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Review Article

Rising gastrointestinal malignancies in North India: a comprehensive review

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ABSTRACT

Gastrointestinal (GI) malignancies, including cancers of the esophagus, stomach, colorectal region, gallbladder and liver, pose a significant public health challenge in North India, with rising incidence driven by unique regional factors. This comprehensive review synthesizes current literature to analyze the epidemiology, risk factors, clinical characteristics and management challenges of GI cancers in North India. Esophageal cancer, predominantly squamous cell carcinoma, exhibits high incidence in areas like Mizoram, while gastric cancer is prevalent in the Kashmir Valley. Colorectal cancer is increasing due to urbanization and lifestyle changes and gallbladder cancer is a major concern in the Ganges River belt. Liver cancer, primarily hepatocellular carcinoma, is linked to chronic hepatitis infections. Key risk factors include dietary habits (e.g., smoked meats, high-fat diets), tobacco use, *Helicobacter pylori* infection, hepatitis B and C and environmental carcinogens. Advanced-stage diagnosis, limited access to diagnostic tools and inadequate region-specific research hinder effective management. Preventive strategies, such as *H. pylori* eradication, hepatitis B vaccination and lifestyle modifications, alongside enhanced screening and genomic research, are critical for reducing the burden. This review underscores the need for collaborative efforts to improve early detection, treatment access and region-specific guidelines to address this growing epidemic.

Keywords: Epidemiology, Gastrointestinal malignancies, North India, Preventive strategies, Risk factors

INTRODUCTION

GI malignancies, encompassing cancers of the esophagus, stomach, liver, gallbladder, pancreas, small intestine and colorectal region, represent a significant and escalating public health challenge in India, with North India bearing a disproportionate burden. According to GLOBOCAN 2012, GI cancers accounted for approximately 227,000 new cases and 182,000 deaths in India, underscoring their substantial contribution to cancer-related morbidity and mortality.[1] North India, including states such as Jammu and Kashmir, Delhi, Rajasthan, Uttar Pradesh, Bihar and the north eastern states, exhibits distinct epidemiological patterns driven by a complex interplay of dietary habits, environmental exposures, genetic predispositions and socio-cultural factors.

These malignancies, particularly esophageal, gastric, colorectal, gallbladder and liver cancers, are rising at an alarming rate, necessitating a deeper understanding of their epidemiology, risk factors, clinical presentation and management challenges. This comprehensive review synthesizes recent literature to provide a detailed analysis of the rising incidence of GI malignancies in North India, supported by numerical citations, tables and figures to elucidate key findings.

EPIDEMIOLOGY OF GI MALIGNANCIES IN NORTH INDIA

The epidemiology of GI malignancies in North India reflects regional variations in incidence, prevalence and histological patterns, influenced by local risk factors and healthcare disparities. Below, authors discussed the major GI cancers prevalent in the region.

Esophageal cancer

Esophageal cancer is the most common GI malignancy in North India, constituting approximately 31% of GI cancers in a hospital-based study from Jaipur, Rajasthan.[2] The age-standardized incidence rate (AAR) is particularly high in the northeastern states, with Aizawl district in Mizoram reporting an AAR of 126.9 per 100,000 among males, one of the highest globally.[3] Squamous cell carcinoma (SCC) is the predominant histological subtype, accounting for over 90% of cases, in contrast to adenocarcinoma, which is more common in Western populations.[2] The male-to-female ratio is approximately 2:1 and the disease typically affects individuals aged 50–70 years, often presenting at advanced stages due to non-specific symptoms like dysphagia and weight loss.[4]

Gastric cancer

Gastric cancer ranks as the second most prevalent GI malignancy in North India, with a prevalence of 15% in Jaipur and significantly higher rates in north eastern states like Mizoram, where it accounts for 30% of all cancers.[5] The age-adjusted incidence rate ranges from 3.0 to 13.2 per 100,000 across India, with the highest rates in the northeast.[3] Adenocarcinoma is the dominant histological type (94.18%), with the antrum being the most common site (60%).[6] The Kashmir Valley is a recognized high-risk area, where gastric cancer is the leading cancer among males, driven by unique dietary and environmental factors.[7]

Colorectal cancer

Colorectal cancer (CRC) is witnessing a rising trend in North India, with rectum cancer (14.3%) and colon cancer (6%) contributing significantly to the GI cancer burden.[2] While the overall incidence remains lower than in developed countries, urbanization, adoption of Westernized diets (high in fat and low in fiber) and sedentary lifestyles are driving an increase.[8] A study from North India reported an incidence rate of 53.3 per 100,000 person-years for CRC among patients with Crohn's disease, highlighting the role of chronic inflammation.[8] The disease is increasingly diagnosed in younger populations, with a notable shift toward left-sided tumors.[6]

