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Risk Factors for Peptic Ulcer Disease, A systematic review

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ABSTRACT

A common gastrointestinal ailment known as peptic ulcer disease (PUD) is characterised by the development of erosions or ulcers in the stomach or duodenal lining. It places a heavy burden on people and healthcare systems across the worldThis systematic review seeks to determine and assess the risk factors for developing peptic ulcer disease . Using established search keywords and inclusion criteria, a thorough search across significant electronic databases, such as PubMed, Embase, ScienceDirect, and Scopus, was carried out. The evaluation includes studies that looked at adult population risk factors for peptic ulcer disease and were published during [1999-2022]. Studies that concentrated on adults or certain ulcer aetiologies were disregarded. The results of the review imply that a number of risk factors have a role in the emergence of the condition known as peptic ulcers. Studies have repeatedly shown that the infection with H. pylori, also known as Helicobacter is a substantial risk factor for developing peptic ulcer disease. Other elements were also noted as significant causes, including the use of nonsteroidal anti-inflammatory medications (NSAIDs), smoking, drinking, stress, and senior age.

Additionally, it was shown that concomitant illnesses such diabetes mellitus, chronic pulmonary obstructive disease (COPD), chronic renal disease, chronic liver disease, and chronic renal failure increased the risk of peptic ulcer disease. Poor dietary practises and unpredictable eating patterns were among the lifestyle variables linked to an increased risk. Being aware of these risk factors is essential for peptic ulcer disease management, early identification, and prevention. The burden of this illness may be lessened with appropriate screening methods, lifestyle changes, and focused therapies. To further understand the processes behind these warning signs and how they interact to cause peptic ulcer disease, more study is always requiredFinally, this systematic review offers a thorough evaluation of the risk variables connected to peptic ulcer disease. The results underline the need of identifying and managing risk factors that can be modified including H. pylori infection, NSAID use, and poor lifestyle choices, in order to decrease the incidence and negative effects of peptic ulcer disease. Future Research should concentrate on creating specific preventative measures and improving treatment methods for people with a risk of developing peptic ulcer disease.

Key Words : Peptic Ulcer, Risk Factor, H. pylori, (NSAIDs) Non-steroidal anti-inflammatory drugs.

INTERODUCTION

A typical illness in gastroenterology is peptic ulcer disease (PUD). Incidence rates for PUD range from 10% to 19%, and 4 million individuals worldwide are affected each year. PUD incidence was estimated to be between 1.5% and 3%.[1] Helicobacter pylori (H. pylori) infection, which impacts gastrointestinal illnesses including PUD and gastritis, was the subject of the majority of PUD investigations.[2,3] PUD sufferers who have a perforated peptic ulcer (PPU) also have a terrible abdomen and a significant risk of long-term disease and death.[4] Other than H. pylori infection, there are a number of risk variables associated with peptic ulcers, such as socioeconomic, environmental, emotional, and other possible factors. Various risk factors, including age, lack of schooling, a low income or low salary, household member crowding, unemployment, marital strain, a blue-collar household, meal intake regularity, skipping breakfast, cigarette smoking, heavy alcohol consumption, a large body mass index (BMI), nonsteroidal painkillers (NSAIDs), musculoskeletal pain, headache,

psychological and physical stress, and others, have been identified by numerous studies of sociodemographic characteristics and peptic ulcers.[5] Smoking is a significant risk factor for PUD.[6]Drinking alcohol was connected to PUD.[7]However, numerous research did not support the link between PUD and smoking and alcohol consumption.[8]Omeprazole, pantoprazole, and lansoprazole are examples of proton pump inhibitors that are universally acknowledged as the best pharmaceutical treatment for both gastric and duodenal ulcers of the stomach.[9] It is widely established that consumption treatment (NSAIDs) is linked to a higher incidence of peptic ulcers and non-variceal upper gastrointestinal haemorrhage. According to research, NSAID overuse may also have negative effects on the colon. Additionally, an ageing population is using these treatments more often. Numerous studies showed that taking proton pump inhibitors (PPIs) does not prevent the mild intestinal mucosal damage brought on by NSAIDs, but it does lessen upper GI injury and the chance of upper GI problems.[10]

