Acta Biomed 2020; Vol. 91, N. 3: e2020002 DOI: 10.23750/abm.v91i3.9796 



# Elevated transaminases in a COVID-19 positive patient at term of gestation: a case report

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**Summary.** *Background:* The coronavirus disease 2019 (COVID-19) pandemic is caused by the severe acute respiratory syndrome 2 virus (SARS-CoV-2) and it is spreading worldwide with an alarming high transmission rate. SARS-CoV-2 usually attacks the lungs causing a wide range of symptoms ranging from mild dyspnea to severe shortness of breath requiring intubation. Elevation of liver transaminases in the patients' sera has been described in up to 53% of the COVID-19 positive patients. The underlying pathogenic mechanisms of the virus on the liver cells are unclear and only few hypotheses are currently available. Data on COVID-19 in pregnant women are lacking and the management of COVID-19 pregnant women is challenging. An elevation of the transaminases during pregnancies infected by SARS-CoV-2 has never been described before. *Methods:* Here we presented the case of a 29 years-old patient at 38 weeks of gestation COVID-19 positive with elevated transaminases. *Results:* The patient showed a progressive decrease of transaminases after the delivery of the fetus. We provided details about the daily transaminases trend, the therapy used and the maternal/neonatal outcomes. *Conclusions:* We speculate that in our case the delivery of the fetus contributed to the normalization of the liver enzymes. In patients affected by COVID-19, at term of gestation, with elevated transaminases, delivery of the fetus is an appealing option. If confirmed by larger studies, our proposed management might be incorporated in the obstetrical management guidelines for COVID-19 positive patients. (www.actabiomedica.it)

**Key words:** COVID-19, SARS-Cov-2, pregnancy, liver injury, transaminases, newborn

## Background

The coronavirus disease 2019 (COVID-19) is the disease caused by the novel coronavirus called "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2). From the city of Wuhan, China, in December 2019, the virus spread outside of Asia rapidly and the World Health Organization (WHO), on March 11th, declared a pandemic emergency. This virus is highly contagious and is mainly transmitted through droplets. To date there is no vaccine and no specific treatment available and the approach to the patient has been changed (1–3). The clinical course in the majority of cases is transient and paucisymptomatic with mild fever, dyspnea, cough, body aches, headache and diarrhea; in a minority of patients it can lead to respiratory failure and in 2-9% of affected individuals it can be fatal (4). The exact underlying molecular pathogenetic mechanism is still unclear, some researchers hypothesized that the virus can trigger an excessive immune reaction with abnormal cytokine release, and consequently a harsh tissue damage (5). Indeed, the interleukin-6 (IL-6) is elevated in cases of complicated COVID-19 and could trigger the so-called "cytokine storm", an inflammatory syndrome that can affect multiple organs of the human body (3). The gold

standard for the diagnosis is the SARS-CoV-2 reverse transcriptase (RT)-qPCR from the nasopharyngeal secretions. Other laboratory values such as total white blood cell and lymphocyte count are inconsistently altered and are not specific for COVID-19 (6,7). Several studies reported an impairment of liver function tests with an elevation of alanine and aspartate aminotransferase (ALT and AST), gamma glutamyl transferase, alkaline phosphatase, and total bilirubin in the serum (7,8). COVID-19 has been poorly studied during pregnancy with only few reports available to date. A case of transaminases elevation during pregnancy affected by COVID-19 has never been reported before. Here we report a case of a 29 years-old patient at 38 weeks of gestation, COVID-19 positive with elevated transaminases. We provide details regarding her transaminases trend, treatment and outcome in the effort of shining some light on the pathogenesis and the management of this new disease.

## Methods

Our patient signed a written informed consent form for her case to be published. Our study is in accordance with the Declaration of Helsinki, in accordance with the Consensus-based Clinical Case Reporting Guideline Development (http://www.equator-network.org/) (9), and the Committee on Publication Ethics (COPE) guidelines (http://publicationethics.org/).

## Results

A 29-year-old gravida 3 para 2002 at 38 weeks and 2 days of gestation presented to the obstetric emergency triage complaining of irregular uterine contractions and was incidentally found to have fever (body temperature of 101 °F). No other symptoms were present such as cough, chills, body ache, vaginal bleeding, loss of amniotic fluid at the time of admission. However, upon further questioning, the patient admitted a recent history of upper respiratory congestion and non-productive cough started 3 days earlier. The patient had no pertinent past medical or surgical history. The prenatal care had been non complicated. The patient was tested for COVID-19, Influenza A and B virus and RSV with nasopharyngeal swab PCR and considered a "Patient under investigation" (PUI). A complete blood cell (CBC) count, complete metabolic panel (CMP), urine and blood cultures, were collected. The laboratory values resulted significant for elevated AST and ALT (2046 and 1375 U/L), and low absolute lymphocyte count (0.6 K/UL). A chest X ray (CXR) was performed on admission and showed multifocal bilateral infiltrates. (Fig.1).

