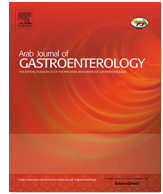




Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



## Original article

# Covid-19 pandemic in Egyptian children with liver diseases: Incidence and impact on health care service delivery in a low/middle income country



Hala Abdullatif<sup>a</sup>, Wafaa Elakel<sup>b</sup>, Sherif Baroudy<sup>a</sup>, Hanaa El-Karaksy<sup>a</sup>, Engy A. Mogahed<sup>a,\*</sup>

<sup>a</sup> Department of Paediatrics, Faculty of Medicine, Cairo University, Cairo, Egypt

<sup>b</sup> Tropical Medicine Department, Cairo University and National Hepatology and Tropical Medicine Research Institute, Cairo, Egypt

## ARTICLE INFO

## Article history:

Received 31 August 2021

Accepted 10 January 2022

## Keywords:

COVID-19

Health care services

Lockdown

Pandemic

Pediatric liver diseases

## ABSTRACT

**Background and study aims:** The coronavirus disease 2019 (COVID-19) pandemic has had considerable effects on health care services given the need for re-allocation of resources and interruption of medical care. COVID-19 poses a challenge to patients with liver disease who are at risk of infection and more severe disease course. The current study aimed to assess the incidence of COVID-19 in children with liver diseases and evaluate the extent to which health care delivery was affected during lockdown.

**Patients and methods:** This cross-sectional analytical study conducted at the Pediatric Hepatology Unit, Cairo University Children's Hospital utilized a questionnaire to determine the incidence of COVID-19 in patients with liver diseases and the impact of COVID-19 on the patients' liver condition and health care service delivery. A presumed score was implemented to identify patients with probable COVID-19.

**Results:** Data from 349 children with liver diseases were analyzed. The overall incidence of COVID-19 was 8%. Patients with documented and probable COVID-19 were compared to improbable COVID-19 cases. Notably, COVID-19 cases were younger and had higher incidence rates of cholestatic liver diseases. COVID-19 patients experienced significantly higher rates of hepatic complications (43%) and had significantly greater need for medical services during the lockdown. All COVID-19 patients recovered after a median (IQR) duration of 3 (4) days, except for one patient who succumbed to COVID-19 and hepatic complications.

**Conclusions:** COVID-19 affected the younger hepatic patients with cholestatic disorders of infancy. Hepatic complications were more common among COVID-19 infected children. Alternative ways of communication require development to prioritize patients who needs a hospital visit and monitoring. Clinical scores may help diagnosis of COVID-19 in low/middle income countries like Egypt to compensate for the deficient laboratory diagnostic facilities.

© 2022 Pan-Arab Association of Gastroenterology. Published by Elsevier B.V. All rights reserved.

## Introduction

Coronavirus disease 2019 (COVID-19) is caused by the recently identified coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. Since the announcement of the 1st COVID-19 case in Egypt on February 2020, the number of cases has increased to 214,639, with 12,653 deaths already having occurred during the preparation of this manuscript in April 2021 [2].

The main manifestations of COVID-19 include fever, cough, lymphopenia, ground-glass chest opacities, diarrhea, and

abdominal pain [1]. Systemic viral infections can be associated with elevated transaminases, which may reflect general immune activation or inflammation caused by circulating cytokines, a phenomenon called "bystander hepatitis." This phenomenon may also be observed among patients with COVID-19 [1,3].

The COVID-19 pandemic poses a huge challenge to health care systems. Patients with preexisting medical conditions have been identified as populations at risk for a severe disease course. Patients with advanced liver diseases and those who receive immunosuppressive therapies either due to autoimmune liver diseases or after liver transplantation represent vulnerable cohorts who are at increased risk of infection and/or a severe course of COVID-19 [4]. Studies have warned that reduced access to diagnosis and treatment can lead to increased morbidity in patients with

\* Corresponding author at: 2B Sama City, Katamya, Cairo 11439, Egypt.

