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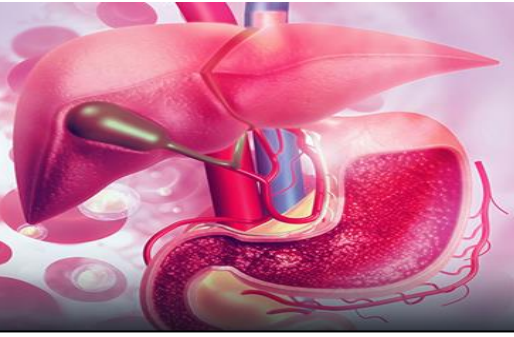

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Best Regards,

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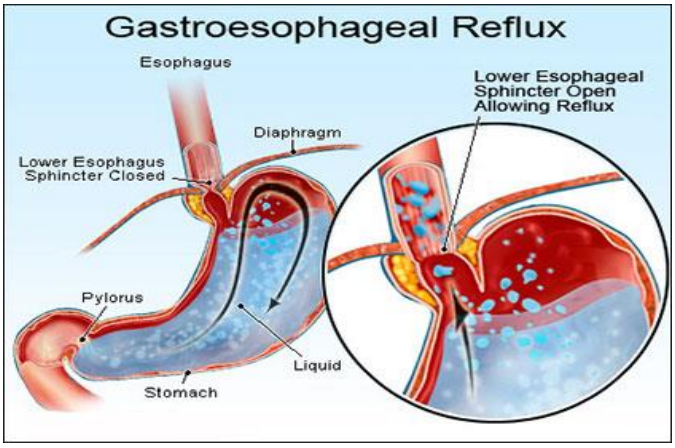
Metabolic Dysfunction-Associated Steatotic Liver Disease and Gastroesophageal Reflux Disease

INTRODUCTION- Gastroesophageal reflux disease (GERD) is a prevalent chronic condition affecting approximately 20% of the population, characterized by the regurgitation of gastric contents into the esophagus. It is commonly associated with risk factors such as obesity, decreased esophageal acid clearance, and motor abnormalities.[1] However, despite efforts to manage these risk factors, controlling GERD progression remains challenging. Recently, metabolic dysfunction-associated steatotic liver disease (MASLD), previously known as non-alcoholic fatty liver disease (NAFLD), has emerged as a potential risk factor for GERD. MASLD, affecting around 25% of the global population, is strongly linked to obesity and insulin resistance and can progress to severe liver conditions. While an association between MASLD and GERD has been suggested, the causal relationship remains unclear, particularly across different ethnic groups.[2] This study explored the potential causal association between MASLD and GERD using genome-wide association study (GWAS) genetic data.



Gastroesophageal Reflux Disease

METHODS- A two-sample bidirectional Mendelian Randomization (MR) analysis was performed using genetic data for Metabolic Associated Steatotic Liver Disease (MASLD) proxies and GERD. MASLD-related data, including non-alcoholic fatty liver disease (NAFLD) and liver fat percentage, were sourced from large genome-wide association studies (GWAS), while GERD data were obtained from 602,604 participants. For MASLD proxies, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels were used, with GERD data from 948 cases and 177,516 controls. Genetic instruments were selected using significance thresholds of $p < 5.0 \times 10^{-6}$ for NAFLD and $p < 5.0 \times 10^{-5}$ for GERD, followed by clumping to exclude confounding SNPs and harmonization of exposure and outcome datasets. Statistical analyses were conducted using inverse variance weighting (IVW) and sensitivity methods in R with 'TwoSampleMR' and 'MR-PRESSO', reporting odds ratios (ORs) and 95% confidence intervals (CIs).

