

**MEKELLE UNIVERSITY**

**COLLEGE OF HEALTH SCIENCES**

**DEPARTMENT OF INTERNAL MEDICINE**

**CLINICAL INDICATIONS OF UPPER GASTROINTESTINAL  
ENDOSCOPY AND THEIR PREDICATING VALUE OF UPPER  
GASTROINTESTINAL MALIGNANCY IN ACSH, NORTHERN  
ETHIOPIA.**

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## LIST OF ABBREVIATIONS

- ACG --American College of Gastrology
- ACSH-Ayder Comprehensive Specialized Hospital
- APD –Acid Peptic Disease
- BSG-British Society of Gastroenterology
- CA –Cancer
- CLD- Chronic Liver Disease
- CSFs - Clinically Significant Findings
- DU-Duodenal Ulcer
- EAC -Esophageal Adenocarcinoma
- EC -Esophageal Cancer
- ECG- Echocardiography
- ESCC -Esophageal Squamous Cell Carcinoma
- EGD-Esophago Gastro Duodenoscopy
- ESG-European Society of Gastroenterology
- EVL- Endoscopy Varicial Ligation
- FD -Functional Dyspepsia
- GC-Gregorian Calendar
- GERD-Gastro Esophageal Reflux Disease
- GI-Gastro Intestinal
- GIT-Gastro Intestinal Tract
- GOO-Gastric Outlet Obstruction
- H.PYLORI-Helicobacter Pylori
- ICU- Intensive Care Unit
- NPV-Negative Predictive Value
- PPI-Proton Pumping Inhibitor
- PPV-Positive Predictive Value
- PUD -Peptic Ulcer Disease
- ROC- Receiver Operating Characteristic
- SPSS- Statistical Package for the Social Sciences
- UD -Uninvestigated Dyspepsia

- UGID-Upper Gastro Intestinal Disease
- UGIE-Upper Gastro Intestinal Endoscopy
- Yr -Year

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## **ABSTRACT**

**Background:** In a resource-limited setup like Ethiopia, Alarm symptoms are generally accepted as an indication for prompt endoscopy, and these are effective and inexpensive tools to optimize diagnostic yield and identify malignant lesions in patients with upper GI complaints. However, previous studies noted that the sensitivity of alarm features for predicting cases with upper GI malignancies is unsatisfactory (29). Some studies on other part of Ethiopia have yielded mixed results. So far, there has been no study done in Ayder that assessed to what extent the indications of upper GI endoscopy could help identify patients with significant UGI pathologies or malignancies.

**Methods:** Facility based cross-sectional study was conducted in patients who underwent upper GI endoscopy at GI clinic in ACSH from Jan 2019 and Jun 2024 was included in the study. Descriptive statistics were used as appropriate. Data analysis was done using SPSS 27.0 statistical software. Bivariate and multivariate analysis was done to identify significant indications of upper GI malignancy, finally, statistical significance was declared at p-value  $\leq 0.05$ .

**Results:** A total of 1,484 patients underwent complete upper gastrointestinal tract endoscopic evaluation during the study period. The median age of the patients was 38 years. Males accounted for 70.4% of the patients. Dyspepsia (21.6%) was the most common indication for endoscopic evaluation. Esophagitis (15.2%) were the most common pathology. The prevalence of upper GI malignancy recorded in our endoscopy cases 11.2%, and of those, 71.1 % had confirmed cancer of the stomach, the esophagus and the duodenum. It was statistically significant giving our study subjects a 7.9% ( $p < 0.001$ ) prevalence of cancer. Gastric cancer was accounting 62.7%, esophageal cancer 27.1%, duodenal cancer 5.08 % and gastro esophageal junction cancer 5.08%. The majority 77.1% of them had one or more alarm symptoms. The sensitivity, specificity, PPV and NPV of having any alarm features for predicting malignancy were 77.1%, 62.1%, 16.4% and 96.6%, respectively. The individual alarm symptoms such as an unexplained loss of weight, persistent vomiting and dysphagia were statistically significant correlation with a UGI malignancy ( $P = 0.001$ ). Based on receiver operating characteristic curve, the optimal age for screening of malignancy was 39.5 years in this population.