E-mail address: [engy.mogahed@kasralainy.edu.eg](mailto:engy.mogahed@kasralainy.edu.eg) (E.A. Mogahed).

liver diseases. Moreover, we may witness a delayed surge in hospitalizations related to decompensated liver disease after the COVID-19 pandemic has receded [5].

The current pandemic requires unusual allocation of health care resources, which may negatively impact the care of patients with chronic liver disease (CLD). Thus, hepatologists are facing an enormous challenge to promote telemedicine in outpatient settings, avoid nosocomial dissemination of the virus, and simultaneously maintain standard care for patients [4]. Patients throughout Egypt are not universally provided with high levels of care for liver disease, promoting the need for some patients to travel for hundreds of kilometers to access tertiary care centers [6].

The Pediatric Hepatology Unit in the Specialized Children's Hospital of Cairo University, Egypt represents one of the largest and highly specialized tertiary care centers for pediatric hepatology in the country. We receive around 700 new cases annually and serve approximately 60–70 children with different presentations of acute and chronic hepatic conditions at each outpatient clinic. During the accelerated COVID-19 rates in Egypt during March 2020 and the associated lockdowns, hospital staff at our institution faced several challenges. Reduced staffing promoted a temporary halt in work at the hepatology outpatient clinics, inpatient department, medication refill, elective procedures, and liver transplantation. Our major concern was that reduced access to health care facilities during the global COVID-19 pandemic might have caused increased morbidity in children with liver diseases.

The current study primarily aimed to assess the incidence of COVID-19 in children with liver diseases and compare different groups of patients according to their vulnerability to COVID-19. Our secondary objective was to evaluate the extent to which health care delivery was affected by the quarantine. Moreover, we aimed to evaluate the patients' opinions regarding remote consultations in case of a second lockdown.

## Patients and methods

This single center, cross-sectional, analytical study was conducted at the Pediatric Hepatology Unit of Cairo University Children's Hospital, Egypt. Accordingly, a questionnaire survey regarding COVID-19 was provided to the guardians of children with liver diseases in order to evaluate the consequences of the pandemic after the lockdown in our unit from March to July 2020. The study protocol was approved by the ethical committee and institutional review board of Kasr Alainy School of Medicine.

A representative convenient sample of pediatric patients with liver diseases whose contact phone numbers could be retrieved from the archives of the Pediatric Hepatology Unit was included. Patients whose guardians were unable to comprehend the proposed questionnaire were excluded from the study.

Data were collected by contacting the patients' parents/guardians through the phone or during their visit to the Pediatric Outpatient Clinic. Informed verbal consent was obtained from the patients' parents/guardians after explaining the nature of the study. The questionnaire directed to the parents included the following three main categories.

### Demographic data

The name, sex, age, residence, whether the patient was a chronic case or a newcomer, and diagnosis were determined.

### Incidence of COVID-19 in patients and their families

The questionnaire obtained information regarding the history of the documented COVID-19 in the patient or family member and

the month in which the infection occurred; number of household contacts who had COVID-19; number of family members sharing the house; whether the patient or any of the patient's close contacts had symptoms suggestive of COVID-19 (respiratory symptoms, fever, diarrhea, headache, malaise, etc.); whether the patient or a family member needed hospitalization for COVID-19 or was treated at home; how COVID-19 was detected (laboratory tests, swab, and chest imaging); and how recovery from COVID-19 was confirmed (negative swab or symptom resolution).

Patients were subdivided into a probable and improbable COVID-19 group. This classification was based on our proposed score, which considers the wide range of symptoms associated with COVID-19 and the role played by contacts in transmission of infection. The total score was 7, with 5 points assigned for symptoms and 2 for presence of infected contacts. Symptoms were divided into five categories: (1) Fever; (2) headache, myalgia, and/or fatigue; (3) sore throat; (4) cough and/or respiratory distress; and (5) diarrhea and/or abdominal pain. One point was assigned for each category. Contact with a confirmed COVID-19 case was assigned 2 points, whereas contact with a suspected case was assigned 1 point. Patients with an overall score  $\geq 3$  were considered as probable COVID-19 cases, whereas those with a score of  $\leq 2$  were considered improbable COVID-19 cases.