RESULTS- Genetic screening for MASLD and GERD-related indicators revealed distinct findings across populations. No significant causal relationship was found between NAFLD or liver fat percentage and GERD (IVW: OR = 1.054, 95% CI, p = 0.236; OR = 0.977, 95% CI, p = 0.258, respectively). However, genetically

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predicted GERD was associated with an increased risk of NAFLD (IVW: OR = 1.485, 95% CI, p < 0.001) and liver fat percentage (IVW: OR = 1.244, 95% CI, p < 0.001). Sensitivity analyses confirmed the robustness of these results, with no heterogeneity or pleiotropy detected. A significant positive association was found between genetically predicted ALT and GERD (IVW: OR = 2.305, 95% CI, p = 0.008), but no causal link was observed between AST and GERD (IVW: OR = 0.973, 95% CI, p = 0.926) (Figure 1). Additionally, no causal relationship between GERD and ALT or AST was noted. After addressing heterogeneity by removing outliers, GERD remained positively associated with ALT (IVW: OR = 1.009, 95% CI, p = 0.020), with no significant pleiotropy detected. Both populations showed robust results in sensitivity analyses.

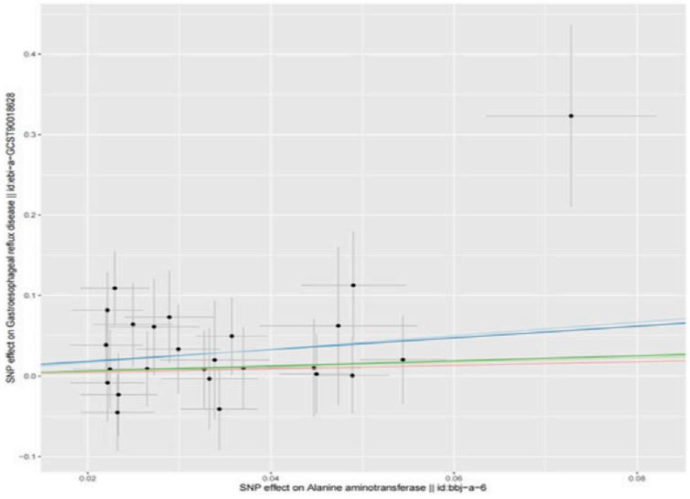

Figure 1: Scatter plot of Mendelian randomization analysis showing association between ALT and GERD

DISCUSSION- The current study establishes a causal relationship between MASLD and GERD through Mendelian Randomization (MR) analysis. It demonstrates that GERD increases the risk of MASLD, while no causal effect of MASLD on GERD was found. A positive association between ALT (a MASLD proxy) and GERD was observed, but no causal link was found between GERD and ALT/AST levels. These findings contrast with previous research suggesting a connection between NAFLD and GERD.[3] The use of ALT/AST as MASLD proxies may introduce bias, as they do not fully reflect the complexity of MASLD, and genetic or metabolic differences between populations may explain the observed discrepancies. Further research is needed to explore the mechanisms underlying these relationships.[4]

CONCLUSION- This study found a reverse causality between MASLD and GERD in one population, while bidirectional causality was observed between a MASLD proxy (ALT) and GERD in another. These findings offer new insights into cross-ethnic genetic research on MASLD and GERD.

Genetically predicted ALT is positively associated with GERD, highlighting a potential link between MASLD and GERD.

REFERENCES

1. Shaqran TM et al. Epidemiology, Causes, and Management of Gastro-esophageal Reflux Disease: A Systematic Review. Cureus. 2023 Oct 21;15(10): e47420.
2. Su C et al. Metabolic dysfunction-associated steatotic liver disease and gastroesophageal reflux disease: a mendelian randomization study in European and East Asian populations. Front Genet. 2024 Dec 5; 15:1428334.

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3. Al Hashmi K et al. Metabolic dysfunction-associated fatty liver disease: current therapeutic strategies. Front Nutr. 2024 Mar 19; 11:1355732.
4. Eslam M et al. A new definition for metabolic dysfunction-associated fatty liver disease: An international expert consensus statement. J Hepatol. 2020 Jul;73(1):202-209.

