Role of the Gut Microbiome in Gastric Cancer: A Systematic Review

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Abstract- Background: Gastric cancer is one of the leading causes of cancer-related mortality worldwide and continues to pose a major health burden in India, particularly in the Kashmir region. Although *Helicobacter pylori* infection is a well-established etiological factor, eradication of *H. pylori* alone does not completely eliminate gastric cancer risk, suggesting the involvement of additional microbial factors.

Materials and Methods: A systematic review of published literature was conducted using PubMed, Scopus, and Embase databases. Human studies evaluating gut or gastric microbiome alterations in gastric cancer and precancerous lesions were included. Relevant data were extracted and analyzed qualitatively.

Aims and Objectives:

1. **To study the role of gut and gastric microbiome in gastric cancer**
2. **To assess microbiome alterations across different stages of gastric carcinogenesis**
3. **To evaluate the clinical relevance of microbiome dysbiosis**

Results: Thirty-two studies were included in the review. Gastric cancer patients consistently demonstrated reduced microbial diversity with enrichment of pathogenic bacteria such as *Fusobacterium*, *Prevotella*, *Streptococcus*, and *Lactobacillus*. Dysbiosis was observed from chronic gastritis to advanced carcinoma.

Conclusion: Gut and gastric microbiome dysbiosis plays a significant role in gastric carcinogenesis. Recognition of microbiome alterations may aid in early diagnosis and preventive strategies, particularly in high-risk regions like Jammu and Kashmir.

Keywords: Gastric cancer, Gut microbiome, Gastric microbiota, Dysbiosis.

I. INTRODUCTION

Gastric cancer remains the fifth most common malignancy and the fourth leading cause of cancer-related deaths globally. In India, especially in the Kashmir valley, the incidence of gastric cancer is considerably high, likely due to dietary habits, smoking, environmental exposure, and chronic *Helicobacter pylori* infection [1,2].

Gastric carcinogenesis is classically explained by the Correa cascade, progressing from chronic gastritis to intestinal metaplasia, dysplasia, and carcinoma [3]. While *H. pylori* infection plays a pivotal role, only a minority of infected individuals develop gastric cancer, and cancer risk persists even after eradication therapy [4]. This indicates the involvement of additional microbial and host-related factors.

Advances in sequencing technologies have demonstrated that the stomach harbors a complex microbial ecosystem rather than being sterile. Alterations in gut and gastric microbiome composition, termed dysbiosis, may promote chronic inflammation, immune dysregulation, and malignant transformation [5,6]. This systematic review aims to summarize available evidence regarding the role of gut microbiome in gastric cancer.

II. MATERIALS AND METHODS

The present study is a systematic review of published literature conducted using PubMed, Scopus, and Embase databases.

Inclusion Criteria

1. Human studies on adults (≥18 years)
2. Studies evaluating gut or gastric microbiome in gastric cancer or precancerous lesions
3. Observational studies and clinical trials
4. English-language publications

Exclusion Criteria

1. Animal or in-vitro studies
2. Case reports, editorials, narrative reviews
3. Pediatric studies

Relevant articles were screened, and data were extracted regarding study design, population, microbiome source, sequencing method, and key findings.

III. RESULTS

A total of 1,246 records were identified through database searching. After screening and eligibility assessment, 32 studies were included in the final analysis.

Table 1: Summary of the studies included in the systematic review showing year of publication, country, study design, source of microbiome sample and method of microbiome analysis.

Author	Year	Country	Study Design	Microbiome Source	Method
Ferreira RM et al.	2018	Portugal	Case-control	Gastric biopsy	16S rRNA
Coker OO et al.	2020	China	Cross-sectional	Gastric tissue	16S rRNA
Yu G et al.	2019	China	Cohort	Stool	Metagenomics
Liu X et al.	2022	Korea	Case-control	Stool	Shotgun sequencing
Wang Z et al.	2021	China	Case-control	Gastric mucosa	16S rRNA

Microbiome Alterations in Gastric Cancer

Most studies reported reduced alpha diversity in gastric cancer patients compared to healthy controls [7,8]. Increased abundance of potentially pathogenic bacteria such as *Fusobacterium nucleatum*, *Prevotella*, *Streptococcus*, and *Lactobacillus* was consistently observed [9,10]. Protective commensal bacteria were significantly depleted.