**Conclusion:** Dyspepsia was the most common indication for EGD followed by screening varices of CLD patients. Clinically significant endoscopic findings were common. Esophagitis, pan gastropathy and esophageal varices were the common endoscopic finding. Of those, malignancies gastric CA followed by esophageal CA were common. Alarm symptoms were highly prevalent which was significantly higher among patients in the abnormal endoscopic group, particularly in upper GI malignancy group than in the

normal endoscopic group. There were inconsistent in finding between endoscopy and biopsy result. Being age above 39.5 and female, and certain alarm features (persistent vomiting, dysphagia, and unexplained weight loss) were independent predictor of UGI malignancy.

**Keywords:** Endoscopy, alerms symptoms, upper GI malignancies and Ethiopia.

# 1. INTRODUCTION

## 1.1 Background

The term “upper gastrointestinal (GI) symptoms” is commonly used to describe a wide range of complaints including dyspeptic and gastro esophageal symptoms, as well as peptic ulcer disease (PUD) (1).

Upper gastrointestinal (UGI) symptoms are among the commonest complaints for which patients seek medical attention mainly the gastroenterology services.

Upper gastrointestinal (GI) malignancy was still a health problem in all over the world. Upper gastrointestinal (GI) cancers, mainly including gastric cancer (8.2% of total cancer deaths) and esophageal cancer (5.3% of total cancer deaths), are the leading cause of cancer-related deaths worldwide (2).

The frequency of gastric cancer is considered rare in sub-Saharan Africa despite the high prevalence of *Helicobacter Pylori* (3). In Ethiopia, available works of literature put gastric cancer 9th among all cancers in incidence (4), but it is 4th most common cancer among upper GI cancers in the Sudan (33-35). Previous local study in Ayder hospital shown that Gastric cancer was found in (9.4%) of Upper GI complaint (5), which is higher than Other studies in Ethiopia have shown a prevalence of gastric cancer ranging from 0.3-8.8% (6,7,8). Esophageal cancer incidence varies globally, with its highest across the “esophageal cancer belt”, Countries of the East and South Africa and Asia (2).

Previous studies have shown that upper GI cancers always go through the stages of precancerous lesions, which can be defined as common conditions associated with a higher risk of developing cancers over time. The detection of the precancerous lesions before cancer occurs could significantly reduce morbidity and mortality rates (9).

Currently, endoscopy remains an important step in the diagnosis and management of upper GI symptoms. Upper GI endoscopy is a procedure that uses a small, flexible camera with a light source to examine the upper GI tract. It gives an excellent view of mucosal surfaces of the oesophagus, stomach, and proximal duodenum. Observations are made looking for focal benign or malignant lesions diffuse mucosal changes, luminal obstruction, motility, and extrinsic compression by contiguous structures (10).

If these lesions are identified in the early stages, the success rate of treatment and the quality of life will improve. However, endoscopy is an invasive procedure that is relatively expensive. Therefore, the selective use of endoscopy in high-risk patients would be the most cost-effective approach. The large burden of inappropriate referrals for endoscopy of patients with Upper GI complaint leads to both unacceptable consumption of health resources and detrimental increase of waiting time for clinically indicated patients (11, 12).

However, the treating physicians fear missing clinically significant endoscopic findings in patients with no warning symptoms if endoscopy is not conducted, and it is unclear whether a substantial proportion of cases with symptoms would be missed (12).

Traditionally, clinicians are alerted to the possibility of malignancy by the history and physical examination; alarm features on the clinical evaluation include chronic gastrointestinal bleeding, progressive unintentional weight loss, progressive difficulty swallowing, persistent vomiting, iron deficiency anemia, lymphadenopathy or epigastric mass. Alarm features, also called *alert features, red flags, or warning signs*, are specific features thought to be associated with serious gastroenterologic disease such as underlying malignancy or significant pathology such as a stricture or ulcer. Current guidelines recommend that, in the initial evaluation of patients with upper GI complaint, the decision to perform endoscopy should be based on older age >60 yrs (13). and alarm features because it is generally believed that these factors indicate a higher probability of malignancy being present (14).

Several studies have sought to determine the utility of alarm features in predicting serious upper GIT disease, with conflicting results (15). In a systematic review and meta-analysis of 15 studies with 57,363 patients, the overall sensitivity and specificity of the alarm features in predicting GI malignancy on endoscopy were 0-83% and 40-98% respectively, while the sensitivity and specificity with just clinical diagnosis of upper GI malignancy by a physician were 11-53% and 97-98% respectively, leading the authors to conclude that the alarm features only have limited value for predicting underlying malignancy,(16) Other workers have documented a similar finding (17). In contrast, some authors document a good predictive value of the alarm features in patients with dyspepsia when endoscopy is performed, and support the use of endoscopy in these patients (18, 19).