Prevalence and associated factors of Asymptomatic Peptic Ulcer Disease in Cirrhosis

INTRODUCTION- Cirrhosis represents a significant global health concern, ranking as the 15th leading cause of disability-adjusted life-years (DALYs) worldwide, particularly affecting individuals aged 25 to 49 years.[1] It is frequently associated with several complications, including peptic ulcer disease (PUD), which occurs more commonly in cirrhotic patients than in the general population. PUD in this context often remains asymptomatic until it progresses to severe complications, such as gastrointestinal (GI) bleeding, which accounts for 30% of GI bleeding cases in cirrhosis. Despite its clinical relevance, the role of Helicobacter pylori infection in cirrhotic patients with PUD is not well understood.[2] This study aims to investigate the epidemiology of asymptomatic PUD in cirrhotic patients undergoing upper gastrointestinal endoscopy for variceal screening, with a focus on identifying region-specific contributing factors influenced by sociodemographic, genetic, and nutritional variations.

METHODS- This cross-sectional study was conducted among cirrhotic patients aged 18 years and above undergoing upper GI endoscopy for variceal screening. Those with incomplete records, recent use of proton pump inhibitors, H2 receptor antagonists, antibiotics, anticoagulants, hepatocellular carcinoma, and peptic ulcers were excluded. The sample size was 296, determined through convenience sampling. Data were collected using a pretested questionnaire covering demographics, liver disease details, and risk factors for PUD. PUD diagnosis was based on endoscopic findings, and cirrhosis severity was assessed using the Child-Pugh classification. H. pylori infection was assessed via stool antigen and serology tests. Descriptive statistics, normality, multicollinearity tests, and bivariate/multivariate logistic regression were used for statistical analysis

RESULTS- Among the 296 cirrhotic participants, 71.6% were male, with a median age of 35 years (range: 18–78 years). Most participants (58.8%) resided in rural areas. The primary etiology of cirrhosis was hepatitis B virus (46.6%), followed by alcohol consumption (18.9%). Cirrhosis severity, based on the Child–Pugh classification, included 35.8% in class A, 47.6% in class B, and 16.6% in class C (Table 1). The prevalence of PUD was 19.6%, with 8.1% having duodenal ulcers, 6.1% gastric ulcers, and 5.4% both types. The duodenal ulcer group had a sex ratio of 1.2:1, while the gastric ulcer group had 0.49:1. H. pylori infection was present in 59.1% of cirrhosis patients and 79.3% of PUD cases. Factors significantly associated with PUD included H. pylori infection, Child–Pugh class C, alcohol consumption, NSAID use, smoking, ascites, cirrhosis etiology, and hypoalbuminemia. In multivariate analysis, H. pylori infection, moderate/heavy alcohol consumption, and Child–Pugh class C were independently linked to asymptomatic PUD ($p < 0.05$).

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Variable	Category	Frequency (n)	Percentage (%)
Etiology of Cirrhosis	HBV	138	46.6
	HCV	36	12.2
	Alcohol Liver Disease	56	18.9
	Unknown Cause	54	18.2
	Other Causes	12	4.1
Child-Pugh Classification	A	106	35.8
	B	141	47.6
	C	49	16.6

Table 1. Clinical Characteristics of Study Participants

DISCUSSION- The current study reported a 19.6% prevalence of PUD in patients with liver cirrhosis, which was consistent with existing literature, where the prevalence of PUD in cirrhosis ranges from 11.7% to 39%.[2] Additionally, H. pylori infection was identified as a significant risk factor for PUD in these patients. This finding aligns with a meta-analysis that identified H. pylori infection as the primary risk factor for PUD in cirrhotic individuals.[3] Similarly, Calvet et al. also found a positive correlation between H. pylori infection and PUD in this patient group.[2]

CONCLUSION- Liver cirrhosis patients are at increased risk for asymptomatic peptic ulcers, with *H. pylori* infection, higher alcohol consumption, and Child-Pugh class C liver disease as key risk factors. These findings highlight the need for targeted interventions, such as *H. pylori* eradication and counselling on alcohol use, to reduce morbidity in this population.

Liver cirrhosis patients are at an increased risk for asymptomatic peptic ulcers with H. pylori, alcohol use, and advanced liver disease as key risk factors.