### Impact of the COVID-19 pandemic on the patients' liver condition and health care service delivery

The questionnaire obtained data regarding the date of the last visit to the hepatology unit; history of an interruption in follow-up visits due to COVID-19 lockdown; interruption in medication administration (due to unavailability or financial burdens); need for any medical care or hospitalization during the lockdown; whether the patient could find an alternative medical facility during the lockdown; whether the patient suffered a complication related to his liver disease during the lockdown (jaundice, encephalopathy, ascites, lower limb edema, and bleeding); parents'/guardians' suggestions on how to consult our unit members regarding their medical condition in case of second lockdown/curfew (through a phone call, WhatsApp, and email).

### Statistical methods

Responses of patients' relatives were collected and entered into an excel sheet and converted to IBM SPSS Statistics for Windows, Version 24. Armonk, NY: IBM Corp. Categorical data were presented as numbers and percentages. Study groups were compared using the Chi-square test or Fischer's exact test as appropriate. Age was presented as median and interquartile range (IQR) and was compared using the Mann-Whitney *U* test. In all tests, *P* values  $< 0.05$  indicated statistical significance. Assuming that a flow of 1200 children into the hepatology clinic per month, the probability of having COVID-19 was 50%, with a 5% error margin and 95% confidence level. Thus, the recommended sample size was 292 children.

## Results

This cross-sectional analytical study included data obtained from a convenient sample of 349 pediatric patients at the Pediatric Hepatology Unit. The patients aged from 5 months to 18 years. Cholestatic liver disorders were the most common diagnosis in the study group (24.4%). Other demographic characteristics of the studied patients are detailed in Table 1.

COVID-19 was documented in five patients (1.4%), among whom 4 were confirmed via a positive nasopharyngeal polymerase

**Table 1**  
Baseline characteristics of the studied children (N = 349).

Characteristic	
Sex	
Male; N (%)	183 (52.4)
Female; N (%)	166 (47.6)
Age in years; Median (IQR)	10 (8)
Residence	
Urban; N (%)	163 (46.7)
Rural; N (%)	186 (53.3)
Person who answered the questionnaire	
Mother; N (%)	186 (53.3)
Father; N (%)	144 (41.3)
Other; N (%)	19 (5.4)
Diagnosis of liver condition	
Cholestatic disorders of infancy; N (%)	85 (24.4)
- Biliary atresia (Post-Kasai portoenterostomy); N (%)	28 (8)
- Alagille syndrome; N (%)	13 (3.7)
- Other cholestatic disorders; N (%)	44 (12.6)
Hepatitis C virus (treated); N (%)	67 (19.2)
Autoimmune hepatitis; N (%)	59 (16.9)
Wilson disease; N (%)	36 (10.3)
Glycogen storage disease; N (%)	25 (7.2)
Recipients of liver transplant; N (%)	19 (5.4)
Miscellaneous; N (%)	58 (16.6)
- Extra-hepatic portal vein obstruction	11 (3.2)
- Fibrocystic liver disorders	9 (2.6)
- Hepatitis B virus	7 (2)
- Sinusoidal obstruction syndromes	2 (0.6)
- Crigler-Najjar syndrome type I	2 (0.6)
- Galactosemia	2 (0.6)
- Tyrosinemia	1 (0.3)
- Niemann-Pick disease	1 (0.3)
- Non-alcoholic fatty liver disease	1 (0.3)
- Hydatid cyst	1 (0.3)
- Operated choledochal cyst	1 (0.3)
- No definite diagnosis reached	20 (5.7)
Status	
New comers; N (%)	8 (2.3)
Patients following at the site; N (%)	341 (97.7)

chain reaction (PCR) swab test for COVID-19 and 1 developed anosmia. Regarding the hepatic diagnosis of these five patients, four had cholestatic disorders of infancy, and one had Budd Chiari syndrome. Ascites was present in four of the five patients.

