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Review Article

Helicobacter Pylori: Gastric Carcinoma and Other Gastrointestinal Neoplasms

Dr Arjun Aravindh[1], Dr Debananda Sahoo[2], Sarika Baburajan Pillai[3], Dr. John Abraham[4], Dr. V. Bharathi[5], Dr. T.S Durga Prasad [6] and Dr. Veena Maheshwari [7*]

[1]*Department of general surgery, Sree balaji medical college and hospital, Chennai, India.*

[2]*Associate Professor, Department of General Medicine, AIIMS, BHUBANESWAR, Odisha-751019.*

[3]*Pasteur Institute of India, Coonoor, The Nilgiris, Tamilnadu -643103.*

[4]*Assistant Professor, Department of Family Medicine, St. Johns National Academy of Health Sciences, Bangalore, India- 560034*

[5]*Assistant Professor, Department of Microbiology, Vivekanandha Arts and Science College for Women, Veerachipalayam, Sankari West (PO), Sankari - TK, Salem District, Tamilnadu - 637 303.*

[6]*Professor and Head, Department of Pharmacy Practice, Sri Padmavathi School of Pharmacy, Tiruchanoor, Tirupati, Andhra Pradesh – 517503.*

[7*]*Assistant professor, Department of Biotechnology, Bhavan's College (Autonomous), Munshi Nagar Andheri-West Mumbai-400058, Maharashtra.*

Abstract: Gastric cancer (GC) remains a critical global health issue, with rising morbidity and mortality rates. Recent epidemiological studies have deepened our understanding of the correlations between GC and other gastrointestinal illnesses, enhancing diagnosis and treatment options. This review highlights key developments in the use of "serological biopsy" for cancer risk assessment, focusing on biomarkers such as pepsinogen, gastrin, and Helicobacter pylori (H. pylori) antibodies. These markers have demonstrated effectiveness in identifying early gastric diseases and predicting infection risks, particularly in high-risk regions. Serologic biopsy is poised for widespread adoption as a non-invasive and cost-effective diagnostic method, offering improved patient monitoring and individualized treatment strategies. Perioperative chemotherapy has emerged as a standard treatment for GC, showing significant improvements in survival, reduced tumor recurrence, and better surgical outcomes. This combination therapy has shifted treatment paradigms by optimizing preoperative tumor reduction, thereby enhancing surgical efficacy. The development of personalized medicine based on serologic biomarkers promises further advances in tailoring treatment to individual cancer characteristics. The review also explores the contentious association between H. pylori and various gastrointestinal cancers, including gastric mucosa-associated lymphoid tissue (MALT) lymphoma, esophageal carcinoma, and colorectal carcinoma. H. pylori has been implicated in the development of MALT lymphoma, with studies showing that eradicating the bacterium can lead to lymphoma remission. The bacteria's potential role in gastric and esophageal cancers remains debated, as conflicting studies have presented varying degrees of correlation. Similarly, the relationship between H. pylori and colorectal cancer, as well as its association with other gastrointestinal malignancies, requires further exploration. This review covers key epidemiological insights into GC, preventive strategies for colorectal cancer, and emerging diagnostic and treatment indicators for both gastric cancer and lymphoma. It also discusses the evolving understanding of H. pylori's role in gastrointestinal carcinogenesis and its potential impact on future cancer prevention strategies.

Keywords: Biomarkers, Colorectal carcinoma, Esophageal carcinoma, Gastric MALT lymphoma, Pancreatic carcinoma, Cancer prophylaxis

***Corresponding Author**

Dr. Veena Maheshwari , Assistant professor, Department of Biotechnology, Bhavan's College (Autonomous), Munshi Nagar Andheri-West Mumbai-400058, Maharashtra.

