Original Article

Frequency of Gastrointestinal Cancers Based on Upper and Lower Endoscopic Findings in Zahedan, 2019- 2021

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ABSTRACT

Background:
Gastrointestinal (GI) cancers represent a significant portion of Iran's cancer burden. Regional epidemiological data from Southern Iran remain limited. This study aimed to determine the frequency and characteristics of major GI cancers diagnosed via endoscopic procedures in Zahedan.

Materials and Methods:
In this retrospective cross-sectional study, we analyzed all endoscopic and colonoscopic procedures (N=6,124) performed at Ali Ibn Abi Talib Hospital between 2019-2021. Data from patients with pathologically confirmed malignancies were extracted and analyzed using SPSS software version 26.

Results:
Malignancy was confirmed in 315 cases (5.14%). Esophageal cancer was most frequent (38.7%), followed by gastric (35.9%) and colorectal cancer (24.8%). The mean age was 61 years, with 56.2% male predominance. Sex distribution differed significantly: esophageal cancer was more prevalent in women (P=0.044), while gastric cancer predominated in men (P=0.014). Histologically, squamous cell carcinoma characterized most esophageal cancers (57.4%), while adenocarcinomas accounted for most gastric (85.8%) and colorectal cancers (88.5%).

Conclusion:
This study reveals a distinct GI cancer profile in Southern Iran, with high esophageal cancer frequency showing a unique gender distribution. These findings emphasize the need for region-specific screening strategies and warrant further investigation into underlying risk factors.

Keywords: Epidemiology, Esophageal cancer, Gastric cancer, Colorectal cancer, Endoscopy, Iran

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INTRODUCTION

Cancer constitutes a major global health challenge and is a leading cause of mortality worldwide, significantly impeding progress in life expectancy (1). According to World Health Organization (WHO) estimates from 2019, cancer ranked as the first or second leading cause of death before age 70 in 112 countries and third or fourth in 23 others (2). This escalating burden reflects demographic and societal trends, including population aging and growth, as well as the prevalence of key risk factors, many of which are intertwined with socioeconomic development (1).

Within the spectrum of oncological diseases, gastrointestinal (GI) cancers represent a substantial component of global incidence and mortality. GLOBOCAN 2020 estimates documented approximately 19.3 million new cancer cases worldwide, with colorectal cancer (10.0%) and stomach cancer (5.6%) among the most frequently diagnosed (3). In terms of mortality, GI cancers remain formidable, with the colorectal (4.9%), liver (3.8%), and stomach (3.7%) cancers featuring prominently among the deadliest malignancies (3). The prognosis for many GI cancers, such as esophageal cancer, with a five-year survival rate of around 15%, remains particularly dire, often due to late-stage diagnosis (4, 5).

The Islamic Republic of Iran mirrors this concerning global picture, experiencing a rising incidence of GI cancers. These malignancies account for about 25% of all common cancers nationally and are responsible for nearly half (44.4%) of all cancer-related deaths, underscoring their disproportionate impact on the nation's health (6,7). The etiology of GI cancers is multifactorial, involving a complex interplay of non-modifiable and modifiable risk factors. Advanced age, male sex, and a positive family history are established non-modifiable risks. Crucially, modifiable factors including dietary habits high in salted foods, pickles, and smoked products; low consumption of fruits and vegetables; sedentary lifestyles; tobacco use; alcohol consumption; and infections such as *Helicobacter pylori* play a significant role in the Iranian context (8, 9).

A particularly critical etiological factor for upper gastrointestinal cancers in Iran, especially in certain high-risk regions, is the consumption of opium and its derivatives. After five decades of epidemiological research across three continents, the evidence has culminated in a definitive conclusion: opium causes cancer (10). In 2020, the International Agency for Research on Cancer (IARC) Monographs Volume 126 formally classified opium consumption as carcinogenic to humans (Group 1), establishing a causal link with cancers of the esophagus, stomach, lung, larynx, and urinary bladder (11) This classification was based on sufficient evidence in humans and marked the culmination of years of investigation into the carcinogenic properties of opium.