PATHOPHYSIOLOGY OF PEPTIC ULCER DISEASE

The formation of ulcers in the mucosal layer of the stomach and duodenum is a result of a complex interaction of several elements that make up the pathophysiology of peptic ulcer disease (PUD). For this frequent gastrointestinal condition to be effectively managed and treated, it is important to comprehend the underlying causes. An outline of the major pathophysiological features of PUD will be given in this section.[11,12]

1. Helicobacter pylori Infection: One of the main etiological causes of PUD is H. pylori. It colonises the stomach mucosa and causes inflammation. The bacteria releases a number of enzymes and toxins that compromise the mucosal protective layer, allowing stomach acid and other abrasive substances to harm the underlying tissues, H.pylori infection triggers inflammatory response and cytokines [13]

2. Imbalance between Aggressive and Defensive Factors**:** A number of factors are imbalanced in the aetiology of PUD. such as the release of stomach acid and defence mechanisms that shield the mucosal lining. increased generation of acid, Infection with H. pylori or overstimulating acid-secreting cells can overwhelm the body's defences, causing harm to the mucous membrane and ulcer development.[14]

3.Gastric Acid Secretion**:** Food digestion depends heavily on gastric acid, which is predominantly generated by the parietal cells inside the stomach. Excessive acid exposure to the stomach and duodenal mucosa results from excessive acid output, whether brought on by H. pylori infection or other factors, making them more susceptible to ulceration [15]

4. Mucosal Integrity and Protective Factors: The stomach mucosa is well protected by the production of mucus, its release of bicarbonate, and other defensive mechanisms. between epithelial cells, and tight junctions. Reduced mucus production or reduced bicarbonate secretion are two examples of how these protective elements are disrupted, which degrade the mucosal barrier's integrity and increase the risk of injury.[16]

5. Non-steroidal anti-inflammatory drugs (NSAIDs): suppress the cyclooxygenase enzymes, which results in less prostaglandin synthesis that is protective. As a result, the stomach mucosa's ability to balance its protective and harmful components is upset, making it more vulnerable to damage.[17]

RISK FACTORS:

Helicobacter pylori (H. pylori) Infection: One of the most prevalent causes for peptic ulcers is H. pylori infection. This bacteria colonises the stomach mucosa, causing persistent inflammation, rupturing the barrier that serves as protection, and the development of ulcers. Peptic ulcers are considerably more likely to occur in people with H. pylori infections than in healthy individuals.[18]

NSAIDs: Nonsteroidal Anti-Inflammatory Drugs: NSAIDs, which include medications such as ibuprofen, aspirin, and naproxen, are frequently used to treat pain and reduce inflammation. NSAID usage that is prolonged and excessive can affect the stomach mucosa by preventing prostaglandin formation and upsetting the harmony between beneficial and detrimental elements. NSAIDs are a key contributor to the development of ulcers, especially in people who use them often or in high dosages.[19]

Smoking: Smoking cigarettes is linked to a higher chance of developing peptic ulcer disease. Smoking has been proven to increase the inflammation brought on by H. pylori, decrease mucosal blood flow, and impair the healing process and raise the risk of ulcer recurrence. The first step in lowering the risk and enhancing ulcer outcomes is to stop smoking.20,21.

Alcohol Consumption: An increased risk of peptic ulcers has been associated with excessive alcohol drinking. Alcohol irritates the stomach mucosa, boosts the production of acid, and weakens the mucosal defences. Additionally, excessive alcohol use may increase the impact of other risk factors like H. pylori infection or NSAID usage, increasing a person's susceptibility to ulcer development. 20,21

Psychological Stress: Although psychological stress may not always result in peptic ulcers, It can lead to ulcers getting worse and coming back. Stress may increase mucosal blood flow, increase stomach acid output, and harm people's general health, increasing their risk of ulcer formation and slower recovery.[19,20]