REFERENCES

1. Devarbhavi H et al. Global burden of liver disease: 2023 update. Journal of hepatology. 2023 Aug 1;79(2):516-37.
2. Lema GD et al. Epidemiology of asymptomatic peptic ulcer disease diagnosed during screening endoscopy in patients with cirrhosis. J Int Med Res. 2024 Dec;52(12):3000605241305258.
3. Vergara M et al. Helicobacter pylori is a risk factor for peptic ulcer disease in cirrhotic patients. A meta-analysis. Eur J Gastroenterol Hepatol 2002; 14: 717–722

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Elevated Fecal Biomarkers of Colorectal Epithelial Cell Activity in Irritable Bowel Syndrome

INTRODUCTION- Irritable bowel syndrome (IBS) is a prevalent functional gastrointestinal disorder affecting over 40% of the global population, with a notably higher incidence in females. It is characterized by chronic abdominal pain and altered bowel habits,[1] and remains a complex condition with a heterogeneous pathophysiology, where immune activation plays a central role. Despite efforts to manage symptoms with anti-inflammatory treatments such as mesalazine, clear therapeutic benefits have yet to be established. While Mucosal Patch Technology (MPT) has identified signs of rectal inflammation, it is limited to assessing only a small segment of the gut.[2] This study aimed to explore fecal biomarkers of immune activity, focusing on colorectal eosinophils, neutrophils, and epithelial cells, to better understand the immune mechanisms underlying IBS and identify potential targets for more effective treatments.

METHODS-

Fecal samples were collected from adult IBS patients (≥18 years) enrolled in a randomized, controlled, multicentre trial (NCT01699438) evaluating mesalazine (2400 mg daily) versus placebo over 8 weeks. IBS is classified according to the Rome IV criteria, and include IBS subtypes based on the predominant bowel pattern: diarrhea (IBS-D), constipation (IBS-C), mixed (IBS-M), or unsubtyped (IBS-U), and moderate symptom severity is defined by an IBS-SSS score of ≥175. Exclusion criteria included systemic inflammatory diseases, other GI disorders, and recent use of NSAIDs or antibiotics. Fecal samples from healthy subjects were obtained from a previous ulcerative colitis study with health assessed via a questionnaire. Fecal markers reflecting immunologic and epithelial activity, including calprotectin, Myeloperoxidase (MPO), Eosinophil derived neurotoxin (EDN), Eosinophil cationic protein (ECP), Human neutrophil lipocalin (HNL), and Human phospholipase BII-precursor (HPLBII-P), were measured using ELISA and Western blotting, with imprecision <10%. Data were analyzed using Mann-Whitney U, Wilcoxon signed-rank, or Kruskal-Wallis tests, and correlations between biomarkers and IBS symptom scores were assessed using Spearman's rank order correlation.

RESULTS- Fecal samples from 165 IBS patients (69% female, median age 46) and 44 healthy subjects (50% female, median age 44) were analyzed. IBS patients were classified into 19% IBS-C, 35% IBS-D, and 46% IBS-nonC/nonD subtypes. No differences were observed in age or sex distribution between groups. Fecal

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concentrations of EDN, HNL (pab/765), and HPLBII-P were higher in IBS patients, while ECP concentrations were lower compared to healthy subjects. No differences were found in calprotectin and MPO levels. Within IBS subtypes, HPLBII-P was lower in IBS-C compared to IBS-D. Mesalazine treatment increased EDN and HNL (pab/765) levels, and decreased ECP levels, with no significant effect on HPLBII-P (Figure 1). There were no correlations between fecal biomarkers and total IBS-SSS, but abdominal bloating was negatively correlated with HPLBII-P. In IBS-D, HNL (pab/765) correlated with abdominal pain intensity. Correlations between biomarkers indicated common origins for eosinophil and epithelial markers, while neutrophil markers showed limited correlations in IBS patients.

