Impact of COVID-19 on the clinical status of patients with Wilson disease

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Abstract

The coronavirus disease 2019 (COVID-19) pandemic has greatly impacted health systems. Many guidelines on chronic liver diseases have been released to optimize the use of medical resources and patient management. However, most of these guidelines have been established through expert consensus because the existing data do not provide strong evidence for developing effective recommendations. As Wilson disease (WD) is a rare chronic liver disease, the impact of COVID-19 on the clinical status of patients with WD is unclear. The present study showed a marked shortage of medical resources for clinically managing patients with WD during the pandemic. Although patients with WD who consistently took anticopper therapy showed no significant differences in hepatic and extrahepatic markers before and after the pandemic, their complication incidences, especially the infection incidence, were significantly increased during the study period. Therefore, patients with WD should be encouraged to adhere to anticopper therapy and be closely monitored to prevent infections and other complications. The present study provides a clinical basis for further managing WD during the pandemic.

Key Words: Coronavirus disease 2019; Wilson disease; Clinical status; Complications; Infections; Anticopper therapy

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TO THE EDITOR

Many countries have enforced social distancing and strict stay-at-home strategies to reduce the spread of coronavirus disease 2019 (COVID-19). However, these measures often negatively affect patients with other diseases[1,2]. Many guidelines on chronic liver diseases have been released to optimize the use of medical resources and patient management[3]. Most of these guidelines have been established through expert consensus because the existing data do not provide strong evidence for developing effective recommendations.

Given the high copper deposition in the livers of patients with Wilson disease (WD), these patients often develop liver injury and cirrhosis. Because WD has clinical features that are distinct from those of liver diseases caused by other etiologies and medical resources have been in short supply during the pandemic, the clinical features of patients with WD should be examined to improve their management. Therefore, we conducted a before-after study to investigate the clinical features of these patients before and during COVID-19.

We reviewed the medical records of patients with WD who were hospitalized for routine office visits or emergency visits at the First Affiliated Hospital of Guangdong Pharmaceutical University from 1 January 2018 to 3 September 2020. In China, the diagnostic criteria for WD are similar to those of the diagnostic scoring system for WD. During the COVID-19 pandemic, the number of WD inpatient visits dropped from 198 to 95, indicating a 52.02% decrease from the number of WD inpatient visits during the same period in 2019. These data indicate that the ongoing pandemic has led to a marked shortage of medical resources for clinically managing patients with WD. Medical data on 68 patients with WD who were hospitalized at our hospital during and before the pandemic were analyzed. All of these patients underwent anticoagulation therapy during the pandemic. Most of them (83.82%) had developed cirrhosis before and during COVID-19.

The hepatic and extrahepatic status of patients who consistently used anticoagulation therapy during the pandemic did not significantly deteriorate (Table 1). However, owing to lifestyle changes and delayed screening for complications during the pandemic, the complication incidence increased significantly in these patients during the study period (23.53% vs 11.76%, \(P = 0.021\)). Notably, most complications (22/24) occurred in patients with WD-associated cirrhosis. Among the complications, infections were the most prevalent (11.8% vs 1.5%, \(P = 0.016\)). Although the community mitigation measures for COVID-19 are thought to reduce the incidence of respiratory infections in the general population[4], our data showed that the incidence of respiratory infections in patients with WD increased during the pandemic (7.4% vs 0%, \(P = 0.063\)).

Following the COVID-19 outbreak, the Chinese government implemented strong strict measures, and most citizens, except those involved in essential services, were ordered to stay at home. These measures helped keep the pandemic under control in China. However, the lockdown and movement restrictions often led to reduced physical activity, prolonged sedentary behaviors, imbalanced nutritional intake, poor mental health and delayed routine follow-up visits in these patients[5]. These changes were associated with cirrhosis-associated immune dysfunction and accounted for the...
Table 1 Clinical features and complications in patients with Wilson disease before and after coronavirus disease 2019