Endoscopy capacity is severely limited in eastern sub-Saharan Africa, despite a high burden of gastrointestinal disease (19). In Ethiopia, although four decades have passed since endoscopic

evaluation of the gastrointestinal tract has been started, Service is offer in few teaching hospitals and private centers, all in the countries (20). In Ayder according previous study, by February 2015, more than 2,500 procedures had been performed from the starting of service in 2011 (5).

Moreover, there is limited data on endoscopy and endoscopic findings in Ethiopian patients with warning signs; therefore, it's not yet obvious whether to heed or adjust such advice. Some African studies have yielded mixed results.

To the best of my knowledge, there has been no study done in Ayder hospital on addressing this subject. Therefore, In this study we answered the questions -How much patients with upper GI symptoms who underwent upper GI endoscopy have significant endoscopy finding, particularly upper gastrointestinal cancer and what was the diagnostic accuracy of clinical indications or alarm features and age threshold for predicting malignancy. This will help to improve the role of age and alarm features in clinical decision making concerning which patients should be done or referred to do endoscopy in our environment. The data obtained in this study, may be used by concerned bodies for planning and evaluating appropriateness of referral and to guarantee improvement in the quality of patient care.

## 1.2 STATEMENT OF THE PROBLEM

Upper gastrointestinal tract disorders are prevalent worldwide, encompassing neoplastic and non-neoplastic lesions like infections and inflammation (21).

Many patients with UGI symptoms are referred to gastroenterologist for consultation and endoscopy. Given the large burden of these patients, the appropriate role of endoscopy in the evaluation of these patients is both a concern to the gastroenterologist and an essential determinant of health care cost, especially in a developing country like Ethiopia where resources are limited (22).

The majority of upper gastrointestinal (UGI) disorders in Africa are uninvestigated with patients often treated symptomatically. This creates a challenge as treatable diseases including malignancies are often missed only to present in very advanced stages (23).

Upper gastrointestinal cancer is a prevalent and life-threatening disease, significantly impacting the well-being of individuals worldwide. According to the latest global cancer statistics report of 2020, esophageal cancer ranked seventh in terms of incidence and sixth in terms of mortality rate, while gastric cancer ranked fifth in incidence and fourth in mortality rate (24). In Ethiopia, hospital records show that there are more than 150,000 cancer cases per year and currently cancer accounts for 4% of all deaths (25).

Both the public's understanding of cancer and the availability of early detection methods are lacking in developing countries. As a result, patients frequently receive a cancer diagnosis in its advanced or deadly stages (26). If these lesions are identified in the early stages, the success rate of treatment and the quality of life will improve (27). The current standard method for diagnosis of upper GI cancers is upper GI endoscopy and biopsy. However, endoscopy is an invasive procedure that is relatively expensive (11,13).

Therefore, the selective use of endoscopy in high-risk patients would be the most cost-effective approach. The large burden of inappropriate referrals for endoscopy of patients with Upper GI complaint leads to both unacceptable consumption of health resources and detrimental increase of waiting time for clinically indicated patients (11, 12). Moreover, the treating physicians fear missing clinically significant endoscopic findings in patients with no warning symptoms if endoscopy is not conducted, and it is unclear whether a substantial proportion of cases with symptoms would be missed. This leads to over use of endoscopy (12).

Despite the fact that symptoms or clinical indications are not as precise as a diagnostic tool such as e.g. laboratory data, because of their subjective and individual nature, quantifying the association between symptoms and upper GI cancer and comparing the relative diagnostic values is useful knowledge for the clinician. (28)

However, previous studies noted that the sensitivity of alarm features for predicting cases with upper GI malignancies is unsatisfactory. (29) Furthermore, most previous studies have investigated populations in western countries, where prevalence of upper GI malignancies is low.

So far, there has been no study done in Ayder, which assessed to what extent the indications of upper GI endoscopy could help identify patients with significant UGI pathologies or malignancies. Some studies on other part of Ethiopia have yielded mixed results.

The aim of this study was to determine the associations between indications or alarm features and significant endoscopy findings especially of upper GI malignancy in patients who underwent upper GI endoscopy in Ayder.