The Golestan Cohort Study, a large-scale prospective investigation conducted in northeastern Iran, has provided some of the most compelling evidence for this association. This study demonstrated that regular opium use is significantly associated with an increased risk of developing esophageal cancer (HR: 1.38, 95% CI: 1.06–1.80), gastric cancer (HR: 1.36, 95% CI: 1.03–1.79), and pancreatic cancer, with the latter showing a particularly strong dose-response relationship (HR: 2.66 for high-dose use, 95% CI: 1.23–5.74) (12). The study further revealed that opium use accounts for a substantial fraction of upper GI cancers in regions where consumption is prevalent, with clear dose-response patterns based on frequency, duration, and cumulative use (12). These findings from the Golestan region are particularly relevant to other parts of Iran with similar cultural and geographical characteristics, including Sistan and Baluchestan province.

A critical aspect of GI cancer epidemiology is its significant geographical heterogeneity, driven by regional variations in genetics, environment, culture, and lifestyle. Studies from different parts of Iran, such as those in Northern and Central provinces, have revealed varying patterns of incidence and histology for cancers of the esophagus, stomach, and colorectum (13,14). This regional variation necessitates localized epidemiological studies, as data from one region cannot be reliably extrapolated to another. The Sistan and Baluchestan province in southeastern Iran is a particularly compelling and under-investigated region. Characterized by a unique ethnic composition, distinct socioeconomic challenges, and specific local customs, including the not-uncommon practice of opium consumption, the population of Zahedan, its capital, may harbor a distinct profile of GI cancer risk and presentation (10,12). The province's potential inclusion in the high-risk "Asian Esophageal Cancer Belt" further underscores the urgency of focused research (6).

In this context, endoscopic procedures (upper endoscopy and colonoscopy) serve as the cornerstone for the early detection and diagnosis of GI cancers. They enable direct visualization of the mucosal lining, identification of precancerous lesions (e.g., Barrett's esophagus, adenomatous polyps), and procurement of histological samples, thereby facilitating interventions that can reduce both incidence and mortality (4,15,16). Despite the established value of endoscopy, a significant knowledge gap exists regarding the specific characteristics of GI cancers in Zahedan. This study is critically needed due to the unique demographic and epidemiological profile of the Sistan and Baluchestan province, where a distinct ethnic

composition, socioeconomic challenges, and the prevalence of established carcinogenic exposures such as opium use likely create a cancer landscape different from other Iranian regions (10,12). Current national data obscures these local variations, leading to health policies that may not address the community's specific vulnerabilities. This research is therefore essential to generate foundational, region-specific evidence on the prevalence and pathology of GI cancers, which will directly inform the development of targeted screening programs and optimize resource allocation to ultimately reduce mortality in this underserved population.

MATERIALS AND METHODS

Study Design

A retrospective cross-sectional study was conducted to analyze the epidemiological and histopathological characteristics of GI cancers diagnosed through endoscopic procedures at a tertiary care center in Southeastern Iran.

The study was conducted at Ali Ibn Abi Talib Hospital, the major tertiary care referral center in Zahedan, Sistan and Baluchestan province. The study population comprised all patients who underwent esophagogastroduodenoscopy (EGD) and/or colonoscopy between March 2019 and March 2021. This hospital serves as the primary GI diagnostic and therapeutic center for the entire southeastern region of Iran.

Ethical Considerations

The study protocol was approved by the Ethics Committee of Zahedan University of Medical Sciences (Ethical Code: IR.ZAUMS.REC.1400.145). Due to the retrospective nature of the study and the use of anonymized data, the ethics committee waived the requirement for informed consent, in compliance with the principles of the Declaration of Helsinki.

Inclusion and Exclusion Criteria

Inclusion criteria consisted of: (1) Complete medical records with demographic data; (2) Successful completion of EGD and/or colonoscopy with adequate documentation; (3) Availability of histopathological reports for suspicious lesions.