Gallbladder cancer

Gallbladder cancer (GBC) is a major public health concern in North India, particularly among women in states like Uttar Pradesh and Bihar, where it constitutes 41% of pancreatobiliary malignancies.[2] The Ganges River belt, encompassing eastern Uttar Pradesh and Bihar, is a high-risk region, potentially due to environmental carcinogens in water and soil.[9] GBC is often diagnosed at advanced stages (stage III or IV), with a mean overall survival of 42.8 months post-R0 resection following neoadjuvant chemotherapy (NACT).[10] The female predominance (2:1 ratio) is linked to gallstone disease and chronic inflammation.[9]

Liver cancer

Liver cancer, primarily hepatocellular carcinoma (HCC), is increasing in North India, with an annual percent change (AAPC) in incidence of 3%–7% from 2003 to 2017.[11] Chronic hepatitis B virus (HBV) infection, prevalent in 2–5% of the Indian population, confers a nearly 100-fold risk of HCC.[12] Hepatitis C virus (HCV) infection and alcohol-related liver disease also contribute significantly. HCC is often diagnosed late, with a five-year survival rate of less than 10% in advanced cases.[11]

RISK FACTORS

The rising incidence of GI malignancies in North India is driven by a combination of dietary, infectious, genetic and environmental factors, which are often region-specific.

Dietary and lifestyle factors

Dietary habits unique to North India significantly contribute to GI cancer risk. In the Kashmir Valley, consumption of smoked meats, salted tea (locally known as "noon chai") and high-fat diets is strongly associated with esophageal and gastric cancers.[13]

Tobacco use, including chewing (e.g., gutkha, pan masala) and smoking local cigarettes ("meiziol") or tobacco-infused water ("tuibur"), is linked to a 2.1–2.3 odds ratio for gastric cancer.[13]

The adoption of Westernized lifestyles, characterized by high-fat, low-fiber diets and sedentary behavior, is driving the increase in CRC incidence, particularly in urban areas like Delhi.[8] Alcohol consumption, prevalent in some northern states, is a significant risk factor for HCC.[12]

Infectious agents

Infectious agents play a critical role in GI malignancies. *Helicobacter pylori* infection, prevalent in 56–89% of gastric cancer cases in North India, is a major risk factor, with the CagA-positive strain strongly associated with adenocarcinoma development.[14] Chronic HBV and HCV infections are the leading causes of HCC, with HBV prevalence particularly high in rural North India.[12] The synergistic effect of HBV and aflatoxin exposure (from contaminated grains) further elevates HCC risk.[11]

Genetic and environmental factors

Genetic polymorphisms, such as -765G>C in the COX-2 gene and NAT2 variants, increase susceptibility to esophageal and gastric cancers in North Indian populations.[15] Environmental carcinogens, including nitrosamines found in tobacco products and salted tea, are significant in high-risk areas like Kashmir.[13] Poor socioeconomic conditions, limited access to clean water and exposure to environmental toxins in the Ganges belt are implicated in the high incidence of GBC.[9]

CLINICAL CHARACTERISTICS AND DIAGNOSTIC CHALLENGES

GI malignancies in North India are frequently diagnosed at advanced stages, contributing to poor prognosis. For gastric cancer, 47.6% of cases present at stage III and 36.1% at stage IV, with common symptoms including abdominal pain, anemia and weight loss.[6] Esophageal cancer patients often present with dysphagia and malnutrition, complicating treatment.[2] GBC and HCC are typically detected at metastatic stages, with imaging (e.g., CT, MRI) revealing extensive disease.[10,11] The five-year survival rate for gastric cancer is approximately 20–22%, while for HCC, it is less than 10% in advanced cases.[5,11] Diagnostic challenges include limited access to advanced modalities like endoscopic ultrasound and PET-CT, particularly in rural areas. Cancer registries in North India are sparse, with incomplete data hindering epidemiological studies.[3] Non-specific symptoms and low awareness delay patient presentation, exacerbating outcomes.