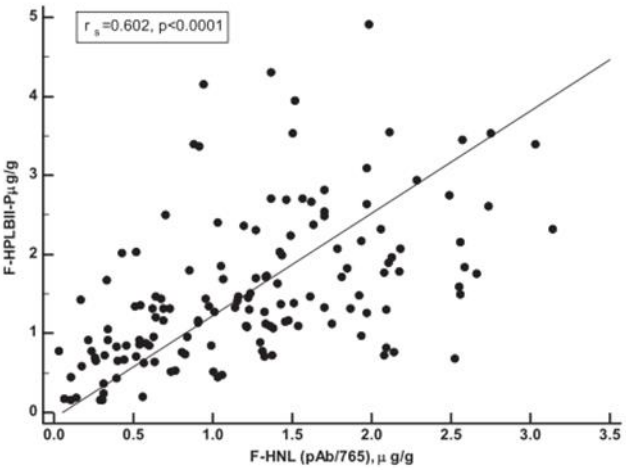

Figure 1: Correlation between fecal concentrations of HNL (pab/765) and HPLBII-P in IBS patients.

DISCUSSION This study found elevated levels of eosinophil and epithelial-derived biomarkers (EDN, HNL (pab/765), HPLBII-P) in IBS patients, indicating impaired gut epithelial integrity, which aligns with previous research linking HNL and HPLBII-P to colorectal epithelial cells.[3] After mesalazine treatment, both EDN and HNL (pab/765) levels increased, suggesting enhanced epithelial activity. These findings contrast with previous reports of mesalazine-induced eosinophilia, as the unaltered neutrophil biomarkers (calprotectin, MPO) imply that mesalazine's effects may predominantly affect epithelial cells rather than immune activation. This provides a novel perspective, challenging prior studies that suggested mesalazine primarily stimulates eosinophil activity in IBS.[2]

CONCLUSION- The lack of neutrophil and eosinophil involvement in IBS suggests that local epithelial cell activity, rather than inflammation, may play a key role in the disease. EDN, HNL (pab/765), and HPLBII-P could serve as potential fecal biomarkers for studying and monitoring IBS.

The negative correlation between the novel biomarker human phospholipase BII-precursor (HPLBII-P) and bloating and the presence of this biomarker in intestinal epithelial cells suggest a physiological role of HPLBII-P in intestinal activities.

REFERENCES

1. Shaikh SD et al. Irritable bowel syndrome and the Gut Microbiome: A Comprehensive Review. J Clin Med. 2023 Mar 28;12(7):2558.
2. Venge P et al. Elevated Fecal Biomarkers of Colo-Rectal Epithelial Cell Activity in Irritable Bowel Syndrome. Neurogastroenterol Motil. 2024 Dec 17:e14984.
3. Xu S et al. Tissue localization and the establishment of a sensitive immunoassay of the newly discovered human phospholipase B-precursor (PLB-P). J Immunol Methods. 2010 Feb 28;353(1-2):71-7.

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Case Report on Blunt Trauma-Induced Complete Esophageal Avulsion

INTRODUCTION- Thoracic esophageal rupture due to blunt trauma is an extremely rare and severe condition, associated with high morbidity and mortality. Such injuries are often the result of blunt trauma to the chest or chest and abdomen,[1] with an incidence of 0.001% in trauma cases. Complete esophageal avulsion, particularly from the gastroesophageal junction, is exceptionally rare in adults due to the esophagus's protected position within the thoracic cavity. The clinical challenges of diagnosing and managing these injuries are highlighted by the limited literature on blunt esophageal avulsions. Morbidity and mortality remain high, with complications such as pneumonia, sepsis, and esophageal stenosis. Prompt identification and surgical intervention are critical for improving outcomes. Historical data predominantly focus on penetrating trauma, further underscoring the rarity of blunt esophageal injuries.[2] This report examines a rare case of blunt traumatic complete esophageal avulsion in an adult, contributing to the understanding of its presentation, management, and postoperative course.