Age and Gender: Although peptic ulcers can happen at any age, the risk seems to rise with ageing.Older people are more likely to have been exposed to risk factors such H. pylori infection or NSAID usage over a longer period of time. In addition, men are more likely than women to have peptic ulcers, however this difference is less noticeable as people become older.[21]

Other Medical Conditions: Several illnesses, including chronic kidney disease, chronic obstructive pulmonary disease, also known as (COPD), and liver cirrhosis, are linked to a higher risk of developing peptic ulcers, as is Zollinger-Ellison syndrome (a rare illness marked by excessive acid production). These disorders alter mucosal defence systems, raise stomach acid production, or put people at higher risk for additional risks.[22]

ETIOLOGY AND PATHOPHYSIOLOGY

H. pylori infection and NSAID's usage are the two primary risk factors for PUD, however not everyone with these conditions will eventually acquire the condition.[23] Nearly half of the worldwide population has H. pylori colonisation.[24] Typically acquired in childhood, the organism endures until treated. A lower socioeconomic position, filthy environment, or crowding are risk factors for contracting the illness. H. pylori is more widespread among several ethnies and is more prevalent in poorer nations. In all age groups, the prevalence of H. pylori has decreased during the past five years in the United States. However, there are disparities based on ethnicity, with rates of infection exceeding 60% in the population of Mexican Americans and just 30% in that of non-Hispanic whites.[25] In the mucosal layer, H. pylori induces an inflammatory response that includes neutrophils, lymphocytes, plasma cells, and macrophages and results in epithelial cell degeneration and damage. With little to no inflammation in the corpus, gastroenteritis is typically more severe in the antrum. To check for H. pylori, all patients with peptic ulcers should be examined.[26] Endoscopy is invasive, however it enables for biopsy and offers a range of test options, including histology, culture, and quick urease test. Acid-suppressing drugs like proton pump inhibitors can influence all tests other than serology and provide false negative results.[27]

DIAGNOSIS

When patients exhibit symptoms such epigastric stomach discomfort, burning, postprandial fullness, or early satiety, the diagnosis is initially made on the basis of clinical suspicion.[28] Traditionally, individuals with duodenal ulcers report stomach pain that worsens when they are hungry, two to three hours after eating, or at night. In contrast, people with stomach ulcers describe post-meal abdominal discomfort, nausea, and vomiting. Elderly adults frequently have little symptoms, and some PUD patients who are untreated may experience occasional symptoms because of spontaneous healing before relapsing because of ongoing risk factors such continuing use of NSAIDs or H. pylori infection.[29] Anti-secretory medication may be initiated as an empiric course of treatment if the clinical symptoms point to a potential peptic ulcer illness and no warning signals are present. Additionally, since H. pylori is a frequent cause of PUD, a test and treat strategy using a non-invasive H. pylori test (stool antigen or urea breath test) is advised for patients under the age of 55 who do not have any alarming symptoms, in areas where gastric cancer is uncommon and the prevalence of H. pylori is higher than 20%.[30] Endoscopy is advised to make a diagnosis in elderly individuals and those with warning symptoms. GI bleeding, a decrease in weight, rapid satiety, dysphagia or odynophagia, a family history of upper GI carcinoma, iron deficient anaemia, or the onset of new upper GI symptoms in people over the age of 55 are alarming signs.[31]

MATERIAL AND METHOD

We followed the Preferred Reporting Items for Systematic Reviews when conducting this review. Up to 2023, a thorough literature search was carried out using electronic databases including Medline, PubMed, and PubMed Central (PMC). Utilising the general keywords "risk factor" AND "peptic ulcer," we looked for pertinent research.

INCLUSION CRITERIA

We incorporated full-text publications and papers with human participants that were published in English between 1999 and 2023. Cohort studies, case-control studies, RCTs, systematic reviews, and conventional reviews were all included.

EXCLUSION CRITERIA

Grey literature, case reports, case series, animal studies, overlapping research, non-English-language studies, and studies whose complete texts are not publicly available.

