



Case report

Hyperbilirubinemia with mild COVID-19 patient: A case report

Rawand Abudlrahman Essa^{a,b}, Sirwan Khalid Ahmed^{a,b,*}, Dunya Hars Bapir^c,
Chawan Pirot Abubakr^d

^a Department of Adult Nursing, College of Nursing, University of Raparin, Iraq

^b Rania Teaching Hospital, Sulaimaniyah, Iraq

^c Department of Medical Laboratory, College of Science, University of Raparin, Iraq

^d Department of critical care nursing, College of Nursing, Urmia University of Medical Science, Iran



ARTICLE INFO

Keywords:
Bilirubin
COVID-19
Jaundice
Case report

ABSTRACT

Introduction and importance: Increased total serum bilirubin rarely reported in mild COVID-19 patients. It occurs mostly in severe cases, particularly in those who have liver diseases and admitted to an intensive care unit. The main cause of increased liver biochemistries in Covid-19 patients related to used drugs, the presence of the ACE2 receptor in the liver, and robust inflammatory response. However, limited studies available regarding to jaundice in COVID19 patients.

Case presentation: Here we present a case of hyperbilirubinemia in a mild asymptomatic COVID-19 patient, the patient was diagnosed by RT-PCR three days prior to presentation fever, dark urine, and of acute onset of jaundice. The patient was diagnosed by physical examination and laboratory findings, and treated successfully by high-quality natural honey.

Clinical discussion: A recent studies of COVID-19 increased total serum bilirubin have been reported, mostly after the appearance of the COVID-19 symptoms. The case in the current study was a 48-year-old male patient who was diagnosed with mild COVID-19 three days prior to presentation. After 2 days increased total serum bilirubin. **Conclusion:** Honey is a natural medicine to treat Jaundice in mild COVID-19 patients. However, significant data on larger studies are still lacking to decide. Our case guides for the clinical treatment of conjunctival icterus in mild COVID-19 patients.

1. Introduction

The severe acute respiratory syndrome (SARS-CoV-2) named (COVID-19), that appeared out of Wuhan, China in December 2019, the present universal pandemic is largely responsible for both a rising number of cases and deaths worldwide [1,2]. The most frequent medical presentation is respiratory with cough, difficulty breath, and fever [3]; as well as gastrointestinal symptoms such as nausea, vomiting, abdominal pain, rising bilirubin level, and elevated liver enzymes have been reported [3,4]. Recent studies showed that 11%–23% of COVID-19 patients had abnormal bilirubin levels [5–7]. Furthermore, most studies showed that aspartate aminotransferase AST, alanine aminotransferase ALT levels were abnormal between 14% and 53% COVID-19 patients [3,5,7,8]. In severe cases, the level of bilirubin is higher than in mild cases of COVID-19 [8–10].

To our knowledge, Iraqi research does not currently exist, showing hyperbilirubinemia with COVID-19. Here we report an unusual

presentation of a 48-year-old male patient who had hyperbilirubinemia 3 days after confirmed COVID-19. Without a relevant past medical history, gastrointestinal and other system diseases with a normal liver function test. This report has been written in the line with SCARE 2020 criteria [11].

2. Case report

A 48-year-old male patient was admitted to the emergency room at Rania Teaching Hospital Kurdistan-Region Iraq country, with chief complaint fever, dark urine and acute onset jaundice for duration two days prior to hospitalization. With no past medical history Diseases, drugs, alcohol, smoking, surgery. Systems examination otherwise was insignificant. The patient was diagnosed with mild COVID-19 three days prior to presentation to the emergency room by Nasopharyngeal RT-PCR. No respiratory symptoms (cough, difficulty breath) were present. He had no abdominal pain, vomiting, and nausea. Furthermore, he did

* Corresponding author at: Sara-Rania, 772, Kurdistan region, Iraq.

E-mail address: sirwanahmed777@gmail.com (S.K. Ahmed).

<https://doi.org/10.1016/j.ijscr.2021.105958>

Received 9 April 2021; Received in revised form 27 April 2021; Accepted 28 April 2021

Available online 3 May 2021

2210-2612/© 2021 The Author(s). Published by Elsevier Ltd on behalf of IJS Publishing Group Ltd. This is an open access article under the CC BY-NC-ND license

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

not recently intake acetaminophen or any other drugs, except vitamin C, and vitamin D3.

A physical examination revealed that the patient was obese with conjunctival icterus, without abdominal tenderness, splenomegaly, and hepatomegaly. His temperature was (38.5 °C) normal range (36.1 °C to 37.2 °C), blood pressure of 129/86 mmHg normal range (120/80 mmHg), pulse rate 93 beats per minute normal range (60 to 100 bpm), respiratory rate 17 breath/min with 97% SPO2 on room air. In addition, abdominal, chest, cardiovascular, neurological systems, and radiological findings were normal. Laboratory test results were as the follows: elevated Total serum bilirubin level were 5.5 mg/dL normal range (0.1 to 1.2 mg/dL) mg/dl, with normal serum aspartate aminotransferase (AST) 15 U/L normal range (6 to 34 U/L), Alanine aminotransferase (ALT) 32 U/L normal range (29 to 33 unit per liter U/L), gamma-glutamyl transferase (GGT) 17 U/L normal range (9 to 48 U/L), serum albumin 4.2 g/dl normal range (3.4 to 5.4 g/dL). Alkaline phosphate 86 U/L normal range (44 to 147 U/L), and platelets 254.000 normal range (150.000 to 400.000 per microliter). In addition, complete blood count, total protein, international randomized ratio were normal. Abdominal ultrasound was normal. The patient received treatment under first author guidance with natural high-quality honey 300 mg per day without any adverse effects. Three weeks later, total serum bilirubin (TSB) level 0.9 mg/dL, and he was released from the emergency room with close monitoring (Table 1).

