

Alexander J Kaye, MD, MBA¹; Reena Razdan, MD¹; Sarah Meyers, DO²; and Sushil Ahlawat, MD^{1,3}

¹Department of Medicine, Rutgers New Jersey Medical School, Newark, NJ, ²Department of Psychiatry, Rutgers Robert Wood Johnson Medical School, Piscataway, NJ, ³Division of Gastroenterology and Hepatology, Rutgers New Jersey Medical School, Newark, NJ

Introduction

- Acute alcoholic hepatitis is associated with high morbidity and mortality
- Between 2010-2014, the incidence of admissions for acute alcoholic hepatitis was seen to increase each year
- There is a strong association between alcohol use disorder and generalized anxiety disorder (GAD)
- GAD has a lifetime prevalence of 6.2% for patients between the ages of 18 and 64 years old
- Currently, little data exist about the association between acute alcoholic hepatitis and GAD, and the outcomes of alcoholic hepatitis patients with comorbid GAD

Aim

- The purpose of this study is to assess the outcomes of acute alcoholic hepatitis in patients with GAD

Methods

- Hospitalized acute alcoholic hepatitis patients from the National Inpatient Sample database from 2014 were selected
- Diagnoses were identified with ICD-9 CM codes
- SPSS Premium Edition was used for analysis
- Patient demographics and outcomes of acute alcoholic hepatitis were compared between the groups with and without GAD
- The outcomes of interest were inpatient mortality, acute hepatic failure, sepsis, acute respiratory failure, acute kidney injury, acute deep vein thrombosis, hepatic encephalopathy, and hypotension/shock
- Chi-square tests and independent t-tests were used to compare proportions and means respectively
- Multivariate logistic regression analysis was performed to determine if GAD is an independent predictor for the outcomes, adjusting for age, sex, race, and Charlson Comorbidity Index

Table 1: Patient Demographics and Characteristics

| Variable | With GAD | Without GAD | P-value |
|---|-----------------|-----------------|---------|
| N = 9,931 | N = 1,954 | N = 7,977 | |
| Patient age, mean (SD) | 44.6 (11.3) | 47.1 (11.7) | <0.001 |
| Sex, N (%) | | | <0.001 |
| Female | 838 (42.9%) | 5,463 (68.5%) | |
| Male | 1,116 (57.1%) | 2,514 (31.5%) | |
| Race, N (%) | | | <0.001 |
| White | 1,495 (83.2%) | 5,194 (69.3%) | |
| Black | 109 (6.1%) | 894 (11.9%) | |
| Hispanic | 127 (7.1%) | 941 (12.6%) | |
| Asian or Pacific Islander | 11 (0.6%) | 91 (1.2%) | |
| Native American | 22 (1.2%) | 143 (1.9%) | |
| Other | 33 (1.8%) | 235 (3.1%) | |
| Length of stay, in days (SD) | 4.7 (4.4) | 4.9 (5.0) | 0.094 |
| Total hospital charges, in \$ (SD) | 28,323 (38,012) | 34,965 (63,879) | <0.001 |
| Charlson Comorbidity Index (SD) | 0.45 (0.80) | 0.51 (0.91) | 0.001 |

Results

Table 2: Multivariate Regression Analysis of Outcomes

| Outcomes | *Adjusted odds ratio | 95% Confidence Interval | P-value |
|-----------------------------------|----------------------|-------------------------|---------|
| Inpatient mortality | 1.32 | 0.85 – 2.05 | 0.221 |
| Acute hepatic failure | 1.87 | 1.25 – 2.80 | 0.002 |
| Sepsis | 1.57 | 1.15 – 2.15 | 0.005 |
| Acute respiratory failure | 1.43 | 1.06 – 1.93 | 0.020 |
| Acute kidney injury | 1.59 | 1.30 – 1.95 | <0.001 |
| Acute deep vein thrombosis | 0.59 | 0.25 – 1.41 | 0.238 |
| Hepatic encephalopathy | 1.60 | 1.29 – 1.98 | <0.001 |
| Hypotension/shock | 1.25 | 1.10 – 1.43 | <0.001 |

*Adjusted for age, sex, race, and the Charlson Comorbidity Index

Discussion and Conclusion

- This study indicates that GAD is associated with an elevated risk of acute hepatic failure, acute respiratory failure, acute kidney injury, hepatic encephalopathy, and hypotension/shock in patients hospitalized with acute alcoholic hepatitis
- Some evidence has found that the medications used to treat GAD, including SSRIs, have the potential to be hepatotoxic. In a patient experiencing acute alcoholic hepatitis, anxiolytics may have a role in worsening the clinical outcomes
- Prior studies have demonstrated increased psychologic stress has been linked to increased alcohol intake, which may cause the findings seen in the study if GAD patients are having increased alcohol intake, elevating the risk of a more severe hepatic injury
- GAD is known to be a state of chronic inflammation. Pro-inflammatory cytokines have been found to induce stellate cell activation and lead to progressive fibrosis. This possible expedited damage to the liver may also help explain the results of this study
- Careful outpatient screening for alcohol use disorder in GAD patients with appropriate referrals to psychiatrists for treatment has the potential to reduce the number of patients presenting with severe complications of acute alcoholic hepatitis

References

- Doshi, S. D., Stotts, M. J., Hubbard, R. A., & Goldberg, D. S. (2021). The changing burden of alcoholic hepatitis: rising incidence and associations with age, gender, race, and geography. *Digestive diseases and sciences*, 66, 1707-1714.
- Smith, J. P., & Book, S. W. (2010). Comorbidity of generalized anxiety disorder and alcohol use disorders among individuals seeking outpatient substance abuse treatment. *Addictive behaviors*, 35(1), 42-45.
- Kessler, R. C., Petukhova, M., Sampson, N. A., Zaslavsky, A. M., & Wittchen, H. U. (2012). Twelve-month and lifetime prevalence and lifetime morbid risk of anxiety and mood disorders in the United States. *International journal of methods in psychiatric research*, 21(3), 169-184.
- Costello, H., Gould, R. L., Abrol, E., & Howard, R. (2019). Systematic review and meta-analysis of the association between peripheral inflammatory cytokines and generalised anxiety disorder. *BMJ open*, 9(7), e027925.
- Esper, L. H., & Furtado, E. F. (2013). Gender differences and association between psychological stress and alcohol consumption: A systematic review. *J Alcohol Drug Depend*, 1(3), 116-20.
- Hosseini, N., Shor, J., & Szabo, G. (2019). Alcoholic hepatitis: a review. *Alcohol and Alcoholism*, 54(4), 408-416.
- Lucena, M. I., Carvajal, A., Andrade, R. J., & Velasco, A. (2003). Antidepressant-induced hepatotoxicity: Expert opinion on drug safety, 2(3), 249-262.