### 1.3 SIGNIFICANCE OF THE STUDY

Symptoms of upper gastrointestinal (UGI) disorders are among the commonest complaints for which patients seek medical care. The majority of patients with upper GI symptoms in Africa are uninvestigated with patients often treated symptomatically. This creates a challenge as treatable diseases including malignancies are often missed only to present in very advanced stages. SSA is projected to have a more than 73% increase in gastrointestinal cancers (including esophagus, stomach, liver and colorectal) by 2030, away more than the 59% global estimate (23).

Upper gastrointestinal endoscopy (UGIE) is one of the most commonly performed diagnostic procedures and offers valuable information in patients with UGI disorders. Establishing etiology of UGI diseases leads to more effective treatment and subsequently decreases morbidity and mortality rates. Based on this the approach for assessing and managing patients with UGI disorders focuses on recognizing high risk patients including those with upper GI symptoms older than 55 years and those with one or more alarm features.(30)

In a resource-limited setup like Ethiopia, particularly in Tigray region, Alarm symptoms are generally accepted as an indication for prompt endoscopy, and these are effective and inexpensive tools to optimize diagnostic yield and identify malignant lesions in patients with upper GI complaints. Moreover, it has an implication on reducing referrals for endoscopy would help ease departmental pressures and waiting times in over- stretched public healthcare systems, while facilitating quicker diagnosis and management. It would also have economic implications.

However, previous studies noted that the sensitivity of age and alarm features for predicting cases with upper GI malignancies is unsatisfactory (29).Some studies on other part of Ethiopia have yielded mixed results

So far, there has been no study done in Ayder, that assessed to what extent the indications of upper GI endoscopy could help identify patients with significant UGI pathologies or malignancies. Some studies on other part of Ethiopia have yielded mixed results.

The aim of this study was to determine the associations between indications or alarm features and significant endoscopy findings especially of upper GI malignancy in patients who underwent upper GI endoscopy in Ayder. Therefore, in this study we answered the questions -How much patients with upper GI symptoms who underwent upper GI endoscopy have significant endoscopy finding, particularly upper gastrointestinal cancer and what was the diagnostic

accuracy of clinical indications or alarm features and age threshold for predicting malignancy. This will help to improve the role of age and alarm features in clinical decision making concerning which patients should be done or referred to do endoscopy in our environment. The data obtained in this study, may be used by concerned bodies for planning and evaluating appropriateness of referral for endoscopy and to guarantee improvement in the quality of patient care.

## 2. LITERATURE REVIEW

### 1. INDICATIONS FOR UPPER GASTROINTESTINAL ENDOSCOPY AND FINDINGS

The benefits of performing an endoscopic procedure regardless of indication—screening, surveillance, diagnostic or therapeutic must be balanced against the potential harms. Studies have questioned the appropriateness of indications for UGIE and have shown that inappropriate indications range from 5% to 49% (31,32). These unnecessary UGIE expose patients to the risks of the procedure and results in increased waiting period and increased health care expenses. The American Society for Gastrointestinal Endoscopy (ASGE) guidelines have been used to define the appropriateness of the indications (32). Alarm symptoms are generally accepted as an indication for direct endoscopy. This is reflected in several guidelines for treatment of patients with dyspeptic symptoms

Alarm features, also called alert features, red flags, or warning signs, are specific features thought to be associated with serious gastroenterologic disease, which may include underlying malignancy or significant pathology such as a stricture or ulcer (33).

However, according to the results of previous studies, the sensitivity of alarm symptoms to predict upper GI malignancies is not satisfactory (34). The predictive effect of alarm symptoms requires further research.

#### A. GLOBAL

There are many reports in the literature on the indications and findings of UGIE mainly from the teaching hospitals and few private hospitals.

In Turkey, A retrospective study was performed (from 2010 to 2015), Total of 6243 patients underwent a complete UGIE over the period, of this 2548 of the patients were male and 3695 were female. The mean age of the patients was  $49.37 \pm 16.90$  years. The indications for EGD were dyspeptic symptoms for 72.8% of females and 70.4% of males. Anemia was the indication for 12.1% of females and 11.8% of males. Other indications included gastrointestinal bleeding, dysphagia, nausea and vomiting, gastroesophageal reflux disease symptoms and weight loss (35). which was in agreement with other published findings in Bangladesh, the patients underwent esophagogastroduodenoscopy mainly because of dyspepsia 226 (37.5%) (36), Unlike this study,

prospective observational study was conducted from India, Commonest indication for EGD was epigastric pain in 614 (68.2%) patients (37).

