenced on a treatment regimen comprising tablets azithromycin, hydroxychloroquine, amoxicillin with clavulanic acid, ivermectin, Vitamin D₃, Vitamin C, and zinc.

### Table 1: Liver and renal tests results at admission, discharge, and two weeks postdischarge

| Blood tests               | At admission | At discharge | Two weeks postdischarge | Reference range |
|---------------------------|--------------|--------------|-------------------------|-----------------|
| Liver function test       |              |              |                         |                 |
| Total bilirubin (µmol/L)  | 15.9         | 16.4         | 13.9                    | ≤17             |
| Direct bilirubin (µmol/L)| 7.3          | 6.2          | 8.9                     | ≤4.3            |
| AST (IU/L)                | 127.0        | 90.0         | 42.7                    | ≤40             |
| ALT (IU/L)                | 130.0        | 124.0        | 40.3                    | ≤40             |
| ALP (IU/L)                | 324.0        | 304.0        | 281.0                   | ≤270            |
| Total protein (g/L)       | 70.0         | 72.0         | 72.0                    | 64-83           |
| Albumin (g/L)             | 40.0         | 42.0         | 42.0                    | 35-52           |
| Fasting glucose (mmol/L)  | 4.9          | 5.7          | 5.7                     | 4.2-6.4         |
| Serum electrolytes, urea and creatinine | | | | |
| Sodium (mmol/L)           | 142.0        | 140.0        | 143.1                   | 135-155         |
| Potassium (mmol/L)        | 5.1          | 4.7          | 4.91                    | 3.4-5.3         |
| Chloride (mmol/L)         | 100.0        | 104.0        | 105.4                   | 98-106          |
| Bicarbonate (mmol/L)      | 26.0         | 28.0         | 24.7                    | 23-31           |
| Urea (mmol/L)             | 4.6          | 5.6          | 3.2                     | 2.1-7.1         |
| Creatinine (mg/dL)        | 1.1          | 1.0          | 0.6                     | 0.6-1.1         |

AST=Aspartate transaminase, ALT=Alanine transaminase, ALP=Alkaline phosphatase

### Table 2: Full blood count at admission, discharge, and two weeks postdischarge

| Blood tests     | At admission | At discharge | Two weeks postdischarge | Reference range |
|-----------------|--------------|--------------|-------------------------|-----------------|
| Haemoglobin (g/dL) | 13.0         | 13.3         | 14.9                    | 13-17           |
| Packed cell volume (%) | 42.0         | 43.0         | 43.5                    | 38-52           |
| White blood cell count | 3.1          | 3.1          | 4.6                     | 4000-10,000x10⁹/L |
| Red blood cell count | 5.68         | 5.68         | 5.6                     | 4.5-5.9x10⁹/L   |
| Platelet        | 140.0        | 140.0        | 160.0                   | 150-400x10⁹/L   |
| Neutrophil (%)  | 31.0         | 42.0         | 52.0                    | 50-65           |
| Lymphocyte (%)  | 54.0         | 48.0         | 39.4                    | 25-40           |
| Eosinophil (%)  | 0            | 1.0          | 1.0                     | 1-6             |
| Monocyte (%)    | 15.0         | 9.0          | 7.6                     | 2-8             |
| Basophil (%)    | 0            | 0            | 0                       | <1              |
| MCHC (g/dL)     | 32.0         | 33.2         | 34.3                    | 31.7-36         |
| MCH (pg)        | 24.0         | 26.0         | 28.6                    | 27-32           |
| MCV (fL)        | 74.0         | 76.0         | 86.7                    | 84-96           |

MCHC=Mean corpuscular haemoglobin concentration, MCH=Mean corpuscular haemoglobin, MCV=Mean corpuscular volume
By the second day on admission, all presenting symptoms had abated, and he was continued on the prescribed medication regimen for 9 days and eventually tested negative for SARS-CoV-2 by day 15 of admission and was discharged home according to the national COVID-19 treatment protocol with a blood pressure of 118/79 mmHg, SPO$_2$ of 96% on room air, and other normal vital signs. Laboratory investigation results prior to discharge, and follow-up laboratory investigations done 2 weeks after discharge are detailed in Tables 1 and 2. Figure 1 shows the trend in liver enzymes over the course of treatment and after discharge.

**Discussion**

Liver impairment was previously established in patients with SARS and MERS.$^6$ This has also been reported with SARS CoV-2 leading to abnormal levels of ALT and AST in a number of studies.$^7$ Reports state that it may be linked to the upregulation of the angiotensin-converting enzyme-2 receptors which are also present in the hepatocytes and cholangiocytes, and is believed to contribute to the abnormal liver enzymes in COVID-19 patients.$^8$

Few cases of reactivation of hepatitis B virus infection have been reported in the literature leading to acute hepatitis.$^9$ An earlier report highlighted the need for clinicians to be aware of the possibility of an initial presentation of COVID-19 infection as an acute nonicteric hepatitis prior to respiratory symptoms.$^4$ Our case has also illustrated the fact that dormant or inactive hepatitis B infection in patients could be reactivated in the presence of COVID-19 coinfection. Therefore, physicians should be particularly alert when managing individuals with a known history of chronic asymptomatic hepatitis B infection because of the risk of reactivation and development of acute hepatitis in the presence of COVID-19 coinfection.

A recent research report of about 123 COVID-19 patients in Wuhan China, noted a 21.8% prevalence of co-infection with HBV in severe cases of COVID-19 infection and 50.9% hepatic injury with deranged liver enzymes in patients without HBV co-infection.$^{10}$ It has been suggested that liver injury in COVID-19 patients could be due to direct viral injury, drug toxicity or systemic inflammation.$^{11}$ At the end of 2015, over 257 million people were living with chronic hepatitis B virus infections; this would be a substantial proportion of the global population at risk of acute hepatitis if infected with SARS-CoV-2.$^{12}$ Hepatitis B infection is, therefore, an additional risk to outcomes of COVID-19 and should be a consideration in the management of infected patients for optimal outcomes and community health.

It has, therefore, been suggested that the management of COVID-19 infection should require liver function assessment as an indicator of the progress of COVID-19 infection.$^{10}$ There is also a need for further observational studies to determine the frequency of the occurrence of “mild-to-moderate” derangements in liver enzymes during the COVID-19 pandemic and the effects on death rates.$^4$

**Conclusion**

We have reported this case to highlight the fact that acute nonicteric hepatitis may be an observed presentation of COVID-19 infection in patients with a history of chronic hepatitis B infection. It would, therefore, be beneficial to include liver function testing in the management of COVID-19 patients, conduct further studies on hepatic derangements in COVID-19, and maintain vigilance during the pandemic, especially in environments with high prevalence rates of hepatitis B.

**Declaration of patient consent**

The authors certify that they obtained all appropriate consent forms from the patient to publish the case report. In the forms, the patient gave his consent for images and other clinical information to be reported in the journal. The patient understood that his names and initials will not be published, and due efforts would be made to conceal his identity, although anonymity could not be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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