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1. INTRODUCTION

Recent epidemiological research has enhanced the comprehension of this significant connection and correlation between GC and other illnesses, highlighting the main aspects of the disease, diagnosis, and therapy. Gastroenteritis is a significant global health concern, characterized by rising morbidity and death rates. A new research has underscored its importance, particularly regarding its association of GC with other gastrointestinal disorders [1], while enhancing diagnosis and therapy. Comprehensive studies in China have validated the efficacy of "serological biopsy" as a technique for assessing cancer risk [2]. This necessitates the assessment of certain serologic markers, such as pepsinogen, gastrin, and Helicobacter pylori antibodies, which have shown efficacy in detecting early gastric illness and forecasting infection risk. Serologic biopsies may effectively differentiate patients from those at risk [3], enabling improved monitoring and treatment. This is especially crucial in high-risk regions where prompt diagnosis might enhance results. Serologic biopsy has the potential for widespread use in global clinical practice as a noninvasive and cost-effective diagnostic procedure. A remarkable advancement has transpired throughout and the perioperative chemotherapy administered before to and during surgical resection significantly improves survival in these individuals. Consequently, perioperative chemotherapy has emerged as the new standard of treatment, supplanting prior surgical interventions[4]. This therapy combination enhances survival rates, reduces tumor recurrence, and optimizes surgical results by decreasing tumor size prior to surgery. This represents a significant change in the management of gastric carcinoma. These biomarkers enable physicians to customize therapy according to cancer features, facilitating more individualized therapeutic approaches. While more study is need to validate these criteria, the prospect of using precision medicine to enhance therapy efficacy is promising, perhaps augmenting survival rates[5] and diminishing related medicines. To reduce the importance of detecting Helicobacter pylori (H. pylori) in individuals diagnosed with MALT lymphoma, a rare neoplasm intimately was associated with H. pylori. Infection with Helicobacter pylori [6]. Eliminate H. The evidence that H. pylori induces remission in several stomach MALT lymphomas indicates that this bacterium contributes to the pathophysiology of malignancy[7]. This discovery has significant therapeutic implications for the need for early diagnosis and management of H. pylori infection in persons predisposed to MALT lymphoma. The association between H. pylori and GC is contentious[8]. Early reported evidence indicates that these bacteria may induce cancer in different gastrointestinal regions. The precise method by which H. pylori may contribute to different cancers is under investigation; nevertheless, chronic inflammation, DNA damage, and immunological responses induced by viruses are presumed to be significant factors for this H. Pylori induced GC [9]. The results have generated increased interest in comprehending the principal impact of H. pylori beyond gastroenteritis, prompting more investigation into its involvement in the genesis of various gastrointestinal disorders. The correlation between H. pylori and malignancies in organs like as the esophagus, pancreas, and colon remains challenging among researchers. Certain research indicates a positive correlation, whilst others demonstrate no correlation. Some studies have associated E. coli with the development of esophageal adenocarcinoma (EA), whereas others propose that these bacteria may mitigate cancer risk by alleviating gastroesophageal reflux disorder (GERD), a recognized risk factor [10]. The association involving H. The relationship between H. pylori and pancreatic cancer remains ambiguous, with inconsistent data on the illness. Despite this uncertainty, the influence of H. pylori may affect the initiation of stomach cancer has prompted investigations into the bacteria's impact on gastrointestinal health, culminating in ultimate success. The confirmation of serologic biopsy as a dependable diagnostic tool for colon cancer, along with the introduction of perioperative chemotherapy as a localized treatment, has resulted in progress in the fight against intestinal malignancies. As understanding of the overall impacts of H. pylori expands, investigating H. pylori infection will enhance the comprehension of its association with bacterial carcinogenesis, ultimately aiding in the formulation of more effective cancer prevention and treatment techniques.