COMPLICATIONS

PUD can lead to consequences such as persistent discomfort, bleeding, perforation, penetration, blockage of the stomach outlet, and gastric cancer (adenocarcinoma and MALT lymphoma). The most frequent consequence, bleeding, affects 15-20% of individuals. About 40 to 60 percent of acute upper GI bleeding is caused by PUD.[32] Upper GI bleeding is an emergency that has to be assessed and prioritised right away. To better coordinate treatment of critically sick patients, notifying a GI expert early in the examination of a bleeding patient is beneficial. For risk stratification, the Glasgow-Blatchford and Rockall scores have been utilised.[33] All patients suspected of having an upper GI bleed should begin intravenous PPI medication as soon as they arrive at the hospital since IV PPIs lower the likelihood of identifying high-risk stigmata during endoscopy and, consequently, the risk of rebleeding and the requirement for surgery.[34] They function by raising the pH inside the stomach, promoting platelet aggregation, and ensuring clot stability. To enhance endoscopic visualisation and diagnostic yield, prokinetic drugs like erythromycin or metoclopramide might also be taken into account.[35]

CONCLUSION

Due to the drop in H. pylori infections, better accessibility to anti-secretory medication, and more prudent NSAID usage, PUD is a condition with a declining clinical burden. However, because to its persistently high lifetime frequency and variable clinical presentation, PUD must be diagnosed and managed properly in order to prevent and minimise serious sequelae. When assessing PUD, it is important to test for and treat H. pylori as well as prevent mucosal damage brought on by NSAIDs (either by concomitant PPI prophylaxis or by selecting COX-2 selective NSAIDs, if available). The most frequent consequence, PUD haemorrhage, is treated with resuscitation, anti-secretory medication, endoscopy, and administration of antithrombotic drugs.

REFERENCES

1. Malik, T. F., Gnanapandithan, K., & Singh, K. (2022). Peptic Ulcer Disease.[Updated 2021 Jul 29]. *StatPearls [Internet]. Treasure Island(FL): StatPearls Publishing*.
2. Pütsep, K., Brändén, C. I., Boman, H. G., & Normark, S. (1999). Antibacterial peptide from H. pylori. *Nature*, *398*(6729), 671–672. https://doi.org/10.1038/19439
3. Suerbaum, S., & Michetti, P. (2002). Helicobacter pylori infection. *The New England journal of medicine*, *347*(15), 1175–1186. https://doi.org/10.1056/NEJMra020542
4. Chung, K. T., & Shelat, V. G. (2017). Perforated peptic ulcer - an update. *World journal of gastrointestinal surgery*, *9*(1), 1–12. https://doi.org/10.4240/wjgs.v9.i1.1
5. Yim, M. H., Kim, K. H., & Lee, B. J. (2021). The number of household members as a risk factor for peptic ulcer disease. *Scientific reports*, *11*(1), 5274. https://doi.org/10.1038/s41598-021-84892-5
6. Konturek, S. J., Bielański, W., Płonka, M., Pawlik, T., Pepera, J., Konturek, P. C., Czarnecki, J., Penar, A., & Jedrychowski, W. (2003). Helicobacter pylori, non-steroidal anti-inflammatory drugs and smoking in risk pattern of gastroduodenal ulcers. *Scandinavian journal of gastroenterology*, *38*(9), 923–930. https://doi.org/10.1080/00365520310004696
7. Andersen, I. B., Jørgensen, T., Bonnevie, O., Grønbaek, M., & Sørensen, T. I. (2000). Smoking and alcohol intake as risk factors for bleeding and perforated peptic ulcers: a population-based cohort study. *Epidemiology (Cambridge, Mass.)*, *11*(4), 434–439. https://doi.org/10.1097/00001648-200007000-00012
8. Johnsen, R., Førde, O. H., Straume, B., & Burhol, P. G. (1994). Aetiology of peptic ulcer: a prospective population study in Norway. *Journal of epidemiology and community health*, *48*(2), 156–160. https://doi.org/10.1136/jech.48.2.156
9. Zavoshti, F. R., & Andrews, F. M. (2017). Therapeutics for Equine Gastric Ulcer Syndrome. *The Veterinary clinics of North America. Equine practice*, *33*(1), 141–162. https://doi.org/10.1016/j.cveq.2016.11.004
10. Lanas, Á., Carrera-Lasfuentes, P., Arguedas, Y., García, S., Bujanda, L., Calvet, X., Ponce, J., Perez-Aísa, Á., Castro, M., Muñoz, M., Sostres, C., & García-Rodríguez, L. A. (2015). Risk of upper and lower gastrointestinal bleeding in patients taking nonsteroidal anti-inflammatory drugs, antiplatelet agents, or anticoagulants. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association*, *13*(5), 906–12.e2. https://doi.org/10.1016/j.cgh.2014.11.007