The cervical exam was 1/0/-3 (respectively dilatation, effacement, and station). A category 1 fetal heart electronic monitoring was noted, with the tocometry positive for 4 contractions every 10 minutes. The decision was made to start induction of labor with intracervical Cook balloon placement, followed by prostaglandins and oxytocin. Her labor course was uneventful, and the patient had a normal vaginal delivery the following day. The neonatal outcome was as follows: Apgar was 9/9, weight 3630 grams, umbilical cord pH 7.26 with a base deficit of 5. Azithromycin and Rocephin were started on day two of admission. Rocephin was discontinued on hospital day 3 after 3 doses were received, and Azithromycin was administered for a total of 5 days. Treatment with hydroxychloroquine was started as soon as the COVID-19 test result became available on day 4 of hospitalization. A repeated CXR on hospital day 3 showed few patchy parenchymal opacities, not significantly changed compared to

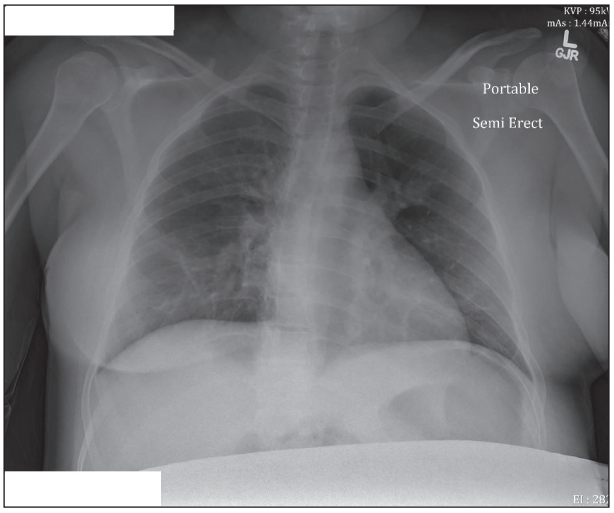


**Figure 1.**

the previous exam (Fig. 2). A CT scan of the chest on hospital day 3 showed no evidence of pulmonary embolism. The body temperature was intermittently elevated from hospital day 1 to 6, and then normalized on day 7 and 8. She received morphine 2 mg IVP PRN for postpartum routine pain control. The transaminases level decreased progressively (Table 1 and Fig. 3). The hepatitis viral panel was negative. The patient was clinically stable during the hospitalization period, with no need for any oxygen therapy and normal O2 peripheral saturation and arterial blood gases. The mother and her baby were discharged home in a stable condition on hospital day 8, the baby nasopharyngeal swab PCR resulted negative for COVID-19. We did not administer paracetamol and we delayed the treatment with hydroxychloroquine out of fear of liver toxicity; we avoided ibuprofen because of anecdotal reports of worse COVID-19 outcomes with it.