1.1 Epidemiologic Perspectives on Gastric Cancer:

Gastrointestinal metaplasia (GIM) is regarded as the principal etiological factor for gastric cancer; yet, there exists debate over the appropriate screening methods for gastric cancer in regions with low incidence rates. A retrospective case-control study at Kaiser Permanente in Southern California included 923 individuals (mean age 68 years) diagnosed with GIM and evaluated their GC status within this cohort [11] Twenty-five of these cases had GC, and 70% were diagnosed with GIM. Eight supplementary instances were identified, averaging 5 years subsequent to the original GIM diagnosis. A genetic predisposition to stomach cancer and pronounced intestinal metaplasia associate due to an elevated incidence of stomach cancer, claiming a need for the surveillance of at risk persons for early detection. Patients diagnosed with alcoholic liver disease (ALD) and control volunteers, matched by age, gender, and body mass index, who underwent esophagogastroduodenoscopy (EGD) for evaluation stomach cancer (GC) screening were reported. The findings indicated that ALD patients with GC were roughly five times more likely to have GC compared to healthy controls [12]. Multivariate logistic analysis identified ALD as an independent risk factor for GC. No notable difference was seen in the frequency of E. coli, gastric adenoma, or malignancy between individuals with alcoholic hepatitis and those without alcoholic steatohepatitis. This investigation revealed that there is no disparity in the incidence of precancerous lesions between the two groups based on histology or serological findings. This research included 142 colon cancer patients who received surgical procedures at Chungnam National University Hospital from 2004 to 2013. Polyps during healthy intervals were assessed. Both cohorts underwent assessment by gastrointestinal endoscopy. The incidence of gastric adenomas or GCs was greater in individuals with colorectal cancer (CRC) compared to controls. A history of alcohol use and stomach cancer was linked to a six fold elevated incidence of gastric adenoma or carcinoma [13]. The results implies the need for upper gastrointestinal cancer screening in colon cancer patients, particularly those with a history of alcoholic consumption and those with poorly defined cancer tumors, even in the absence of colorectal illness.

1.2 Strategies for preventing colon cancer and screening for precancerous conditions:

The efficacy of "serologic biopsy" has been inconsistent owing to variations across diverse regions. A thorough population-based research reported a study of individuals diagnosed with stomach cancer. This study used prospective surveillance by