11. Zhang, B. B., Li, Y., Liu, X. Q., Wang, P. J., Yang, B., & Bian, D. L. (2014). Association between vacA genotypes and the risk of duodenal ulcer: a meta-analysis. *Molecular biology reports*, *41*(11), 7241–7254. https://doi.org/10.1007/s11033-014-3610-y
12. Papatheodoridis, G. V., & Archimandritis, A. J. (2005). Role of Helicobacter pylori eradication in aspirin or non-steroidal anti-inflammatory drug users. *World journal of gastroenterology*, *11*(25), 3811–3816. https://doi.org/10.3748/wjg.v11.i25.3811
13. Hooi, J. K., Lai, W. Y., Ng, W. K., Suen, M. M., Underwood, F. E., Tanyingoh, D., ... & Ng, S. C. (2017). Global prevalence of Helicobacter pylori infection: systematic review and meta-analysis. *Gastroenterology*, *153*(2), 420-429.
14. Sachs, G., Shin, J. M., Munson, K., Vagin, O., Lambrecht, N., Scott, D. R., ... & Melchers, K. (2000). The control of gastric acid and Helicobacter pylori eradication. *Alimentary pharmacology & therapeutics*, *14*(11), 1383-1401.
15. Hooi, J. K., Lai, W. Y., Ng, W. K., Suen, M. M., Underwood, F. E., Tanyingoh, D., ... & Ng, S. C. (2017). Global prevalence of Helicobacter pylori infection: systematic review and meta-analysis. *Gastroenterology*, *153*(2), 420-429.
16. Yandrapu, H., & Sarosiek, J. (2015). Protective factors of the gastric and duodenal mucosa: an overview. *Current gastroenterology reports*, *17*, 1-8.
17. Feldman, M., Cryer, B., Sammer, D., Lee, E., & Spechler, S. J. (1999). Influence of H. pylori infection on meal-stimulated gastric acid secretion and gastroesophageal acid reflux. *American Journal of Physiology-Gastrointestinal and Liver Physiology*, *277*(6), G1159-G1164.
18. Mhaskar, R. S., Ricardo, I., Azliyati, A., Laxminarayan, R., Amol, B., Santosh, W., & Boo, K. (2013). Assessment of risk factors of Helicobacter pylori infection and peptic ulcer disease. *Journal of global infectious diseases*, *5*(2), 60.
19. Li LF, Chan RLY, Lu L, Shen J, Zhang L, Wu WKK, et al. Cigarette smoking and gastrointestinal diseases: the causal relationship and underlying molecular mechanisms (review). Int J Mol Med. 2014;34(2):372–80.
20. Fornai M, Antonioli L, Colucci R, Tuccori M, Blandizzi C. Pathophysiology of gastric ulcer development and healing: molecular mechanisms and novel therapeutic options, peptic ulcer disease, Dr. Jianyuan Chai (Ed.), InTech; 2011, DOI:10.5772/17640. European Union: Rijeka, Croatia.
21. Thorsen, K., Søreide, J. A., Kvaløy, J. T., Glomsaker, T., & Søreide, K. (2013). Epidemiology of perforated peptic ulcer: age-and gender-adjusted analysis of incidence and mortality. *World Journal of Gastroenterology: WJG*, *19*(3), 347.
22. Huang, K. W., Luo, J. C., Leu, H. B., Lin, H. C., Lee, F. Y., Chan, W. L., ... & Chang, F. Y. (2012). Chronic obstructive pulmonary disease: an independent risk factor for peptic ulcer bleeding: a nationwide population-based study. *Alimentary pharmacology & therapeutics*, *35*(7), 796-802.
23. Zhang, B. B., Li, Y., Liu, X. Q., Wang, P. J., Yang, B., & Bian, D. L. (2014). Association between vacA genotypes and the risk of duodenal ulcer: a meta-analysis. *Molecular biology reports*, *41*(11), 7241–7254. https://doi.org/10.1007/s11033-014-3610-y