Exclusion criteria included: (1) Incomplete medical records; (2) Previous history of GI malignancy; (3) History of major GI surgery that could alter cancer risk assessment.

Sampling Method and Sample Size

A complete census method was employed, including all eligible endoscopic procedures performed during the 24-month study period. This approach ensured comprehensive capture of all diagnosed GI malignancies within the specified timeframe. A total of 6,124 endoscopic procedures were initially identified and screened for eligibility.

A standardized data extraction form was developed and validated through pilot testing. The following variables were systematically collected:

• Demographic characteristics: age, sex

• Procedure details: type of endoscopy (EGD/colonoscopy), date of procedure

• Endoscopic findings: location and characteristics of suspicious lesions

• Histopathological data: final diagnosis, cancer type (esophageal/gastric/colorectal), histological classification (adenocarcinoma/squamous cell carcinoma (SCC)/others)

Operational Definitions

• Esophageal cancer: Histologically confirmed malignancy of the esophagus

• Gastric cancer: Histologically confirmed malignancy of the stomach

• Colorectal cancer: Histologically confirmed malignancy of the colon or rectum

• Early-onset cancer: Cancer diagnosed in patients aged <50 years

To ensure data quality, two trained gastroenterologists independently reviewed all endoscopic reports and pathological findings. Any discrepancies were resolved through consensus with a third senior gastroenterologist. Data entry was performed by two independent researchers, with cross-checking for accuracy.

Statistical Analysis

Data analysis was performed using SPSS software version 26 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean ± standard deviation or median with interquartile range based on distribution normality. Categorical variables were expressed as frequencies and percentages. The Chi-square test or Fisher's exact test was used for comparing proportions between groups. A P value < 0.05 was considered statistically significant for all analyses.

All patient data were anonymized and stored on password-protected computers. Access to the database was restricted to the principal investigators, in compliance with Iranian data protection regulations and institutional policies

RESULTS

During the 3-year study period (2019-2021), a total of 6,124 endoscopic and colonoscopic procedures were performed at Ali Ibn Abi Talib Hospital. Among these, suspicious lesions warranting biopsy were identified in 489 procedures (7.98%). Histopathological examination confirmed malignancy in 315 patients, yielding a cancer detection rate of 5.14% among all procedures performed. The cohort of 315 patients with confirmed GI cancers consisted of 177 (56.2%) males and 138 (43.8%) females, with a male-to-female ratio of 1.3:1. The mean age of the

patients at diagnosis was 61.0 ± 14.8 years (Range: 23-95 years).
The mean age of the entire patient population was 41.01 ± 23.41 years, while the average age of patients diagnosed with cancer was approximately 61 years.
Objective 1: Frequency of Upper and Lower Gastrointestinal Tract Cancers
Objective 2: Frequency of Cancers by Age and Sex
Objective 3: Determine and compare the correlation between the prevalence of upper and lower GI cancers and sex

Esophageal cancer was diagnosed in 112 (38.73%) patients, gastric cancer in 113 (35.87%), and colorectal cancer in 78 (24.76%). Synchronous Cancers: 2 (0.6%) (0.63%) presented with multiple cancers (e.g., both stomach and esophagus).

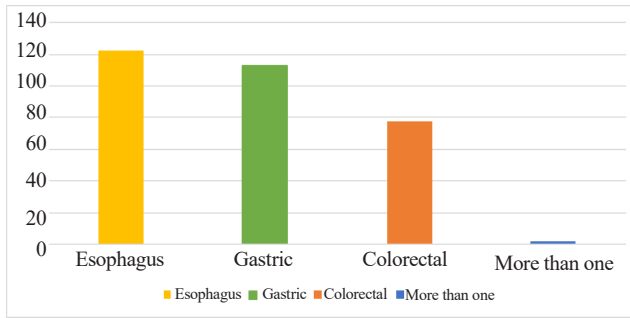

Figure 1. The frequency distribution of diagnosed gastrointestinal cancers according to the malignancy type derived from endoscopy-colonoscopy procedures performed at Ali ibn Abi Talib Hospital between 2019 and 2021

