

N-acetyl Cysteine Use in the Treatment of Ischemic Hepatitis in the Setting of COVID-19 Infection

Vivian Agumadu, MD¹, Gabriela S. Generette, MD¹, Altaf Dawood, MD¹, Nicole Gentile, MD¹, Mario Affinati, MD¹

¹Department of Internal Medicine, University of Illinois College of Medicine, Rockford, IL, USA

Introduction

- Acute liver injury occurs in 15-53% of COVID-19 patients.
- Most often, elevation in transaminases is mild (1-2 times the upper limit of normal).
- Severe liver injury has been described possibly secondary to hepatic ischemia.

Case description

58 year-old male presented to ED with generalized fatigue, chills and cough for 1 week.

- **Past Medical History:**
 - Atrial flutter, adult congenital heart disease, cardiac cirrhosis
- **Past Surgical History:**
 - Open heart surgery, tricuspid valve replacement, cardiac ablation, pacemaker/defibrillator placement
- **Social History:**
 - No smoking, alcohol or illicit drug use
- **Medications:**
 - Warfarin 5 mg QD, Spironolactone 25 mg QD, Losartan 12.5 mg BID
- **Initial testing:** COVID-19 PCR positive
- **Vitals:**
 - BP 133/72 mmHg, HR 73 beats/minute, SpO2 96% on 8 L of nasal canula, Temperature 98 F
- **Pertinent Positive Physical Exam Findings:**
 - General: Not in acute distress
 - Lungs: Bibasilar crackles bilaterally
 - Heart: Regular rate and rhythm, no murmurs
 - Abdomen: Non-tender, non-distended. Bowel sounds present. No hepatosplenomegaly
- **Lab work:**
 - COVID-19 PCR positive
 - WBC 3.6, Hgb 15.8, Plt 32
 - Na 127, K 4.0, Cr 1.2
 - AST 1954, ALT 190, ALP 137, Total bilirubin 0.9 (baseline liver tests 8 months prior were normal)
 - INR 19.1

Case description

- **Lab work cd:**
 - EtOH level, acetaminophen level, salicylate level — normal
 - Urine drug screen — negative
 - Acute hepatitis panel, Hepatitis E IgM — negative
 - ANA, AMA, ASMA, anti-LKM, IGG subclasses, ceruloplasmin — normal
 - Alpha-1 antitrypsin level — normal
 - tTG level — normal
 - HIV, VZV PCR, EBV PCR, HSV PCR and CMV PCR — normal
- **Imaging:**
 - Chest x-ray: No airway opacities. No evidence of pneumothorax or pleural effusion.
 - Abdominal ultrasound: Known liver cirrhosis and ascites without any concerning liver lesion.
 - CT abdomen was not done.
- **Treatment:**
 - N-acetylcysteine (NAC) protocol was initiated with decrease in elevated liver enzymes by half in the first 72 hours and >20 fold of the highest level upon discharge.
 - Supratherapeutic INR was treated with 1 dose of vitamin K. Warfarin was being held.
 - COVID-19 pneumonia was treated with Dexamethasone 6 mg QD for 10 days.