According to the clinical score herein adopted for the diagnosis of COVID-19, 23 cases fulfilled the criteria and exhibited a score of  $\geq 3$ . These patients were referred to as probable COVID-19 cases. Accordingly, the global incidence of COVID-19 in the present study was 8% (28 patients).

Patients with documented and probable COVID-19 were compared to improbable COVID-19 patients according to their demographic data and diagnosis (Table 2). COVID-19 cases were significantly younger and had significantly more cholestatic liver diseases than the non-infected group. Interestingly, patients who were receiving immunosuppressive therapy, such as those with autoimmune hepatitis and recipients of liver transplant, had a lower incidence of COVID-19 (4% and 7%) compared to the cholestatic and miscellaneous groups (54% and 29% respectively). None of the patients with glycogen storage disease contracted COVID-19.

The most common symptom suggestive of COVID-19 in our study group was fever, accounting for 79% of the COVID-19 group and 10% of the non-COVID-19 group, followed by respiratory symptoms (50% vs. 2.5%), sore throat (46% Vs. 1.6%), diarrhea (39% vs. 2%), myalgia and fatigue (32% vs. 0.9%), and anosmia (4% of the COVID-19 group only). Five patients from the COVID-19 group underwent a nasopharyngeal swab test. Chest imaging was done for 18 cases, among whom 10 were for COVID-19 patients. Blood tests for COVID-19 were performed in 21 cases, around half of whom were for the COVID-19 group.

The peak of the COVID-19 cases occurred in July 2020 (32%), followed by May (18%). A total of seven cases (25%) needed admission to isolation hospitals, whereas the remaining 21 patients (75%) recovered after home treatment. Patients who required no hospitalization received only symptomatic treatment at home comprising mainly of oral or rectal acetaminophen. Meanwhile, hospitalized patients with severe pulmonary involvement received additional clarithromycin, zinc, intravenous antibiotics, and dexamethasone. Recovery was confirmed in four patients through a negative nasopharyngeal swab test. One patient died of COVID-19 and complications of his liver condition. The remaining 23 cases (82%) recovered from infection based on the clinical resolution of their symptoms. The median duration (IQR) of the reported illness was 3 (4) days.

Several risk factors for contracting COVID-19 were studied in our patients (Table 3). A total of 18 cases had household contact with a definite diagnosis of COVID-19. Another 10 patients had contacts with clinical manifestations suggestive of COVID-19 for whom the diagnosis was not confirmed via laboratory or radiological methods. The frequency of definite and probable COVID-19 contacts was significantly higher among the COVID-19 group of patients. The number of family members that needed hospitalization and had a history of contact with an infected case were significantly higher among patients who contracted COVID-19 ( $P < 0.01$ ). Conversely, both groups showed no significant difference in either the number of family members sharing a house or the number of infected family members in the same house (Table 3).

Our center is one of the biggest tertiary care centers for pediatric patients with liver disease in Egypt. During the lockdown, both inpatient and outpatient services were halted from March to July 2020. The living donor liver transplantation program was suspended until August 2020. During this period, routine follow-up visits were interrupted in 83.4% of the patients. Moreover, 15 patients (4.3%) discontinued their medications owing to unavailability or financial burdens, whereas 55 patients (15.8%) suffered from complications related to their liver disease during the lockdown. Jaundice was the most common complication encountered, followed by ascites and bleeding. The rate of complications was significantly more frequent in patients with COVID-19 (Table 4). Approximately 30% of the patients needed medical care services during the lockdown but could not reach our unit. Only half of them were able to reach an alternative medical facility. Patients with probable or documented COVID-19 had significantly greater need for medical care during the lockdown ( $P < 0.01$ ). Most of the parents selected phone calls as their preferred method for contacting one of our staff members in case of future lockdown (Table 4).