MANAGEMENT AND TREATMENT PERSPECTIVES

Surgical interventions

Surgical resection remains the cornerstone of treatment for resectable GI cancers. For gastric cancer, D2 gastrectomy with lymphadenectomy is the standard of care, but over 50% of patients are inoperable at presentation due to advanced disease.[6] Esophageal cancer often requires esophagectomy combined with chemoradiation, though outcomes are poor due to late diagnosis.[2] For GBC, neoadjuvant chemotherapy (e.g., gemcitabine-based regimens) improves resectability, with 66.67% of patients achieving R0 resection.[10] Liver resection or transplantation for HCC is limited to early-stage cases, which are rare in North India.[11]

Chemotherapy and targeted therapies

Chemotherapy regimens, such as cisplatin and 5-fluorouracil, are commonly used for gastric cancer, with objective response rates of 30–40% in neoadjuvant settings.[6] For GBC, neoadjuvant chemotherapy improves survival in resectable cases.[10] Targeted therapies, such as trastuzumab for HER2-positive gastric cancer, are underutilized due to limited molecular testing.[6] Imatinib has shown efficacy in gastrointestinal stromal tumors (GIST), with stable disease reported in high-risk cases.[2] For HCC, sorafenib is the standard systemic therapy, but access is limited in resource-constrained settings.[11]

Radiation therapy

Radiation therapy is used as an adjuvant or palliative treatment for esophageal and rectal cancers. For esophageal cancer, chemoradiation with 50–60 Gy improves local control but has limited impact on survival in advanced cases.[2] Stereotactic body radiotherapy (SBRT) is emerging for HCC but is not widely available.[11]

Challenges in management

The lack of randomized controlled trials (RCTs) specific to North Indian populations limits evidence-based practice.

Most treatment protocols are extrapolated from Western studies, which may not account for regional differences in cancer biology.[10] Limited healthcare infrastructure, high treatment costs and inadequate screening programs contribute to poor outcomes. For instance, only 10–15% of North Indian hospitals have access to advanced endoscopic facilities.[6]

Table 1: Incidence rates and key characteristics of major GI malignancies in North India.

Cancer type	Region/State	AAR (per 100,000)	Predominant histology	Male:female ratio
Esophageal cancer	Aizawl, Mizoram	126.9 (males)	Squamous Cell	2:1
Gastric cancer	Mizoram, Kashmir	3.0–13.2	Adenocarcinoma (94%)	1.5:1
Colorectal cancer	North India (Crohn's)	53.3	Adenocarcinoma	1.2:1
Gallbladder cancer	Uttar Pradesh, Bihar	High prevalence	Adenocarcinoma	1:2
Liver cancer	North India	Increasing (3–7%)	Hepatocellular	3:1

Table 2: Clinical presentation and staging of GI malignancies in North India.

Cancer type	Common symptoms	Common stage at diagnosis	5-year survival rate
Esophageal cancer	Dysphagia, weight loss	Stage III–IV	~15%

Continued.

Cancer type	Common symptoms	Common stage at diagnosis	5-year survival rate
Gastric cancer	Abdominal pain, anemia, weight loss	Stage III (47.6%), IV (36.1%)	20–22%
Colorectal cancer	Rectal bleeding, altered bowel habits	Stage II–III	~40%
Gallbladder cancer	Abdominal pain, jaundice	Stage III–IV	~10% (advanced)
Liver cancer	Abdominal pain, jaundice, ascites	Stage III–IV	<10% (advanced)

PREVENTIVE STRATEGIES AND FUTURE DIRECTIONS

Preventive strategies are critical to reducing the GI cancer burden. *Helicobacter pylori* eradication with triple therapy (proton pump inhibitors, amoxicillin, clarithromycin) significantly reduces gastric cancer risk, with studies showing a 50% risk reduction in high-risk populations.[14]

Hepatitis B vaccination programs, implemented in India since 2011, are expected to decrease HCC incidence over time.[12] Lifestyle modifications, including reducing tobacco use, adopting high-fiber diets and increasing physical activity, are essential for CRC prevention.[8]

Future research should focus on large-scale, multi-center RCTs to establish region-specific treatment guidelines. Genomic studies to identify biomarkers, such as CDH1 mutations for gastric cancer or KRAS mutations for CRC, could enable personalized therapies.[15]

Enhanced screening programs targeting high-risk groups (e.g., those with inflammatory bowel disease or chronic HBV infection) and public awareness campaigns are urgently needed. Investment in healthcare infrastructure, including cancer registries and diagnostic facilities, will improve early detection and outcomes.

CONCLUSION

The rising burden of GI malignancies in North India, driven by esophageal, gastric, colorectal, gallbladder and liver cancers, reflects a complex interplay of dietary, infectious, genetic and environmental factors. Advanced-stage presentation, limited diagnostic access and lack of region-specific research exacerbate the challenge.

Preventive strategies, including *H. pylori* eradication, HBV vaccination and lifestyle interventions, offer hope for reducing incidence. Collaborative efforts among researchers, clinicians and policymakers are essential to strengthen screening, improve treatment access and conduct region-specific studies to mitigate this growing epidemic.

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