CASE PRESENTATION- A 50-year-old male truck driver presented to the emergency department with severe, sharp abdominal pain after a fall, where he struck his upper abdomen against a truck step. The pain was constant and aggravated by movement. Initial examination revealed pneumomediastinum and free intraperitoneal air, suggesting potential bowel perforation (Figure 1). Urgent surgical exploration showed complete disruption of the gastroesophageal junction, with esophageal avulsion and gastric contents spilling into the abdomen. A left thoracotomy and resection of 2 cm of the distal esophagus and gastric cardia were performed, followed by end-to-end esophagogastric anastomosis and omental flap reinforcement. Postoperatively, the patient developed respiratory distress and required reintubation but was eventually discharged on day 21. Two months later, he had gastrostomy and jejunostomy tube removal, but at three-month follow-up, he reported worsening symptoms of retrosternal burning, dysphagia, and early satiety. Esophagogastroduodenoscopy (EGD) revealed erosive esophagitis and anastomosis complications. Despite conservative management with pantoprazole and sucralfate, symptoms persisted, and at 15 months, he experienced severe nausea and blood-tinged vomiting. Further evaluation showed mild distal esophageal narrowing and erosive esophagitis. The patient was referred for consideration of surgical revision, with options including esophagectomy, colonic interposition, or Roux-en-Y gastric bypass.

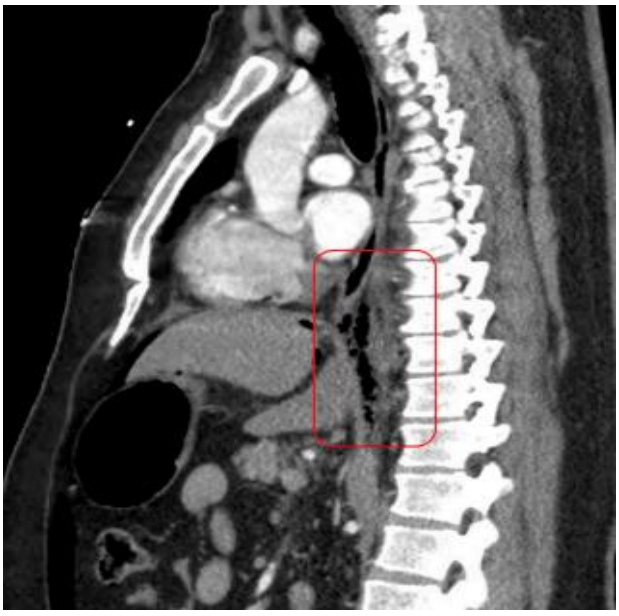

Figure 1. CT showing pneumomediastinum and pneumoperitoneum, suggesting esophageal injury near the GE junction (red box).

DISCUSSION- The surgical approach to blunt esophageal avulsion, particularly complete separation from the gastroesophageal junction, is complex and requires both thoracic and abdominal access. In this case, the operative

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intervention involved a laparotomy and left thoracotomy, with resection of the distal esophagus and gastric cardia, similar to strategies employed in other reported cases of traumatic esophageal injury. However, this contrasts with other studies where less invasive procedures were used, depending on injury severity.[2] Postoperative complications in this case, including severe gastroesophageal reflux and erosive esophagitis, are consistent with findings in the literature, where such injuries commonly result in long-term gastrointestinal issues.[3]

CONCLUSION- Blunt traumatic esophageal avulsion, though rare, necessitates rapid diagnosis and urgent surgical intervention to prevent life-threatening complications. Early recognition, along with a multidisciplinary approach, is crucial for improving survival and minimizing long-term sequelae. Effective follow-up care is essential to ensure optimal patient outcomes.

Blunt traumatic esophageal avulsion demands rapid diagnosis and surgery, with early intervention critical for survival and recovery.

REFERENCES

1. Kim JJ et al. Delayed diagnosis of thoracic esophageal rupture due to blunt abdominal trauma without chest trauma: A case report. J Cardiothorac Surg. 2022 Sep 3;17(1):228.
2. Grabill N et al. Blunt trauma-induced complete esophageal avulsion: A case report on surgical intervention and clinical insights. Trauma Case Rep. 2024 Nov 26; 54:101117.
3. Petrone P et al. Management of esophageal injuries secondary to trauma. Injury. 2017 Aug;48(8):1735-1742.