According to the results, the prevalence of esophageal and

Table 1. Distribution of gastrointestinal cancers by age from a total of endoscopy-colonoscopy procedures performed at Ali ibn Abi Talib Hospital between 2019 and 2021

Cancer \ Age (y)		≤40	41-50	51-60	60≤	Total	P value*
Esophageal cancer	✓	7 (5.6)	15 (12.1)	28 (22.6)	74 (59.7)	123 (100)	0.184
	✗	24 (12.6)	26 (13.6)	34 (17.8)	107 (56)	191 (100)	
Gastric cancer	✓	12 (10.4)	17 (14.8)	22 (19.1)	64 (55.7)	115 (100)	0.889
	✗	19 (9.5)	24 (12)	40 (20)	117 (58.5)	200 (100)	
Colorectal cancer	✓	12 (15.2)	9 (11.4)	12 (15.2)	46 (58.2)	79 (100)	0.224
	✗	19 (8.1)	32 (13.6)	50 (21.2)	135 (57.2)	236 (100)	
Total		31 (9.8)	41 (13)	62 (19.7)	181 (57.5)	315 (100)	

* The Chi-square test results for the numbers in the table were reported in terms of frequency (in percentage).
No significant correlation was observed between the frequency of GI cancers and age.

Table 2. Distribution of gastrointestinal cancers by sex from a total of endoscopy-colonoscopy procedures performed at Ali ibn Abi Talib Hospital between 2019 and 2021

Cancer \ Sex		Male	Female	Total	P value*	OR(95% CI)
Esophageal cancer	✓	61 (49.2)	63 (50.8)	123 (100)	0.044	1.59 (1.01-2.52)
	✗	116 (60.7)	75 (39.3)	191 (100)		
Gastric cancer	✓	75 (65.2)	40 (34.8)	115 (100)	0.014	0.55 (0.34-0.89)
	✗	102 (51)	98 (49)	200 (100)		
Colorectal cancer	✓	41 (51.9)	38 (48.1)	79 (100)	0.374	1.26 (0.75-2.10)
	✗	136 (57.6)	100 (42.4)	236 (100)		
Total		177 (56.2)	138 (43.8)	315 (100)		

*The Chi-square test results for the numbers in the table were reported in terms of frequency (in percentage). The totals for each cancer type exceed 315 because two cases of synchronous cancers are counted in more than one category.

gastric cancers differed significantly by sex. Esophageal cancer was reported to be slightly more common in women than in men, while gastric cancer had a higher prevalence in men. The prevalence of colorectal cancer, however, showed no significant difference based on sex.

Additional Findings:

Determining the frequency of diagnosed cancer types based on pathology reports from all endoscopy and colonoscopy procedures conducted at Ali Ibn Abi Talib Hospital between 2019 and 2021

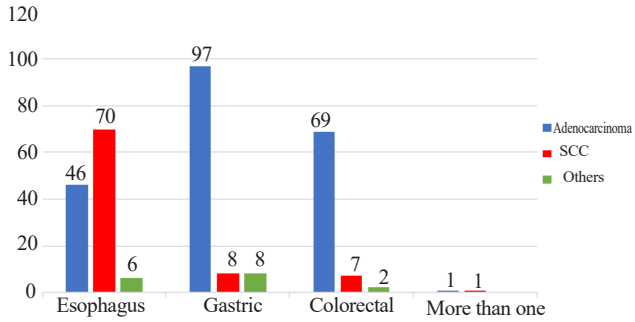

Figure 2. The distribution of diagnosed gastrointestinal cancers according to pathology report derived from endoscopy-colonoscopy procedures performed at Ali ibn Abi Talib Hospital between 2019 and 2021

Table 3. The distribution of diagnosed gastrointestinal cancers according to pathology report derived from endoscopy-colonoscopy procedures performed at Ali ibn Abi Talib Hospital between 2019 and 2021