There was prospective observational study was carried out in China (From January to December 2017) of 4310 (mean age 44, median 42, range 14–86) consecutive patients undergoing upper gastrointestinal endoscopy for evaluation of upper gastrointestinal symptoms, 75.1% had a normal EGD; 13.8% had Significant pathology (peptic ulcer disease 12.3%, gastric cancer 1.2%, and esophageal cancer 0.3%) (38). These results were consistent with another study from China showing that as least a quarter of patients undergoing EGD had significant endoscopic findings (39). These findings contrast with those of western countries where reflux esophagitis and endoscopic suspected esophageal metaplasia are currently the predominant findings. The high prevalence of *H. pylori* and its related diseases, peptic ulcer and malignancy, remains high in China (40), such that in China, in contrast to many western countries, screening for peptic ulcer and malignancy has proven to be cost effective (41).

This prospective study revealed a significantly association between Age, male sex and alarm symptoms and with malignancy. The age cut-off identified for upper gastrointestinal malignancy was 56 years among patients with uncomplicated dyspepsia, which was similar to the combined cutoff of age and gender (38). These results were consistent with another study (42).

There was prospective observational study from India, Which found that alarm features were effective tools to identify malignant lesions in patients with upper GI complaints. Alarm features were present in 206 (22.9%), of which malignant lesions were seen in 46 (22.3%) patients (37). which was unlike the studies conducted in Bangladesh (63.5%) (43, 44). This variation may be due to the study population involved (tertiary vs. primary), health care facilities available, local prevalence of a disease and study design (retrospective vs. prospective). This was somewhat similar to studies conducted across the country (44).

There is an increase in the risk of gastric and esophageal cancer with advancing age, but a cutoff age is currently unavailable. American College of Gastroenterology and the Canadian Association of Gastroenterology recent guidelines suggest that patient >60 years of age presenting with dyspepsia are investigated with UGIE to exclude organic pathology (45).

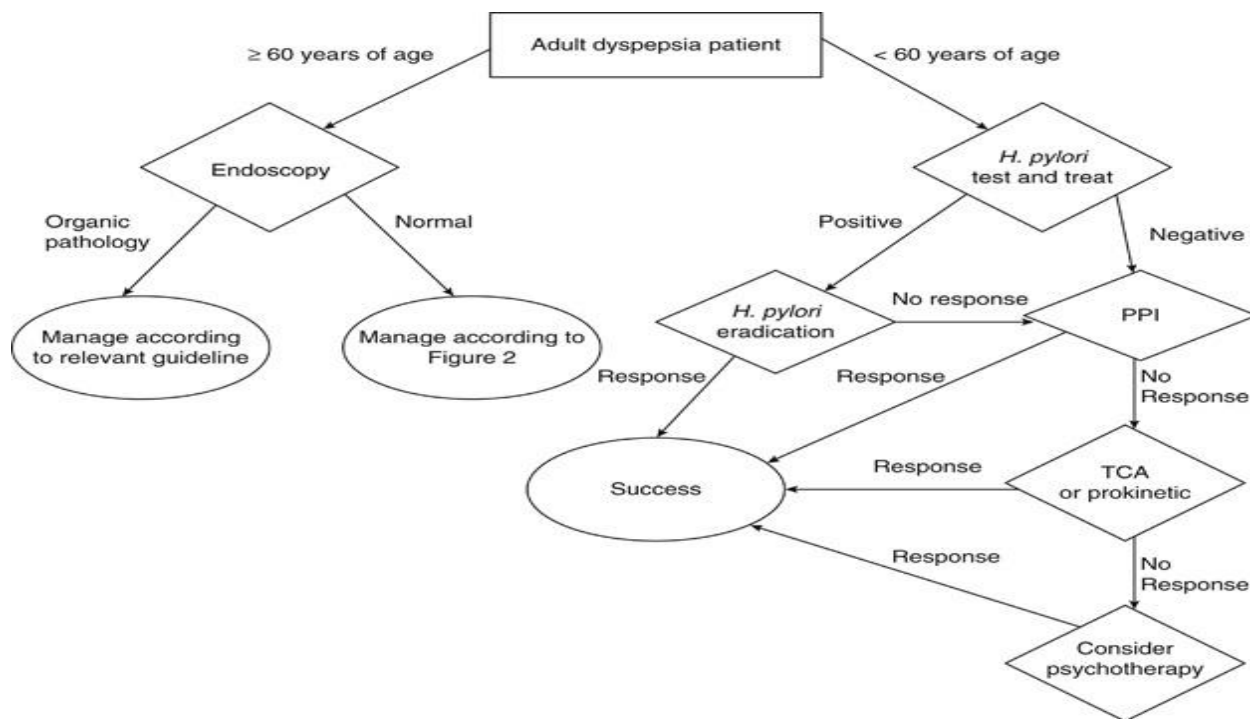


Figure 1:-Algorithm for the management of undiagnosed dyspepsia.