|                                | Before COVID-19 (n = 68) | After COVID-19 (n = 68) | P value |
|--------------------------------|--------------------------|-------------------------|---------|
| **Demographic characteristics**|                          |                         |         |
| Age (yr)                       | 28.00 (23.00–33.00)      | -                      |         |
| Male sex                       | 37 (54.41)               | -                      |         |
| **Hepatic features**           |                          |                         |         |
| Elevated ALT (> 40 U/L)        | 16 (23.53)               | 12 (17.65)              | 0.424   |
| Elevated AST (> 35 U/L)        | 13 (19.12)               | 17 (25.00)              | 0.388   |
| Elevated bilirubin (> 17.1 µmol/L) | 15 (22.06)               | 13 (19.12)              | 0.754   |
| Hypoproteinemia (albumin < 35 g/L) | 10 (14.71)               | 12 (17.65)              | 0.774   |
| Elevated PT (> 15 s)           | 11 (16.18)               | 13 (19.12)              | 0.791   |
| Elevated INR (> 1.5)           | 1 (1.47)                 | 2 (2.94)                | 1.000   |
| Child-Pugh                     |                          |                         | 1.000   |
| A                              | 64 (94.12)               | 65 (95.59)              |         |
| B/C                            | 4 (5.88)                 | 3 (4.41)                |         |
| Cirrhosis                      | 57 (83.82)               | 57 (83.82)              | 1.000   |
| **Extrahepatic features**      |                          |                         |         |
| Neurological manifestations    | 50 (73.5)                | 49 (72.1)               | 1.000   |
| Psychiatric manifestations     | 3 (4.4)                  | 4 (5.9)                 | 1.000   |
| Kayser-Fleischer ring          | 32 (47.1)                | 35 (51.5)               | 0.375   |
| Splenomegaly/splenectomy       | 45 (66.2)                | 47 (69.1)               | 0.688   |
| **Complications**              |                          |                         |         |
| Any complication               | 8 (11.76)                | 16 (23.53)              | 0.021   |
| Ascites                        | 2 (1.5)                  | 5 (7.4)                 | 0.375   |
| Infections                     | 1 (1.5)                  | 8 (11.8)                | 0.016   |
| Respiratory infection          | 0 (0)                    | 5 (7.4)                 | 0.063   |
| Urinary infection              | 0 (0)                    | 1 (1.5)                 | 1.000   |
| Gastrointestinal infection     | 1 (1.5)                  | 2 (2.9)                 | 1.000   |
| SBP                            | 0 (0)                    | 1 (1.5)                 | 1.000   |
| PVT                            | 0 (0)                    | 0 (0)                   | -       |
| Gastroesophageal varices       | 5 (7.4)                  | 7 (10.3)                | 0.500   |
| Variceal bleeding              | 0 (0)                    | 1 (1.5)                 | 1.000   |
| Hepatic encephalopathy         | 0 (0)                    | 0 (0)                   | -       |
| Renal impairment               | 0 (0)                    | 0 (0)                   | -       |
| Liver failure                  | 0 (0)                    | 0 (0)                   | -       |
| HCC                            | 0 (0)                    | 0 (0)                   | -       |

Data are presented as medians (interquartile ranges) or n (%). ALT: Alanine transaminase; AST: Aspartate transaminase; HCC: Hepatocellular carcinoma; INR: International normalized ratio; PT: Prothrombin time; PVT: Portal vein thrombosis; SBP: Spontaneous bacterial peritonitis; COVID-19: Coronavirus disease 2019.

In conclusion, the hepatic and extrahepatic status of patients with WD who adhered strictly to their anticopper therapy during the COVID-19 pandemic did not significantly worsen, but the complication incidence — especially the infection incidence — increased significantly. Therefore, patients with WD should be encouraged to adhere...
to anticopper therapy and be closely monitored to prevent infections and other complications.

REFERENCES

1 Mafham MM, Spata E, Goldacre R, Gair D, Curnow P, Bray M, Hollings S, Roebuck C, Gale CP, Mamas MA, Deanfield JE, de Belder MA, Luescher TF, Denwood T, Landray MJ, Emberson JR, Collins R, Morris EJA, Casadei B, Baigent C. COVID-19 pandemic and admission rates for and management of acute coronary syndromes in England. *Lancet* 2020; **396**:381-389 [PMID: 32679111 DOI: 10.1016/S0140-6736(20)31356-8]

2 Villarreal-Garza C, Aranda-Gutierrez A, Ferrigno AS, Platas A, Aloi-Timeus I, Mesa-Chavez F, Ayensa-Alonso A. The challenges of breast cancer care in Mexico during health-care reforms and COVID-19. *Lancet Oncol* 2021; **22**:170-171 [PMID: 33359740 DOI: 10.1016/S1470-2045(20)30609-4]

3 Bollipo S, Kapuria D, Rabie A, Ben-Yakov G, Lui RN, Lee HW, Kumar G, Siou K, Turnes J, Dhanasekaran R. One world, one pandemic, many guidelines: management of liver diseases during COVID-19. *Gut* 2020; **69**:1369-1372 [PMID: 32499304 DOI: 10.1136/gutjnl-2020-321553]

4 Olsen SJ, Azziz-Baumgartner E, Budd AP, Brammer L, Sullivan S, Pineda RF, Cohen C, Fry AM. Decreased Influenza Activity During the COVID-19 Pandemic - United States, Australia, Chile, and South Africa, 2020. *MMWR Morb Mortal Wkly Rep* 2020; **69**:1305-1309 [PMID: 32941415 DOI: 10.15585/mmwr.mm6937a6]

5 Pinto AJ, Dunstan DW, Owen N, Bonfà E, Gualano B. Combating physical inactivity during the COVID-19 pandemic. *Nat Rev Rheumatol* 2020; **16**:347-348 [PMID: 32355296 DOI: 10.1038/s41584-020-0427-z]

6 Xiang M, Zhang Z, Kuwahara K. Impact of COVID-19 pandemic on children and adolescents' lifestyle behavior larger than expected. *Prog Cardiovasc Dis* 2020; **63**:531-532 [PMID: 32360513 DOI: 10.1016/j.pcad.2020.04.013]