Type / Cancer	Adenocarcinoma	Squamous cell carcinoma	others	Total
Esophageal	46 (37.7)	70 (57.4)	6 (4.9)	122 (100)
Gastric	97 (85.8)	8 (7.1)	8 (7.1)	113 (100)
Colorectal	69 (88.5)	7 (9)	2 (2.6)	78 (100)
More than one	1 (50)	1 (50)	-	2 (100)
Total	213 (67.6)	86 (27.3)	16 (5.1)	315 (100)

According to the results, most esophageal cancers (57.4%) were SCC, while most gastric cancers (85.8%), and colorectal cancers (88.5%) were adenocarcinomas.

Table 4. Determining the average age of patients based on the location of gastrointestinal cancers

Cancer	Average age	Standard deviation	P value*
Esophageal	62.96	13.12	0.478
Gastric	60.68	15.73	
Colorectal	60.18	16.41	

* Kruskal-Wallis Test

1. Most cancers (57.5%, n=181) were diagnosed in patients over 60 years of age. The mean age of patients with esophageal cancer (63.0 ± 13.1 years) was slightly higher than that of patients with gastric (60.7 ± 15.7 years) and colorectal (60.2 ± 16.4 years) cancer. This difference was not statistically significant (P=0.478, Kruskal-Wallis test). A notable finding was that 12 (15.2%) of the 79 colorectal cancer cases were diagnosed in patients under 40 years of age.

DISCUSSION

This retrospective cross-sectional study provides significant insights into the epidemiological and histopathological characteristics of GI cancers in a tertiary care center in Southeastern Iran. Our findings reveal several distinctive patterns that help explain regional variations in GI cancers in Iran and highlight the need to develop targeted healthcare strategies.

The overall cancer detection rate of 5.14% in our endoscopic population aligns with previous Iranian studies. Emani and colleagues (2012) reported suspicious lesions in 8.49% of patients undergoing endoscopic procedures, which is consistent with our finding of 7.98% suspicious lesions (17). However, our cancer confirmation rate of 5.10% demonstrates the significant burden of GI malignancies in this region. The distribution pattern of specific cancers in our cohort esophageal cancer (38.7%) being the most prevalent, followed by gastric (35.9%) and colorectal cancers (24.8%) presents a notable deviation from patterns reported in other Iranian studies. Almasi (2014) in Markazi province reported gastric cancer as the predominant malignancy (51.2%), followed by colorectal (35.4%) and esophageal cancers (13.5%) (18). This discrepancy underscores the substantial regional variation in GI cancer epidemiology within Iran and emphasizes that findings from one geographical region cannot be extrapolated to others.

The high prevalence of esophageal and gastric cancers in our cohort is consistent with the established carcinogenicity of opium. After five decades of research, opium has been definitively classified as a Group 1 carcinogen by IARC, with causal links to esophageal and gastric cancers (10,11). The Golestan Cohort Study provides compelling evidence, demonstrating that regular opium use significantly increases risk for esophageal (HR: 1.38) and gastric (HR: 1.36) cancers, with clear dose-response relationships (12). Given that opium consumption is not uncommon in Sistan and Baluchestan, this exposure likely contributes substantially to the elevated burden of upper GI cancers observed in our population.

The sex distribution in our study reveals intriguing patterns that merit special attention. The higher prevalence of esophageal cancer in women (45.7%) compared with men (34.5%) contrasts with most international literature but finds some support in regional studies. This reversed sex ratio may reflect differential opium exposure patterns, as the IARC Monograph notes that consumption varies by sex and cultural context (11). Opium use among women in certain Iranian populations is not negligible and may contribute to their cancer risk (10,12). Additional factors, such as indoor air pollutants from traditional cooking, may synergize with opium-related carcinogenesis, disproportionately affecting women. Conversely, the male predominance in gastric cancer (42.4% in men vs. 29.0% in women) aligns with global patterns and previous Iranian studies, possibly reflecting higher prevalence of established risk factors such as smoking and *H. pylori* infection among men in this region (8).