gastroscopy and evaluated five gastric serological biomarkers: pepsinogen I (PGI), pepsinogen II (PGII), the PGI/II ratio, Helicobacter pylori resistance, and gastrin 17 (G-17) responses [14]. This study included an extensive system design and risk evaluation conducted over a prolonged duration. In a cross-sectional study, biomarkers such as PGII, the PGI/II ratio, and Helicobacter pylori seropositivity were correlated with the existence of gastropathy, intraepithelial neoplasia, or cancer at the time of enrollment [15]. Subsequent data demonstrated that diminished PGI levels and PGI/II ratios correlate with malignancy risk; but, both low and elevated G-17 levels equally signify cancer risk [16]. The risk prediction model demonstrated that the integration of all five biomarkers enhanced predicted accuracy compared to conventional risk adjustment and was more proficient in detecting precancerous conditions at recruitment. Moreover, higher serologic biopsy scores from these biomarkers correlated with a increased risk of colon cancer throughout the follow-up period. Consequently, "serological biopsy" using these signs may assist in identifying persons at elevated risk for diagnosis, as well as for focused diagnosis and prevention. corpus-predominant gastritis index CGI may serve as a prognostic indicator to identify people with H. pylori infection who are at elevated risk for the condition. Cheng and colleagues a case-control research was performed to assess the prevalence of CGI in Taiwanese patients with nonulcer dyspepsia (NUD, N = 350) in comparison to duodenal ulcer controls (DU, N = 224) [17]. The incidence of CGI was much greater in NUD patients compared to controls (46% vs. 30%, P<.001), particularly in those over 40 years of age. Surgical treatments related to stage III/IV gastric atrophy (OLGA) and intestinal metaplasia (OLGIM) are more prevalent in individuals with non-abdominal dyspepsia (NUD)[18]. Individuals with NUD and CGI had a threefold increased risk of developing spasmolytic polypeptide-expressing metaplasia (SPEM), particularly after the age of 60. The proportion of protease I to protease II has decreased [19]. The eradication of H. pylori led to a substantial reduction in CGI, with no recurrence seen in patients with SPEM or those at OLGA/OLGIM stage III/IV. The researchers determined that, CGI is a superior histological marker of cancer risk compared to OLGA/OLGIM [20]. CGI is the only histological marker that recovers during H. pylori infection. Preventing colon cancer involves a comprehensive approach that combines early detection, regular screening, and lifestyle changes. One of the most effective strategies for early detection is regular colonoscopy, which allows for the identification and removal of precancerous polyps before they develop into malignancies. Colonoscopies are typically recommended for individuals over 50, or earlier for those with a family history of colorectal cancer. Another important screening method is the fecal occult blood test (FOBT), which detects hidden blood in the stool that may indicate the presence of polyps or cancer [21]. Stool DNA testing is a more recent innovation that looks for genetic mutations associated with colorectal cancer, providing another non-invasive screening option. In addition to regular screenings, certain lifestyle changes can significantly reduce the risk of developing colon cancer. Maintaining a healthy diet is key, with a focus on consuming high-fiber foods, such as fruits, vegetables, and whole grains, while limiting the intake of red and processed meats, which have been linked to an increased risk of colorectal cancer. Regular physical activity is also essential, as it helps regulate weight and reduces inflammation, both of which are known risk factors for cancer [22]. Weight management is particularly important, as obesity has been strongly associated with an increased risk of colorectal cancer. Other preventive measures include smoking cessation, as smoking is a well-known risk factor for various cancers, including colon cancer. Studies suggest that regular aspirin use may reduce the risk of colorectal cancer due to its anti-inflammatory effects, although this should be discussed with a healthcare provider [23]. Supplements like calcium and vitamin D have also shown potential in lowering cancer risk, though more research is needed in this area [24]. For individuals with a family history of colon cancer or genetic predispositions, such as Lynch syndrome, increased surveillance and more frequent screenings are recommended to catch any abnormalities at an early stage. By combining these screening techniques with healthy lifestyle choices, the risk of developing colon cancer can be significantly reduced, and early detection can improve treatment outcomes.

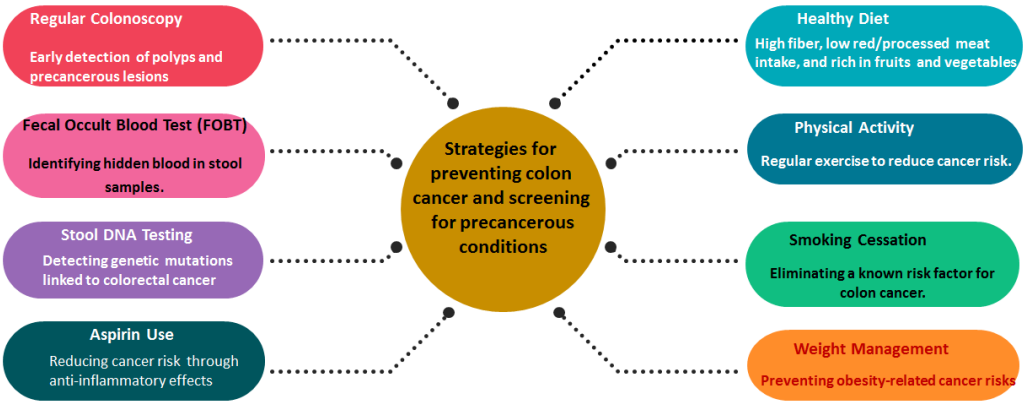

Fig 1: Strategies for preventing colon cancer

1.3 *Gastric Cancer: Indicators for Assessing Treatme nt Effect*

Perioperative chemotherapy has shown general effectiveness in individuals with gastric cancer and localized illness. Precisely identifying those at risk for recurrence poses significant challenges. A retrospective review of the MAGIC research assessed tumor markers and nodal status in 330 breast cancer patients, including those with borderline carcinoma, who received perioperative therapy [25]. The Mandard TRG method evaluates resected tissue, with TRG 1 signifying full tumor regression after neoadjuvant treatment and TRG 5 denoting the absence of tumor regression [26]. Univariate study indicated effectiveness in patients exhibiting pathologic regression was seen; nonetheless, multivariate analysis determined prostate cancer as a significant predictor of overall survival. A further