## B. REGIONAL

In Nigeria, a retrospective study (between August 1st 2017 and July 31st 2018) was conducted, one hundred and fifty-nine gastroscopies were performed during this period, mean age was 47.8 ( $\pm 14.4$ ) years, and 49.1% were male. Dyspepsia was the commonest indication for endoscopy (80.5%), 60.2% of the dyspeptics had at least one alarm feature (46). This is similar to findings by other investigators (47, 48).

The most frequent dyspeptic symptom was epigastric pain/burning sensation (75%), while the commonest alarm features were recent onset dyspepsia in a patient over 45 years (79%) and unexplained weight loss (28.6%) (46). However, lower figures have been reported by some studies (49,33). The high prevalence of alarm features in this study may be attributed to late presentation and poor health seeking behavior.

Endoscopy was normal in 26%. The most frequent significant endoscopic findings were gastritis (49%) and gastric ulcer (17%) and they were not associated with alarm features. Upper gastrointestinal bleeding, persistent vomiting and odynophagia were specific for significant endoscopic findings (46). This was similar to previous findings in Nigeria (50). While others report esophagitis and peptic ulcer disease as the most frequent endoscopic finding (51,44).

In this study, alarm features in the patients with dyspepsia were not associated with any significant endoscopic finding. The pooled sensitivity, specificity, positive predictive value, and negative predictive value of the alarm features were 65%, 49%, 71% and 41% respectively

(46). This was in contrast to studies that report an association between alarm features and abnormal endoscopic findings, such as polyps, and cancers (51, 47), with gastric cancer being eight times more common in those with alarm features than in those without (52).

Similar study conducted, In Ghana, Dyspepsia was the commonest indication occurring in 282(76.0%) patients. The commonest endoscopic diagnosis was gastritis which occurred in 261(70.4%) patients (43). Whereas in Ethiopia a review of 10,000 endoscopies between 1979 and 1994, showed that 59.4% were referred because of dyspepsia (14).

There was a cross-sectional study In South-Western Uganda There were multiple reasons patients present with upper gastrointestinal symptoms but epigastric pain (51.6%) was the most common reason for endoscopy. Which is similar to studies in Jos and Ilorin, Nigeria (53). The most common identifiable lesion at endoscopy in this study was gastritis (40.2%) which is similar to the data from Kenya, and Sudan (54,55). These earlier studies in Kenya and Sudan showed a frequency of gastritis at 25.8% and 36.9% respectively. This disparity may be as a result of the difference in predisposition to risk factors for gastritis among the patients who were studied in these countries.

### C. NATIONAL

The predictive performance of using alarm features to predict UGI pathology has been extensively studied, but the results were inconsistent (56,57). Moreover, the majority of previous research was conducted in Europe, North America or Asian. Conclusions from Western studies may not be applicable in Ethiopia countries where prevalence of UGI diseases remarkably differs.

In Ethiopia, At St Paul hospital millennium medical college GI clinic a retrospective cross-sectional (between January 2012 and December 2019) was conducted; a total of 5753 patients underwent complete upper gastrointestinal tract endoscopic evaluation during the study period. The median age of the patients was 37 years. Males accounted for 63.4% of the patients. Dyspepsia (27.8%) was the most common indication for upper gastrointestinal endoscopic evaluation (20), which was lower than similar local studies conducted in Tikur Anbessa teaching

hospital, in Addis Ababa, and at University of Gondar, northwestern Ethiopia, in which it accounted for 59.4% and 53.8%, respectively (58, 59).

On the contrary, indications like work up for upper GI bleeding (17.1%), variceal screening (16.8%), and follow-up endoscopy (13.7%), of which 89.2% had varices, were higher in this study. This may be due to the fact that SPHMMC, being a center with gastroenterology and hepatology fellowship training program, accepts more patients with liver diseases who have complications and require repeated endoscopic evaluation (20).