3. Discussion

We reported a case of hyperbilirubinemia with a mild COVID-19 patient which rapidly increased total serum bilirubin (TSB). Many systemic reviews of the present studies show total bilirubin as one of the abnormal diagnostic markers in patients with COVID-19. Moreover, many meta-analyses showed that increased total bilirubin levels were related to an unfavourable COVID-19 progression [7,12–15]. In our case, the patient did not have any symptoms, such as fever, difficult breathing, vomiting, diarrhea, nausea and his condition were stable. Therefore, in COVID-19 patients, liver injury has a possible clinical and biological significance [16]. The hepatic injury could be caused directly by the viral infection of liver cells or caused by medication [17]. In contrast, our case did not use any drugs, such as acetaminophen and anti-viral. Altered levels of bilirubin were reported in Covid-19 patients [17], but their dynamics were not clear, especially as regards the severity of the disease [18]. Panagiotis et al. in his pooled analysis showed that concentration of bilirubin is significantly higher in severe COVID-19 patients (SMD: 0.48 μ mol/L; 95% CI, 0.11 to 0.85 μ mol/L, $P = .012$) [18]. Our patient had elevated total serum bilirubin (TSB). Alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), white blood cells, and international randomized ratio (INR) were normal. Contrastingly, in the large cohort of 1099 patients, found an increasing prevalence of abnormal levels and hepatic aminotransferase, higher AST levels, and hepatic injuries in severe COVID-19. They observed increased levels of AST (21%), ALT (22%), and total bilirubin (10%) in COVID-19 patients [5]. Research studies of the interplay of pre-existing liver conditions with COVID-19 require careful assessment. A recent study concluded that abnormal liver enzymes can be a major factor in a large number of COVID-19 patients, especially in mild forms [19]. Our case shows that increased total serum bilirubin can happen in mild COVID-19 patients. It is critical to investigate laboratory TSB test in mild COVID-19 patients. Further studies are required to understand the prevalence of increase total serum bilirubin in mild COVID-19 patients.

4. Conclusion

Abnormal total serum bilirubin is more common in severe COVID-19 patients. Honey is a natural medicine to treat of Jaundice in mild COVID-19 patients. However, significant data on larger studies are still

Table 1
Patient test results during hospitalization.

Laboratory testes	Day 1	Day 5	Day 10	Day 21
TSB	5.5 mg/dL	4.1 mg/dL	2.3 mg/dL	0.9 mg/dL
(ALT) U/L	32 U/L	31 U/L	28 U/L	29 U/L
(AST) U/L	15 U/L	17 U/L	14 U/L	11 U/L
(GGT) U/L	17 U/L	16 U/L	18 U/L	20 U/L
Serum albumin	4.2 g/dl	4. g/dl	4.6 g/dl	4.4 g/dl
Alkaline phosphate	86 U/L	85 U/L	89 U/L	88 U/L
(WBCs) normal range (4.5 to 11.0 $\times 10^9/L$)	9.0 $\times 10^9/L$	8.2 $\times 10^9/L$	7.04 $\times 10^9/L$	7.1 $\times 10^9/L$
Temperature	38.5 °C	38 °C	37.5 °C	37 °C
INR	0.7	0.8	0.6	0.8

Abbreviations: TSB = total serum bilirubin, ALT = Alanine aminotransferase, AST = aspartate aminotransferase, GGT = gamma glutamyl transferase, WBCs = white blood cells, INR = international randomized ratio.

lacking to decide.

Funding

No source to be stated.

Ethical approval

Approval is not necessary for a case report in our locality.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

CRedit authorship contribution statement

Rawand Essa, Sirwan Ahmed: Rotators managing the case, follow up the patient, writing the manuscript and final approval of the manuscript. **Sirwan K. Ahmed, Dunya Bapir, Chawan Pirot Abubaker:** literature review, writing the manuscript, final approval of the manuscript.

Registration of research studies

Not applicable.

Guarantor

Rawand Abdulrahman Essa is the Guarantor of submission.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Declaration of competing interest

There is no conflict to be declared.