## Discussion

COVID-19 has been associated with liver injury in 14%–83% of hospitalized adult patients [1,7–15]. Several mechanisms for liver injury have been implicated, including direct viral cytopathic effects, immune dysfunction, hypoxia, and drug-induced effects [8,15,16]. Accordingly, patients with liver diseases are more prone to detrimental consequences and adverse outcomes when infected with SARS-COV-2 given the vulnerable state of the liver, especially when cirrhotic [17]. To date, limited data has been published exclusively for COVID-19 in children with liver diseases, with most recommendations having been extrapolated from adult studies. Children with COVID-19 experience a wide range of symptoms, which may be indistinguishable from common concurrent illnesses. Moreover, liver diseases in children are entirely different from those in adults in terms of etiology, onset, progression, and outcomes.

**Table 2**  
Comparison between children with liver disease who did and did not have COVID-19.

Characteristic	Total	Documented or probable COVID-19 N (%)	Improbable COVID-19 N (%)	P value
Number (%)	349	28 (100)	321 (100)	
Sex				
Male (N; %)	183	15 (54)	168 (52)	
Female (N; %)	166	13 (46)	153 (48)	1
Age in years (median; IQR)	10 (8)	6 (11)	10 (9)	0.02
Residence				
Urban (N; %)	163	12 (43)	151 (47)	
Rural (N; %)	186	16 (57)	170 (53)	0.7
Diagnosis of liver condition				
Cholestatic disorders of infancy (N; %)	85	15 (54)	70 (22)	
Hepatitis C virus (treated) (N; %)	67	1 (4)	66 (21)	
Autoimmune hepatitis (N; %)	59	1 (4)	58 (18)	
Wilson disease (N; %)	36	1 (4)	35 (11)	<0.01
Glycogen storage disease (N; %)	25	0 (0)	25 (8)	
Recipients of liver transplant (N; %)	19	2 (7)	17 (5)	
Miscellaneous (N; %)	58	8 (29)	50 (16)	

**Table 3**  
Probable risk factors for COVID-19 in both study groups.

Characteristic	Total	Documented or probable COVID-19 N (%)	Improbable COVID-19 N (%)	P value
Number (%)	349	28 (100)	321 (100)	
Number of family members sharing the same house				
2	9	1 (4)	8 (2)	
3	16	1 (4)	15 (5)	0.98
4	69	5 (18)	64 (20)	
5	239	18 (64)	221 (69)	
Family members with COVID-19				
Definite case	18	8 (29)	10 (3)	<0.01
Probable case (by symptoms)	23	13 (46)	10 (3)	
Symptoms suggestive of COVID-19 in family members				
Fever	18	10 (36)	8 (2)	
Respiratory symptoms		6 (21)	8 (2)	0.97
Diarrhea	14	2 (7)	3 (1)	
Fatigue, headache, myalgia	53	1 (4)	2 (1)	
Number of infected family members				
1	24	12 (43)	12 (4)	0.63
2	11	5 (18)	6 (2)	
3	2	0 (0)	2 (1)	
4	2	2 (7)	0 (0)	
5	2	2 (7)	0 (0)	
6+	2	1 (4)	1 (0.3)	
Came into contact with infected persons	29	15 (54)	14 (4)	<0.01
Infected family member that needed hospitalization	4	4 (14)	0 (0)	<0.01

The diagnosis of COVID-19 in children with liver disease necessitates a high index of suspicion considering that acute hepatic decompensation can be the only presentation in these children [18]. This can be compounded by the limited resources and restricted SARS-COV-2 PCR testing. After the implementation of our proposed score together with the few available PCR results, we reported an overall COVID-19 incidence (documented and probable) of 8% among our cohort of children with liver disease. This percentage was approximately comparable to the global incidence of COVID-19 in the pediatric population (7.3%) as reported by the Centers for Disease Control and Prevention in July 2020 [19]. This finding is consistent with that reported in the study conducted by Zhang et al. [15], in which patients with CLD without cirrhosis had similar susceptibility to COVID-19 as those without CLD. However, we noted that the four patients who tested positive for SARS-COV-2 had decompensated liver disease with ascites prior to infection, all of whom required hospitalization. Hepatic decompensation and mortality have been reported to be more common among patients with cirrhosis given the lethal effects of combined cirrhosis and COVID-19 where immune dysregulation and abnor-

mal coagulation are characteristic [20]. Similarly, another Italian study showed high rates of hospitalization and mortality among patients with confirmed COVID-19 and cirrhosis [21].