The pathology most frequently identified was esophageal varices (35.8%), followed by gastritis (18.1%), and duodenal ulcers (10.6%), which were much higher than similar Ethiopian studies from Addis Ababa (9%), Gondar (2.9%) and Mekelle (12.7%); (59,60,5) and studies from other African countries (60). These findings can be explained by the better availability of human and material resources in SPHMMC for the treatment of esophageal varices, such as endoscopic band ligation, compared with the rest of the country, which attracts more referrals of patients with such pathologies.

This report Consistent with previous retrospective cross-sectional study conducted at the same hospital (from September 1, 2015, to August 31, 2017), off 3542 patients seen at GI clinic, dyspepsia was diagnosed in 418 i.e. in 21.6% of cases (61).

Other an institution-based cross-sectional study conducted in Ethiopia (from July to September 2022), 142 patients were selected, with an average age of 48.35 and 52.1% being male. Epigastric pain was the most common reason for an endoscopy. 62% of patients had at least one alarm feature, the most common being unexplained weight loss and UGI bleeding (20). This was similar to what has been reported from Nigeria (60.2%) (46). A 73.9% endoscopic diagnostic yield was obtained based on the fact that 26.1% of patients exhibited normal endoscopic results. Which was similar reports have been made from Gondar (83.4%) and Nigeria (71.4%);(62,46).

The study found a strong association between the presence of alarm features, significant endoscopic findings, and UGI malignancies. The pooled sensitivity and specificity of any alarm feature for any significant finding were 79% and 64.9%, respectively, and for malignancy, 100% and 39.7%, respectively. The presence of the alarm feature was associated with an increase of 6.801 in the odds of developing SEF and an increase of 4.199 in the odds of developing

malignancy (20). This was the same studies from Chinese and Iranian studies (33, 63). Reports from Nigeria were contrast to these findings (46).

#### **D. LOCAL**

A facility-based retrospective cohort study was conducted in Ayder; total patients of 1,994 upper GI endoscopy examinations were included in the study. The mean, minimum and maximum age of the study subjects was 40, 1 and 94 years of age respectively. Common indications for EGD were peptic ulcer disease (32%), dyspepsia (13.2%), esophageal varices (10%), upper gastrointestinal bleeding (8.9%), gastric cancer (5.8%), gastric outlet obstruction (4.5%), esophageal cancer (2.6%) and gastro esophageal reflux disease (GERD) (1.5%). Generally, these findings are consistent with the concept that dyspepsia is a marker for various upper gastrointestinal pathologies that can only be differentiated by upper gastrointestinal endoscopy among other sophisticated and expensive tests (5).

## **2. UPPER GI MALIGNANCY**

The presence of alarm symptoms not only in upper GI malignancy but also in benign conditions, such as peptic ulcer and H. pylori infection, has led to controversy over the diagnostic value of these symptoms. Especially, the fact that young UGSM patients also present with dyspepsia rather than alarm symptoms further complicates this issue. These controversies have led to many studies determining the diagnostic value of alarm symptoms (64).

#### **A. GLOBAL**

In Thailand, Cross-sectional study was conducted a total of 4664 patients (mean age: 52.0±14.4 years, 66% female) were included. Alarm symptoms were presented in 21.6%. The prevalence of active Helicobacter pylori infection was 26.3%. Fifty-eight (1.2%) patients had UGI malignancy (65). Which was similar to that reported from a study conducted in Taiwan (66), but much lower than those reported from studies conducted in China and Iran (58,67,68). The differences between and among studies may be due to differences in the background prevalence of H. pylori infection in the studied populations (69). There was also found a positive association between cancer frequency and increasing age, which was similarly found in a Chinese and a Singaporean study (18).

Patients with alarm features had a higher prevalence of malignancy (OR 22.3, 95% CI 10.5 to 47.4;  $p < 0.001$ ) than those without. The pooled sensitivity, specificity, positive predictive value and negative predictive value of alarm features for UGI malignancy were 87.0%, 79.1%, 4.7%

and 99.8%, respectively. Among all age groups, persistent vomiting had a positive likelihood ratio (PLR) >10, while dysphagia and GI bleeding/anemia had a PLR >10 in patients <50 years old (36). which was consistent with those from a systematic review and meta-analysis of more than 4000 dyspeptic patients with a low reported prevalence of UGI malignancy (0.8%) that showed low pooled sensitivity and specificity of individual alarm features of 67% (95% CI 54% to 83%) and 66% (95% CI 55% to 79%), respectively (34).