24. Papatheodoridis, G. V., & Archimandritis, A. J. (2005). Role of Helicobacter pylori eradication in aspirin or non-steroidal anti-inflammatory drug users. *World journal of gastroenterology*, *11*(25), 3811–3816. https://doi.org/10.3748/wjg.v11.i25.3811
25. Grad, Y. H., Lipsitch, M., & Aiello, A. E. (2012). Secular trends in Helicobacter pylori seroprevalence in adults in the United States: evidence for sustained race/ethnic disparities. *American journal of epidemiology*, *175*(1), 54–59.
26. Chey, W. D., Wong, B. C., & Practice Parameters Committee of the American College of Gastroenterology (2007). American College of Gastroenterology guideline on the management of Helicobacter pylori infection. *The American journal of gastroenterology*, *102*(8), 1808–1825. https://doi.org/10.1111/j.1572-0241.2007.01393.x
27. Narayanan, M., Reddy, K. M., & Marsicano, E. (2018). Peptic Ulcer Disease and *Helicobacter pylori* infection. *Missouri medicine*, *115*(3), 219–224.
28. Feldman, M., Friedman, L. S., & Brandt, L. J. (Eds.). (2020). *Sleisenger and Fordtran's gastrointestinal and liver disease E-book: pathophysiology, diagnosis, management*. Elsevier health sciences.
29. Lanas, A., & Chan, F. K. L. (2017). Peptic ulcer disease. *Lancet (London, England)*, *390*(10094), 613–624. https://doi.org/10.1016/S0140-6736(16)32404-7
30. Agréus, L., Talley, N. J., & Jones, M. (2016). Value of the "Test & Treat" Strategy for Uninvestigated Dyspepsia at Low Prevalence Rates of Helicobacter pylori in the Population. *Helicobacter*, *21*(3), 186–191. https://doi.org/10.1111/hel.12267
31. Talley, N. J., Vakil, N. B., & Moayyedi, P. (2005). American gastroenterological association technical review on the evaluation of dyspepsia. *Gastroenterology*, *129*(5), 1756–1780. https://doi.org/10.1053/j.gastro.2005.09.020
32. Lanas, A., García-Rodríguez, L. A., Polo-Tomás, M., Ponce, M., Quintero, E., Perez-Aisa, M. A., Gisbert, J. P., Bujanda, L., Castro, M., Muñoz, M., Del-Pino, M. D., Garcia, S., & Calvet, X. (2011). The changing face of hospitalisation due to gastrointestinal

bleeding and perforation. *Alimentary pharmacology & therapeutics*, *33*(5), 585–591. https://doi.org/10.1111/j.1365-2036.2010.04563.x

33. Stanley, A. J., Dalton, H. R., Blatchford, O., Ashley, D., Mowat, C., Cahill, A., Gaya, D. R., Thompson, E., Warshow, U., Hare, N., Groome, M., Benson, G., & Murray, W. (2011). Multicentre comparison of the Glasgow Blatchford and Rockall Scores in the prediction of clinical end-points after upper gastrointestinal haemorrhage. *Alimentary pharmacology & therapeutics*, *34*(4), 470–475. https://doi.org/10.1111/j.1365-2036.2011.04747.
34. Strand, D. S., Kim, D., & Peura, D. A. (2017). 25 Years of Proton Pump Inhibitors: A Comprehensive Review. *Gut and liver*, *11*(1), 27–37. https://doi.org/10.5009/gnl15502
35. Laine, L., & Jensen, D. M. (2012). Management of patients with ulcer bleeding. *The American journal of gastroenterology*, *107*(3), 345–361. https://doi.org/10.1038/ajg.2011.480