post-hoc analysis of the MAGIC trial assessed the impact of cytostatic treatment in patients with breast cancer and locoregional illness, concentrating on microsatellite instability (MSI). MSI data were accessible for 300 people, of whom 20 had a high MSI [27]. Among patients who underwent resection, there was no statistically significant difference in overall survival between those with stable microsatellite status (MSS) malignancies and those with high microsatellite instability (MSI) or mismatch repair-deficient tumors (MMRD). Perioperative chemotherapy correlated with a reduced mortality risk in patients with high microsatellite instability, HR 2.18, suggesting a decreased therapeutic response.

1.4 Lymphoma related with gastric mucosa-associated lymphoid tissue

Gastric MALT lymphoma (GML) is analogous to H. pylori infection. A retrospective examination of GML patients from 1993 to 2013 demonstrated that H. pylori eradication treatment facilitated a complete response (CR) [28]. Ninety-two percent of patients with stage IE attained remission, and 83% exhibited a response at a median duration of 7 months. Furthermore, 86% of patients had full remission after 105 months of follow-up. The CR rate was elevated in patients with H. pylori. The response rate was reduced in individuals with lymphoma located in the antrum and body. Relapse transpired in only less patients, often after 2 years, and was more prevalent among individuals with H. pylori reinfection, several surgical interventions, or cancer present in the body.
In stage EII patients, the proportion of effective therapy responses is reduced. In stage EIV, some individuals may undergo therapy or surgery, whilst others have advanced illness. H. pylori was detected in a retrospective study including 345 Korean patients with GML [29]. Patients who tested positive had an elevated CR rate. Individuals afflicted with H. pylori are in poor health. Surgical resection is preferred as the primary therapy for GML, irrespective of disease condition or stage [30]. The prevalence of SPM, particularly GC, was elevated in GML patients relative to the French population [31]. The elevated risk was seen only in individuals undergoing immunotherapy or chemotherapy, while this risk was absent in those treated with H. The treatment for eradicating H. pylori is unaffected. Consequently, prolonged monitoring of patients with GML is advised even post-resection. Moreover, several studies indicates that initial-phase diffuse large B-cell lymphoma (DLBCL) may still be attributable to H. pylori. DLCBL may develop fast if therapy is ineffective, in contrast to Mucosa-associated lymphoid tissue lymphoma [32]. Consequently, indicators of H. pylori association should be identified in gastric diffuse large B-cell lymphoma. A correlation between CagA expression in malignant B cells and the CagA signaling molecules phosphorylated SHP2 and phosphorylated ERK, as well as H. pylori were reported [33]. Gastric H. pylori DLCBL has MALT characteristics independent of H. pylori [34]. MicroRNAs (miRNAs) have shown dysregulation in lymphoma. In a study 384 miRNAs in 10 GMLs, identifying 12 miRNAs were related with gastric cancer, including two instances of reactive lymphadenopathy [35]. In GML, miR-142-3p and miR-155 exhibited considerable expression, but miR-203 shown a decline, suggesting that these miRNAs may function as biomarkers to differentiate between GML and gastritis [36]. Study investigations on miRNA regulation were reported that created animal models of GML using BALB/c mice, who underwent thymectomy three days postnatally and were then infected by Helicobacter pylori. Five miRNAs were identified as overexpressed in GML, including TP53INP1, a protein linked to immune response and pro-apoptotic activity, which is targeted by four of the miRNAs, indicating their involvement in the modulation of GML formation [37].