Table 2: Distribution of major microbiome alterations reported in patients with gastric cancer across the included studies.

Feature	Observation
Microbial diversity	Reduced
Pathogenic taxa	*Fusobacterium*, *Prevotella*, *Streptococcus*
Commensal bacteria	Decreased
Inflammatory profile	Increased pro-inflammatory taxa

Microbiome Changes Across Gastric Carcinogenesis

Progressive dysbiosis was observed across the stages of gastric carcinogenesis, from chronic gastritis to carcinoma [11]

Table 3: Microbiome characteristics observed at different stages of gastric carcinogenesis from chronic gastritis to carcinoma.

Disease Stage	Microbiome Characteristics
Chronic gastritis	Early dysbiosis
Intestinal metaplasia	Reduced diversity
Dysplasia	Pathogenic enrichment
Gastric carcinoma	Severe dysbiosis

IV. DISCUSSION

The present systematic review highlights the important role of gut and gastric microbiome dysbiosis in gastric cancer development. Beyond *H. pylori*, non-*H. pylori* bacteria appear to contribute to carcinogenesis through chronic inflammation, immune modulation, and production of carcinogenic metabolites [12,13].

Enrichment of oral and intestinal bacteria in gastric cancer tissue suggests microbial translocation and altered gastric ecology [9]. Additionally, emerging evidence indicates that gut microbiome composition may influence response to chemotherapy and immunotherapy in gastric cancer [14,15]. Recent evidence suggests that gut microbiome dysbiosis influences carcinogenesis and antitumor immunity across multiple organ systems (Fig 1).

Various host-related and environmental factors such as diet, antibiotics, *Helicobacter pylori* infection, aging, and gastric surgery are known to influence gastric microbiota composition and contribute to dysbiosis (Fig 1).

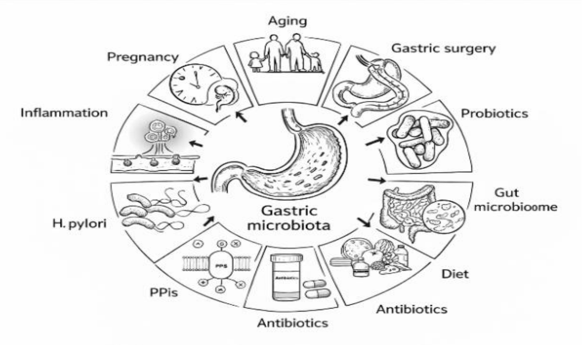

Fig 1: Factors influencing gastric microbiota composition including *Helicobacter pylori* infection, dietary habits, antibiotic and proton pump inhibitor use, inflammation, aging, gastric surgery, probiotics, and gut microbiome interactions.

Relevance to Kashmir and the Indian Subcontinent

Gastric cancer incidence in Kashmir is among the highest in India. Dietary practices such as consumption of salted tea, smoked and pickled foods, dried vegetables, and high salt intake, along with tobacco use, may promote chronic gastric inflammation and microbiome dysbiosis [16,17]. High prevalence of *H. pylori* infection further alters the gastric microbial environment. Understanding regional microbiome patterns may help in identifying high-risk individuals and developing targeted preventive strategies.

V. CONCLUSION

Gut and gastric microbiome dysbiosis plays a crucial role in gastric carcinogenesis. Early recognition of microbial alterations may aid in risk stratification, prevention, and improved management of gastric cancer, particularly in high-incidence regions such as Jammu and Kashmir.

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