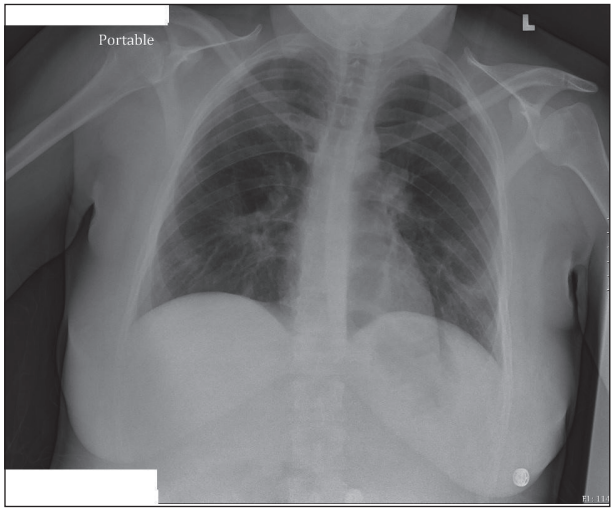


**Figure 2.**

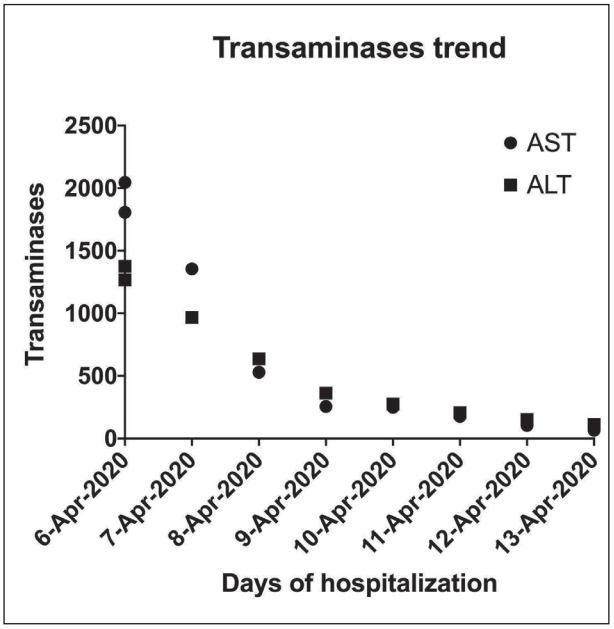


**Figure 3.**

**Table 1.** Trend of transaminases during days of hospitalization

| | AST | ALT |
|---|---|---|
| Day 1 – 4/6/2020 at h 16:50 | 2046 | 1375 |
| Day 1 – 4/6/2020 at h 20:30 | 1806 | 1267 |
| Day 2 – 4/7/2020 at h 9:30 | 1355 | 966 |
| Day 3 – 4/8/2020 at h 5:00 | 529 | 637 |
| Day 4 – 4/9/2020 at h 4:00 | 256 | 362 |
| Day 5 – 4/10/2020 at h 5:00 | 249 | 276 |
| Day 6 – 4/11/2020 at h 3:55 | 177 | 207 |
| Day 7 – 4/12/2020 at h 3:55 | 104 | 152 |
| Day 8 – 4/13/2020 at h 6:00 | 65 | 111 |

AST: Aspartate transaminase, ALT: Alanine transaminase

## Discussion

We report the first case of elevated transaminases in a patient at term of gestation and COVID-19 positive. SARS-CoV-2 attacks preferentially the human lungs causing an upper respiratory infection that could be fatal in some cases (4,10). Liver damage during COVID-19 has been described before in non-pregnant patients (7,8). In these studies, liver damage is mainly transient and can return to normal without any specific treatment (11). Zhang et al. in March 2020 analyzed all the reported cases of COVID-19 with associated description of the AST/ALT trend and reported elevated liver enzymes in 14–53% of the cases. The hepatic involvement seemed to be more frequent in patients with a more severe clinical condition (11). Epidemiologic studies reported a higher proportion

of patients with liver dysfunction in Wuhan, where the virus outbreak arose, than other Chinese regions. The authors speculated that a higher viral load can lead to a more severe liver impairment (12). There is some molecular evidence supporting a direct tropism of SARS-CoV-2 for the liver. The enzyme Angiotensin Converting Enzyme-2 (ACE-2) is the receptor for the virus. This protein is highly expressed on type II alveolar epithelial cells but also on other human cells such as enterocytes, endothelial cells and bile duct cells (13,14). Some reports revealed a moderate microvesicular steatosis with mild lobular and portal activity in liver biopsy specimens of COVID-19 patients (6). In addition, viral RNA was found in stool samples of COVID-19 patients with diarrhea (15). All these findings support the hypothesis that the virus would be able to infect bile duct cells causing a liver alteration. In our case, we think that the liver damage has been caused directly by the virus. We excluded a drug induced liver toxicity because the initial labs were collected before the administration of any therapy, at presentation of the patient in triage. We also excluded the pregnancy conditions typically associated with elevated transaminases at term of gestation, such as hemolysis, elevated liver enzymes and low platelets (HELLP) syndrome and preeclampsia, since the patient had normal blood pressure and there were no other associated laboratory value alterations such as low platelets and there were not associated symptoms such as headache, right upper quadrant pain or scotomata. We do not know why the transaminases normalized during the hospitalization and we propose few hypotheses. One hypothesis is that the delivery of the fetus triggered an immune system reaction that facilitated the elimination of the virus from the maternal body. The therapy with antibiotics and hydroxychloroquine could also have been a factor involved in the transaminases downward trend. Lastly, the virus could have been spontaneously cleared by the maternal immune system, without any influence by the pregnancy status or any administered therapy.

## Conclusion

We speculate that fetal delivery leads to normalization of the liver enzymes in COVID-19 positive pregnant patients. Currently there is not any specific clinical guideline available for cases similar to ours. We suggest to expedite the delivery in COVID-19 positive patient at term of gestation. Larger studies are needed for our conclusions to be incorporated in new clinical guidelines for COVID-19 pregnant patients management.

**Ethics Approval and Consent to Participate:** IRB waived the Ethics approval because of the anonymity of the data. The consent to participate was provided by the patient in written form.

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

**Availability of data and materials:** All data generated or analyzed during this study are included in this published article.

**Funding:** This research received no external funding.

**Authors' contributions:** CN and GS designed and coordinated the work, collected the data, and corrected the manuscript. AS interpreted the patient data regarding the anamnesis. GS supervised the discussion and the conclusions. All authors read and approved the final manuscript.

**Conflict of interest:** Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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Received: 13 May 2020
Accepted: 15 June 2020
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