1.5 The correlation between H. pylori and esophageal carcinoma

The association between H. pylori infection and the onset of esophageal adenocarcinoma (EA) remains a subject of active contention. Epidemiological studies have shown a significant correlation between H. pylori and EA; however, other variables may affect the onset of colon cancer. In a study, the methylation pathways of several proteins in the intestines and esophagus of 68 individuals (33 females and 35 men, mean age 52 years) with histologically confirmed nonspecific (floral type) columnar metaplasia (EA onset) [38]. This research examined the genes death-associated protein kinase (DAPK), thrombospondin-1 (THBS1), CDH1, and p14 to assess their correlation with H. pylori CagA positivity. The findings indicated CpG methylation of this gene in nonspecific columnar metaplasia of the esophagus. The methylation of the DAPK and THBS1 genes correlated with CagA-positive H. pylori infection, indicates that some CagA-positive H. pylori strains may exhibit susceptibility to EA. The prevalence of H.pylori infection among South African patients with (ESCC) is comparable to that of the general population [39]. Helicobacter pylori is incapable of inducing esophageal squamous cell carcinoma (ESCC).

1.6 H. pylori and its association with Colorectalcarcinoma

Colorectal carcinoma is linked to H. pylori infection. A research revealed that H. pylori infection was linked to increased incidence of colon adenomas and multiple intestinal adenomas. A retrospective research including 6,351 Koreans Mean age 51.7 ± 8.1 years underwent colon cancer screening revealed the presence of advanced-stage cancer, including high-risk adenomas and/or infiltrating pylori seropositivity [40]. Group analysis indicated that 1,000 pancreatic cancer patients and 1,754 healthy controls revealed an association between the risk of pancreatic cancer and H. pylori (OR = 1.45; 95% CI = 1.09-1.92), however no increased risk was seen for H. pylori infection. Consequently, colonoscopy was advised for those with H. pylori infection. The early identification of adenomatous cells is crucial in Gastritis associated with Helicobacter pylori [41]. In individuals with early-stage colorectal carcinoma (EGC) who have endoscopic submucosal dissection (ESD), colonoscopy is advised to assess high risk, particularly elevated blood carcinoembryonic antigen (CEA) levels. The elevated incidence of advanced adenoma and a higher blood CEA level among the EGC group were reported. Prior research indicates that the correlation between H. pylori and stomach cancer may differ across various groups [42]. A case-control research using an older, mostly Caucasian cohort study examined the correlation between seropositivity and H. pylori association [43]. The research identified that there is no correlation between H. pylori seropositivity and an elevated risk of colon cancer. Significant changes were seen in comparison to prior research seroprevalence of certain antigens, including VacA and CagA, perhaps due to changes in group characteristics.

2. CONCLUSION

Examination of human intestinal metaplasia may facilitate the early identification of gastric cancer. The follow-up outcomes of the MAGIC research may influence the identification of candidates who may benefit from perioperative chemotherapy. Evaluating MSI status will be crucial for future gastric cancer patients and localized illnesses. Patients with colon cancer exhibiting significant microsatellite instability may be less responsive to perioperative therapy and may be directly impacted. Eradication treatment for H. pylori is essential for stomach MALT lymphoma, irrespective of the illness or its stage. Evidence indicates that the elimination of H. pylori may improve some inflammatory bowel disorders in the lymphatic nodes. More research is necessary to clarify the relationship with H. pylori infection, chronic atrophic gastritis, and malignancy.

3. AUTHORS CONTRIBUTION STATEMENT

Study conception and design: Dr Arjun Aravindh, Dr Debananda Sahoo; data collection: Sarika Baburajan Pillai; analysis and interpretation of results: Dr. John Abraham, Dr. V. Bharathi; draft manuscript preparation: Dr. T.S Durga Prasad and Dr. Veena Maheshwari. All authors reviewed the results and approved the final version of the manuscript.

4. CONFLICT OF INTEREST

Conflict of interest declared none.

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