References

- [1] W.H. Organization, WHO Director-General's Remarks at the Media Briefing on 2019-nCoV on 11 February 2020, World Health Organization, Geneva, 2020. Available via <https://www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020>. Accessed. 10.
- [2] R. Lu, X. Zhao, J. Li, P. Niu, B. Yang, H. Wu, W. Wang, H. Song, B. Huang, N. Zhu, Y. Bi, X. Ma, F. Zhan, L. Wang, T. Hu, H. Zhou, Z. Hu, W. Zhou, L. Zhao, J. Chen, Y. Meng, J. Wang, Y. Lin, J. Yuan, Z. Xie, J. Ma, W.J. Liu, D. Wang, W. Xu, E.

- C. Holmes, G.F. Gao, G. Wu, W. Chen, W. Shi, W. Tan, Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding, *Lancet* 395 (2020) 565–574, [https://doi.org/10.1016/S0140-6736\(20\)30251-8](https://doi.org/10.1016/S0140-6736(20)30251-8).
- [3] C. Huang, Y. Wang, X. Li, L. Ren, J. Zhao, Y. Hu, L. Zhang, G. Fan, J. Xu, X. Gu, Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China, *Lancet* 395 (2020) 497–506.
- [4] K.S. Cheung, I.F.N. Hung, P.P.Y. Chan, K.C. Lung, E. Tso, R. Liu, Y.Y. Ng, M.Y. Chu, T.W.H. Chung, A.R. Tam, Gastrointestinal manifestations of SARS-CoV-2 infection and virus load in fecal samples from the Hong Kong cohort and systematic review and meta-analysis, *Gastroenterology* 159 (1) (2020) 81–95.
- [5] W. Guan, Z. Ni, Y. Hu, W. Liang, C. Ou, J. He, L. Liu, H. Shan, C. Lei, D.S.C. Hui, Clinical characteristics of coronavirus disease 2019 in China, *N. Engl. J. Med.* 382 (2020) 1708–1720.
- [6] Q. Cai, D. Huang, H. Yu, Z. Zhu, Z. Xia, Y. Su, Z. Li, G. Zhou, J. Gou, J. Qu, et al., *J. Hepatol.* (2020).
- [7] N. Chen, M. Zhou, X. Dong, J. Qu, F. Gong, Y. Han, Y. Qiu, J. Wang, Y. Liu, Y. Wei, Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study, *Lancet* 395 (2020) 507–513.
- [8] D. Wang, B. Hu, C. Hu, F. Zhu, X. Liu, J. Zhang, B. Wang, H. Xiang, Z. Cheng, Y. Xiong, Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China, *Jama.* 323 (2020) 1061–1069.
- [9] Z.P. Qian, X. Mei, Y.Y. Zhang, Y. Zou, Z.G. Zhang, H. Zhu, H.Y. Guo, Y. Liu, Y. Ling, X.Y. Zhang, Analysis of baseline liver biochemical parameters in 324 cases with novel coronavirus pneumonia in Shanghai area, *Chin. J. Hepatol.* 28 (2020). E005–E005.
- [10] X. Zhang, H. Cai, J. Hu, J. Lian, J. Gu, S. Zhang, C. Ye, Y. Lu, C. Jin, G. Yu, Epidemiological, clinical characteristics of cases of SARS-CoV-2 infection with abnormal imaging findings, *Int. J. Infect. Dis.* (2020).
- [11] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, A. Kerwan, A. Thoma, A.J. Beamish, A. Noureldin, A. Rao, B. Vasudevan, The SCARE 2020 guideline: updating consensus Surgical CAse REport (SCARE) guidelines, *Int. J. Surg.* 84 (2020) 226–230.
- [12] B.M. Henry, M.H.S. De Oliveira, S. Benoit, M. Plebani, G. Lippi, Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis, *Clin. Chem. Lab. Med.* 58 (2020) 1021–1028.
- [13] G. Lippi, M. Plebani, Laboratory abnormalities in patients with COVID-2019 infection, *Clin. Chem. Lab. Med.* 58 (2020) 1131–1134.
- [14] Q. Ruan, K. Yang, W. Wang, L. Jiang, J. Song, Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China, *Intensive Care Med.* 46 (2020) 846–848.
- [15] A.J. Rodriguez-Morales, J.A. Cardona-Ospina, E. Gutiérrez-Ocampo, R. Villamizar-Peña, Y. Holguin-Rivera, J.P. Escalera-Antezana, L.E. Alvarado-Arnez, D.K. Bonilla-Aldana, C. Franco-Paredes, A.F. Henao-Martinez, Clinical, laboratory and imaging features of COVID-19: a systematic review and meta-analysis, *Travel Med. Infect. Dis.* 101623 (2020).
- [16] C. Zhang, L. Shi, F.-S. Wang, Liver injury in COVID-19: management and challenges, *Lancet Gastroenterol. Hepatol.* 5 (2020) 428–430.
- [17] J. Sun, A. Aghemo, A. Forner, L. Valenti, COVID-19 and liver disease, *Liver Int.* (2020).
- [18] P. Paliogiannis, A. Zinellu, Bilirubin levels in patients with mild and severe Covid-19: a pooled analysis, *Liver Int.* (2020).
- [19] A. Agarwal, A. Chen, N. Ravindran, C. To, P.J. Thuluvath, Gastrointestinal and liver manifestations of COVID-19, *J. Clin. Exp. Hepatol.* (2020).