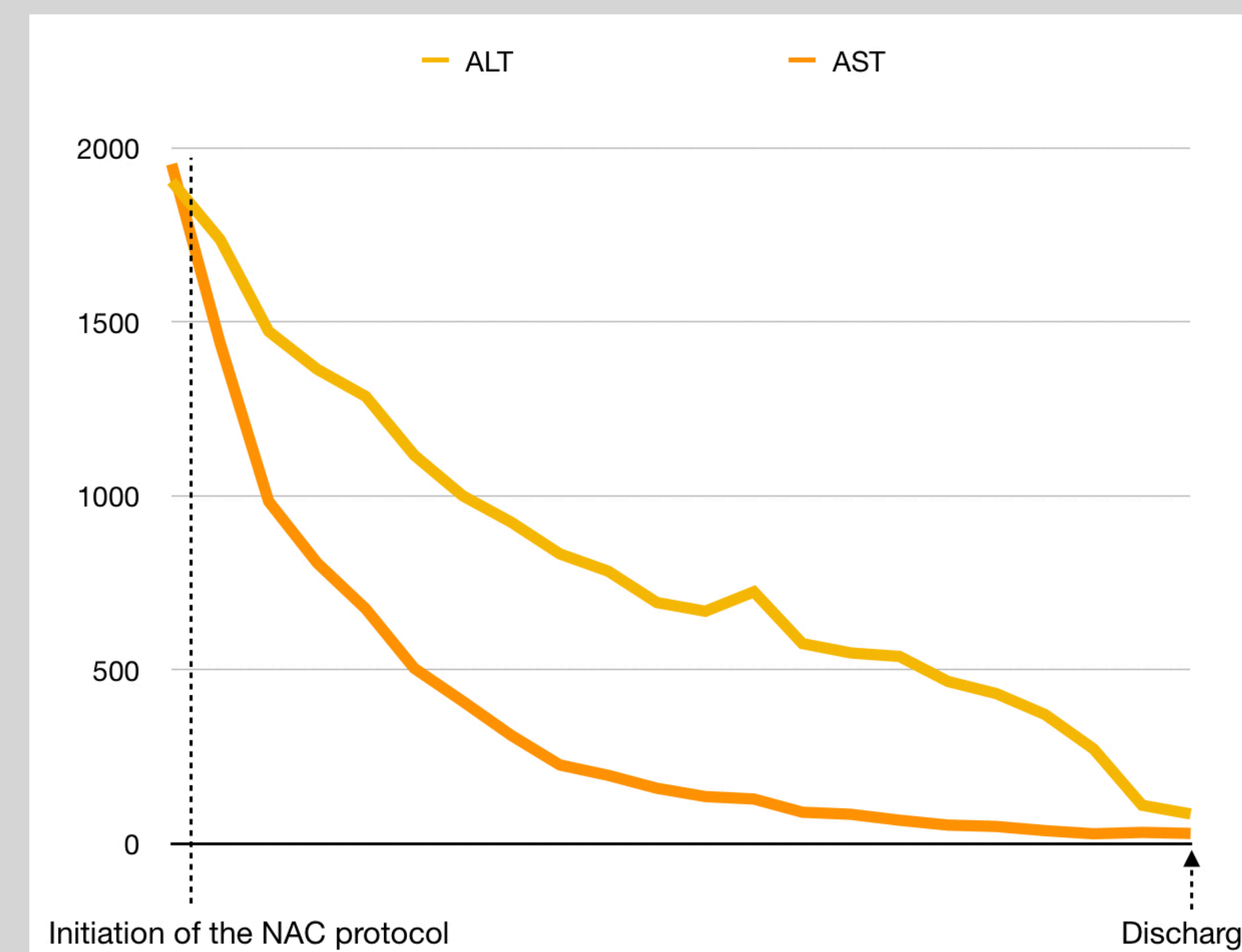


Image 1. Liver enzyme trend after initiation of the NAC protocol

Ischemic Hepatitis (IH)

- It results from insufficient blood flow volume and/or oxygen content to the hepatocytes.
- IH is characterized as a transient, rapid and considerable increase in liver enzymes.
- Acute hypoxic respiratory failure as a result of COVID-19 infection is one of the potential causes of this type of liver injury.
- The liver is one of the most commonly affected organs by COVID-19 infection.
- In the setting of COVID-19 infection, prompt diagnosis and recognition of IH is critical as studies describe mortality rates as high as 50%.
- A study conducted by Maiwall et al. Demo started benefit in the use of NAC in non-acetaminophen liver injury with lower mortality due to liver failure.

Conclusion

We describe our clinical experience with NAC in the setting of COVID-19 infection with severe IH and propose that NAC is considered in the treatment of COVID-19 infection in patients with IH, however further research including prospective clinical trials is needed to better validate this.

References

1. Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, Liu S, Zhao P, Liu H, Zhu L, Tai Y, Bai C, Gao T, Song J, Xia P, Dong J, Zhao J, Wang FS. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *Lancet Respir Med.* 2020 Apr;8(4):420-422. doi: 10.1016/S2213-2600(20)30076-X. Epub 2020 Feb 18. Erratum in: *Lancet Respir Med.* 2020 Feb 25; PMID: 32085846; PMCID: PMC7164771.
2. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, Huang H, Zhang L, Zhou X, Du C, Zhang Y, Song J, Wang S, Chao Y, Yang Z, Xu J, Zhou X, Chen D, Xiong W, Xu L, Zhou F, Jiang J, Bai C, Zheng J, Song Y. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. *JAMA Intern Med.* 2020 Jul 1;180(7):934-943. doi: 10.1001/jamainternmed.2020.0994. Erratum in: *JAMA Intern Med.* 2020 Jul 1;180(7):1031. PMID: 32167524; PMCID: PMC7070509.
3. Huang H, Li H, Chen S, Zhou X, Dai X, Wu J, Zhang J, Shao L, Yan R, Wang M, Wang J, Tu Y, Ge M. Prevalence and Characteristics of Hypoxic Hepatitis in COVID-19 Patients in the Intensive Care Unit: A First Retrospective Study. *Front Med (Lausanne).* 2021 Feb 11;7:607206. doi: 10.3389/fmed.2020.607206. PMID: 33681238; PMCID: PMC7928422.