Younger children with liver disease were at higher risk of contracting COVID-19, with cholestatic disorders being the most common diagnosis among infected children (54%). This can be attributed to the early onset (i.e., during infancy) of most cholestatic disorders. Cholestatic disorders of infancy usually exhibit a progressive course, eventually leading to cirrhosis, placing these children at an incremental risk for COVID-19 and worsening liver condition. Data from adult studies have shown no evidence of increased risk for COVID-19 in adult patients with cholestatic disorders, such as primary biliary cirrhosis and primary sclerosing cholangitis [15]. Nonetheless, these results cannot be inferred to the pediatric population.

Unlike those with cholestatic disorders of infancy, patients receiving immunosuppression, such as those with autoimmune hepatitis and liver transplant recipients, were far less frequently affected by COVID-19 infection (4% and 7% respectively). At the beginning of the pandemic, studies have postulated that patients

**Table 4**  
Assessment of medical services during lockdown in both studied groups.

Characteristic	Total	Documented or probable COVID-19 N (%)	Improbable COVID-19 N (%)	P value
Total	349	28 (100)	321 (100)	
Interruption of follow-up	291	23 (82)	268 (83)	0.79
Non-adherence to liver disease treatment	19	2 (7)	17 (5)	0.95
Cause of non-adherence				
Financial	3	0 (0)	3 (18)	0.47
Unavailability of medication	12	2 (100)	10 (59)	
Hepatic complications during lockdown	55	12 (43)	43 (13)	<0.01
Type of complication				
Jaundice	31	7 (25)	24 (8)	
Ascites	19	10 (36)	9 (3)	
Bleeding	17	4 (14)	13 (4)	
Hepatic encephalopathy	3	1 (4)	2 (0.6)	
Lower limb edema	2	1 (3)	1 (0.3)	
Need for medical care during lockdown	102	22 (79)	80 (25)	<0.01
Availability of medical facility substitutes	52	15 (54)	37 (12)	<0.01
Preferred contact with our medical facility during future lockdown				
Phone calls	310	27 (96)	283 (88)	
Email	23	1 (4)	22 (7)	
WhatsApp	11	0	11 (3)	<0.01
No suggestions	17	1 (4)	16 (5)	

receiving immunosuppressive medications are at higher risk of infection. Nevertheless, D'Antiga [22] reported that although his hospital was in the red zone in Italy with the highest rates of COVID-19, none of the patients receiving immunosuppression developed clinical pulmonary disease. Thus, it was concluded that immunosuppressed patients are at similar risk for COVID-19 as the general population and that immunosuppression may be protective against immune-induced lung injury [10,22]. However, immunosuppression may prolong viral shedding in infected patients [23]. Conversely, a study in Spain reported that 111 liver transplant recipients had twice the risk of acquiring SARS-CoV-2 compared to the general population, albeit having a lower mortality rate than matched general population [24]. Therefore, the updated Associate American Society for the Study of Liver recommendations in November 2020 did not recommend any anticipatory changes in immunosuppression among patients without COVID-19 and highlighted the need to individualize immunosuppressive modification in patients with COVID-19 based on disease severity [25].

Only 1 of the 67 HCV-treated children had probable COVID-19. All enrolled children with HCV were treated with FDA-approved direct acting antivirals (DAAs) sofosbuvir/ledipasvir. HCV and SARS-CoV-2 polymerase have a structural superposition wherein residues that bind to the drug are present in the latter, suggesting the possible usefulness of sofosbuvir in treatment of COVID-19 [26,27]. A multicenter study in Spain showed that among the 341 patients with HCV receiving DAAs, only one patient who was receiving sofosbuvir/velpatasvir tested positive for SARS-CoV-2. Despite the potential theoretical benefits associated with DAAs, further studies are needed to evaluate the age, baseline liver condition, type of DAAs administered, and the severity of COVID-19 in this special population of viral hepatitis [28].

