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Etiologies of Marked Transaminase Elevation: Systematic Review and Proportion Meta-Analysis

Mouhand Mohamed MD¹, Daniel Marino MD ¹ Azizullah Beran MD², Yousef Elfanagely MD¹, Mohamed A Abdallah MD³, Firrah Saeed MD¹, Hamad Mohamed MD, Kittichai Promrat MD¹

¹Warren Alpert Medical School of Brown University, Providence, RI, United States; ² Indiana University, Indianapolis, Indiana, United States.

; ³ Division of Gastroenterology, University of Minnesota, Minneapolis, Minnesota; ⁴ HMC, Doha, Qatar

Introduction

- Among liver injury causes, only a few result in extreme liver enzyme rise, particularly alanine aminotransferase (ALT) or aspartate aminotransferase (AST) levels exceeding 1000 international units per liter (IU/L).
- This review aims to summarize common etiologies of marked transaminitis.

Methods

- A comprehensive search on PubMed, EMBASE, Cochrane Library, and Google Scholar from inception through April 2022 for relevant studies reporting on the frequency of marked transaminitis etiologies (ALT or AST >1000 IU/L).
- A proportion meta-analysis to pool frequencies with the corresponding 95% confidence interval (CI). I^2 adjudicated heterogeneity. The random-effects model was utilized for statistical analysis.

Results

- Four relevant studies, comprising 1138 patients, were included in the analysis.
- The pooled frequency of various etiologies as below:
 - Ischemic hepatitis = 45% (95% CI 34-55%, $I^2=92\%$).
 - Viral hepatitis = 16% (95% CI 3-34%, $I^2=98\%$).
 - Toxin or drug-induced liver injury (DILI) = 13% (95% CI 8-18%, $I^2=85\%$).
 - Acetaminophen-induced liver injury = 8% (95% CI 6-10%, $I^2=9\%$).
 - Pancreaticobiliary causes = 6% (95% CI 1-16%, $I^2=96\%$).
 - Others (procedure-related, autoimmune, rhabdomyolysis, etc.) = 7% (95% CI 2-15%, $I^2=94\%$).
 - Idiopathic = 6% (95% CI 4-7%, $I^2=14\%$).

“Ischemic hepatitis is the most common cause of extreme transaminitis.”

“Extrahepatic-biliary obstruction can lead to marked transaminase elevation.”



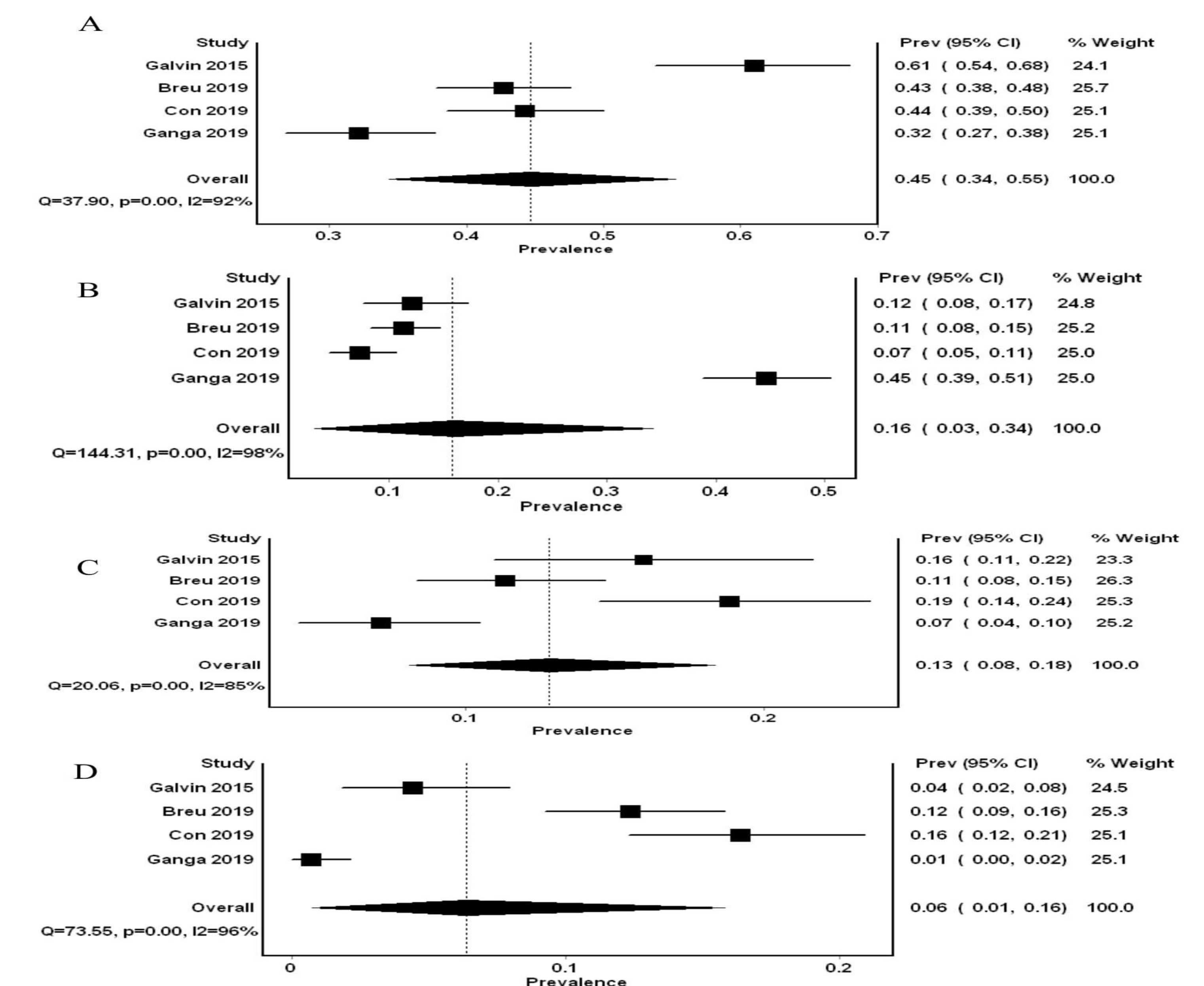
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Discussion

- This is the first meta-analysis to examine etiologies of marked transaminase elevation.
- Liver ischemia is the most common cause of ALT or AST above 1000 IU/L. Other common causes are DILI or toxins, viral hepatitis, and extrahepatic biliary obstruction.
- A notable finding of this review is the presence of extrahepatic biliary obstruction among the common causes of marked transaminitis.



Forest plots summarizing the pooled frequency of (A) ischemic hepatitis, (B) viral hepatitis, (C) drug or toxin injury, and (D) extrahepatic biliary obstruction among patients presenting with extreme transaminase elevation.