The histopathological distribution in our cohort provides additional insights into the regional cancer profile. The predominance of SCC (57.4%) among esophageal cancers reinforces the classification of this region as a high-risk zone for esophageal SCC. The SCC predominance is particularly relevant to the opium hypothesis, as opium derivatives contain carcinogens that preferentially affect the esophageal squamous epithelium (38,39). The IARC Working Group found sufficient evidence for opium-related esophageal SCC, and the Golestan study reported strong associations between opium use and SCC specifically, with substantial population attributable fractions in high-prevalence regions (11,12). Meanwhile, the high proportion of adenocarcinomas in both gastric (85.8%) and colorectal cancers (88.5%) aligns with global trends. Notably, the IARC Monograph also found sufficient evidence for opium-related gastric carcinogenesis, including both intestinal and diffuse adenocarcinoma types (11).

Age distribution analysis reveals that while most cancers (57.5%) were diagnosed in patients over 60 years, the substantial proportion of colorectal cancer cases (15.2%) in patients under 40 years is particularly concerning. This finding is consistent with Rahimi's (2015) review article, which indicated increasing incidence rates of colorectal cancer in Iran, though the high percentage in young adults in our study exceeds previous reports (4). This trend may reflect changing lifestyle factors, genetic predispositions, or possibly delayed diagnosis in younger populations, warranting further investigation.

The Golestan study's demonstration of dose-response relationships with cumulative opium use suggests that early initiation could contribute to earlier cancer development (12).

A key clinical implication is prevention. The Golestan study showed that cessation of opium use for more than 5 years substantially reduces esophageal cancer risk (HR: 0.33) (12). As emphasized in the fiftieth-anniversary review, the carcinogenic effects of opium are partially reversible, offering hope for public health interventions (10,11). Our findings of high esophageal and gastric cancer burden suggest that targeted cessation programs in this region could yield significant reductions in future cancer incidence.

CONCLUSION

Between 2019 and 2021, a suspicious lesion was observed in the hospital of Ali ibn Abi Talib Zahedan. The age group above 44 years accounted for more than half of all types of GI cancers. The most common to least common cancers were, respectively, esophageal cancer, stomach cancer, and finally colorectal cancer. Overall, the prevalence of GI cancers was reported to be higher in men. Also, studies in recent years have shown that esophageal cancer is often of the SCC type, while stomach and colorectal cancers are often adenocarcinomas.

It is suggested that greater public awareness of the risk factors for GI cancers can reduce their incidence, and that people should be encouraged to visit screening centers. It is also recommended that comprehensive insurance policies be considered for diagnostic methods. Additionally, individuals with a positive family history of GI cancers should be identified and monitored more closely.

Limitations

Several limitations of our study should be acknowledged. The retrospective design and single-center data collection may limit generalizability. The absence of detailed information on risk factors such as *H. pylori* infection status, dietary patterns, smoking habits, and family history prevents a more comprehensive analysis of potential etiological factors. Furthermore, as a tertiary referral center, our patient population may represent more advanced cases, which could introduce selection bias. Despite these limitations, our study provides valuable baseline data from an understudied region that can inform future prospective studies. Limitations include the absence of detailed exposure data on opium consumption. Given the established causal role of opium in upper GI cancers (38,40). Future prospective studies should systematically collect information on opium use including frequency, duration, and mode of consumption to quantify its contribution to the local cancer burden and inform evidence-based prevention strategies

Conclusion and Implications

In conclusion, our findings delineate a distinct profile

of GI cancers in Southeastern Iran, characterized by the predominance of esophageal cancer, unusual sex distribution patterns, and concerning rates of early-onset colorectal cancer. These results emphasize the necessity for developing region-specific cancer control strategies, including tailored screening programs and targeted public health interventions. Future studies should focus on prospective designs with comprehensive risk factor assessment to better understand the determinants of these unique epidemiological patterns and to develop effective prevention strategies for this population.

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