Hepatic complications in the form of progressive worsening of CLD or acute decompensation in CLD had been observed in 55 patients (15%) within our cohort. Moreover, 43% of the patients infected with SARS-CoV-2 developed liver complications. This could be attributed to the impact of the lockdown and cessation of medical liver services, with subsequent deterioration of their liver condition, thereby placing them at higher risk for COVID-19. Another possible explanation for the higher rates of complications among patients with COVID-19 is COVID-19-induced acute decompensation of CLD manifesting as ascites, bleeding, and/or encephalopathy [20]. Notably, the only patient with cryptogenic

cirrhosis who succumbed to COVID-19 was on the transplantation list; however, our transplantation services were halted during the lockdown.

Amidst the COVID-19 pandemic, it is mandatory, yet challenging, to weigh the benefits of protecting the patients from infection against the risks of deteriorating unmonitored liver disease [20]. Adjusting to the “new normal” has to be individualized based on the stage of liver disease, associated risk factors, hospital resources, and COVID-19 burden in order to ensure safe and optimum care [25].

The current study has some limitations worth noting. First, only a limited number of nasopharyngeal swabs were utilized to confirm COVID-19. Second, data were collected using a questionnaire depending on information obtained retrospectively from the patient's guardians. However, the questionnaire allowed us to cover the lockdown duration and reach out to a large number of patients. Moreover, this has been the first study to analyze pediatric patients with liver disease during the current pandemic. We attempted to implement a score to diagnose COVID-19 considering the limited number of nasopharyngeal swabs.

In conclusion, COVID-19 has been shown to affect younger patients with cholestatic disorders of infancy. Hepatic complications were more common among those with COVID-19. Given the threat of a second lockdown, alternative methods of communication require further development to avoid unnecessary commuting to and from the hospital and thus prioritizing patients in need of hospitalization as well as close follow-up and monitoring. Clinical scores may help diagnose COVID-19 in low/middle income countries like Egypt to compensate for the deficient laboratory diagnostic facilities.

#### Declaration of competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### Acknowledgements

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## References

- [1] Guan W-J, Ni Z-y, Hu Yu, Liang W-H, Ou C-Q, He J-X, et al. China medical treatment expert group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J* 2020;382(18):1708–20.
- [2] WHO. Health Emergency Dashboard-COVID-19, Egypt status. <https://covid19.who.int/region/emro/country/eg> Accessed 18/4/2021.
- [3] Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020;395(10229):1054–62.
- [4] Boettler T, Newsome PN, Mondelli MU, Maticic M, Cordero E, Cornberg M, et al. Care of patients with liver disease during the COVID-19 pandemic: EASL-ESCMID Position Paper. *JHEP Rep* 2020;2(3):100113. <https://doi.org/10.1016/j.jhepr.2020.100113>.
- [5] Hollander JE, Carr BG. Virtually perfect? Telemedicine for Covid-19. *N Engl J Med* 2020;382(18):1679–81.
- [6] El Kassas M, Abdelkader H, Medhat MA. COVID-19 in Egypt: Through crisis to adaptation; a gastroenterologist's perspective. *Arab J Gastroenterol* 2020;21(3):207–10.
- [7] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020;395(10223):507–13.
- [8] Fan Z, Chen L, Li J, Cheng X, Yang J, Tian C, et al. Clinical features of COVID-19-related liver functional abnormality. *Clin Gastroenterol Hepatol* 2020;18(7):1561–6.
- [9] Felm S, Fisher C, Pakala T, Tong M, Shah D, Schwarzbaum D, et al. Analysis of gastrointestinal and hepatic manifestations of SARS-CoV-2 infection in 892 patients in Queens, NY. *Clin Gastroenterol Hepatol* 2020;18(10):2378–2379. e1.
- [10] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Yi, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395(10223):497–506.
- [11] Hundt MA, Deng Y, Ciarleglio MM, Nathanson MH, Lim JK. Abnormal liver tests in COVID-19: A retrospective observational cohort study of 1827 patients in a major U.S. hospital network. *Hepatology* 2020;72(4):1169–76.
- [12] Phipps MM, Barraza LH, LaSota ED, Sobieszczyk ME, Pereira MR, Zheng EX, et al. Acute liver injury in COVID-19: prevalence and association with clinical outcomes in a large US cohort. *Hepatology* 2020;72(3):807–17.
- [13] Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. *JAMA* 2020;323(20):2052. <https://doi.org/10.1001/jama.2020.6775>.
- [14] Xu L, Liu J, Lu M, Yang D, Zheng X. Liver injury during highly pathogenic human coronavirus infections. *Liver Int* 2020;40(5):998–1004.
- [15] Zhang C, Shi L, Wang F-S. Liver injury in COVID-19: management and challenges. *Lancet Gastroenterol Hepatol* 2020;5(5):428–30.
- [16] Gu J, Han B, Wang J. COVID-19: gastrointestinal manifestations and potential fecal-oral transmission. *Gastroenterology* 2020;158(6):1518–9.
- [17] Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, et al. Factors associated with COVID-19-related death using OpenSAFELY. *Nature* 2020;584(7821):430–6.
- [18] Moon AM, Webb GJ, Aloman C, Armstrong MJ, Cargill T, Dhanasekaran R, et al. High mortality rates for SARS-CoV-2 infection in patients with pre-existing chronic liver disease and cirrhosis: preliminary results from an international registry. *J Hepatol* 2020;73:705–8.
- [19] CDC. Demographic Trends of COVID-19. <https://www.cdc.gov/covid-data-tracker/index.html#demographics>. Accessed December 27, 2020.
- [20] Marjot T, Moon AM, Cook JA, Abd-El Salam S, Aloman C, Armstrong MJ, et al. Outcomes following SARS-CoV-2 infection in patients with chronic liver disease: an international registry study. *J Hepatol* 2021;74(3):567–77.
- [21] Iavarone M, D'Ambrosio R, Soria A, Triolo M, Pugliese N, Del Poggio P, et al. High rates of 30-day mortality in patients with cirrhosis and COVID-19. *J Hepatol* 2020;73(5):1063–71.
- [22] D'Antiga L. Coronaviruses and immunosuppressed patients: the facts during the third epidemic. *Liver Transpl* 2020;26(6):832–4.
- [23] Bhoori S, Rossi RE, Citterio D, Mazzaferro V. COVID-19 in long-term liver transplant patients: preliminary experience from an Italian transplant centre in Lombardy. *Lancet Gastroenterol Hepatol* 2020;5(6):532–3.
- [24] Colmenero J, Rodríguez-Perálvarez M, Salcedo M, Arias-Milla A, Muñoz-Serrano A, Graus J, et al. Epidemiological pattern, incidence and outcomes of COVID-19 in liver transplant patients. *J Hepatol* 2021;74(1):148–55.
- [25] AASLD. Associate American Society for the Study of Liver [online] Clinical best practice advice for hepatology and liver transplant providers during the COVID-19 pandemic: AASLD expert panel consensus statement Last updated 9 November 2020. <https://www.aasld.org/sites/default/files/2020-11/AASLD-COVID19-ExpertPanelConsensusStatement-November092020.pdf> Accessed December 2020.
- [26] Chien M, Anderson TK, Jockusch S, Tao C, Li X, Kumar S, et al. Nucleotide analogues as inhibitors of SARS-CoV-2 polymerase, a key drug target for COVID-19. *J Proteome Res* 2020;19(11):4690–7.
- [27] Jácome R, Campillo-Balderas JA, Ponce de León S, Becerra A, Lazcano A. Sofosbuvir as a potential alternative to treat the SARS-CoV-2 epidemic. *Sci Rep* 2020;10(1). <https://doi.org/10.1038/s41598-020-66440-9>.
- [28] Lens S, Miquel M, Mateos-Muñoz B, García-Samaniego J, Forns X. SARS-CoV-2 in patients on antiviral HBV and HCV therapy in Spain. *J Hepatol* 2020;73(5):1262–3.