In Turkey, Prospective study, evaluated 260 cases (between July 2021 and January 2022). Of these cases, 53.80% (n = 140) had at least 1 alarm symptom, while 46.10% (n = 120) had no alarm symptoms. Anemia was the most common alarm symptom, corresponding to 27.69% (n = 72) of the cases. Those with alarm symptoms had a higher incidence of malignancy (P < .001). The incidence of malignancy was significantly higher in patients aged  $\geq 45$  years and in patients with anemia, dysphagia, weight loss, melena, family history of gastric cancer, positive abdominal mass, and lymphadenopathy (P < .05). The malignancy rate was significantly higher in patients with 3 or more alarm symptoms (P < .05). Anemia and weight loss were found to be predictive factors for gastric cancer (70).which was similar to other study (33).Contrary to these, a study conducted in Nigeria found no correlation between alarm symptoms and endoscopy findings in patients with dyspepsia.

Another Similar prospective observational study from Indian, Dyspepsia was functional in 311(34.6%) patients. EGD revealed benign lesions in 340 (37.8%) and malignancy in 50 (5.5%) patients. Among the malignant lesions, gastric malignancy was present in 28 (56%) and esophageal malignancy in 20 (40%) patients. Alarm features were present in 206 (22.9%), out of which malignant lesions were seen in 46 (22.3%) patients. Altogether, the alarm features had a sensitivity of 92% and specificity of 81.2% for predicting malignancy. The sensitivity and specificity for weight loss were 76% and 90.8%, while that of abdominal mass were 10% and 99.9% respectively. Based on receiver operating characteristic curve, the optimal age for screening of malignancy was 46.5 years in this population (37).

## **B. REGIONAL**

In Rwanda, Retrospective review of histologically-confirmed esophageal and gastric cancers in adults age  $\geq 18$  yrs (between June 2014 and June 2019). There were 149 upper gastrointestinal cancers, of which 137 (92%) were gastric and 12 (8%) were esophageal. Gastric cancer patients had a mean age at presentation of  $56.9 \pm 12.3$  years (range 21 - 87) (71).Which was higher than

what has been reported in earlier studies conducted in Nigeria and Sudan for esophageal cancer at 10.7% and 5.9% respectively and while gastric cancer 3.5% to 6.6% (54,56,51).

Presenting symptoms were epigastric pain (78.8%), weight loss (53.3%), post-prandial vomiting (52.6%), early satiety (29.9%), epigastric mass (24.8%), hematemesis (19.7%) and melena (16.8%). The location was antrum 50.3%, corpus 21.8%, fundus 8%, and cardia 8%. Tumor type was adenocarcinoma in 94.1%. *Helicobacter pylori* infection was present in 108 (78.8%). Esophageal cancer patients had a mean age of  $54.4 \pm 9.5$  years (range 35 - 72). Presenting symptoms were dysphagia (100%) and weight loss (83%). The most common site was lower third esophagus (9/12), and adenocarcinoma cancer subtype accounted for 5/12 (41.6%) cases (71).

### C. NATIONAL

In Ethiopia, At St Paul hospital millennium medical college GI clinic a retrospective cross-sectional was conducted (from September 1, 2015, to August 31, 2017), off 3542 patients seen at GI clinic, dyspepsia was diagnosed in 418 i.e. in 21.6% of cases. The endoscopic diagnosis showed a high prevalence of gastric cancer of 8.8%. Functional dyspepsia was diagnosed in 15.5% and a high prevalence of non-specific Gastro-duodenitis were reported, especially in younger cases with no associated alarm symptoms. Anemia and weight loss were independent predictors for organic causes (61).

In Ethiopia, At St Paul hospital millennium medical college GI clinic a retrospective cross-sectional was conducted (between January 2012 and December 2019), with regard to upper gastrointestinal malignancies, esophageal tumor was slightly predominant than gastric tumor (4.4% vs 4.1%) (20), similar to a study in Gondar, Ethiopia, with comparable prevalence (4.3% vs 3.6%)(6). A higher proportion of gastric tumor (5%) than of esophageal tumor (5% vs 1.3%) was found in an Indian study (37). A study in Ghana reported a lower prevalence of gastric tumor (2.1%)(51). These differences observed with studies from other countries could be from population's difference in lifestyle, dietary factors and genetics. Consistent with a local study in Gondar, Ethiopians living in different parts of the country have comparable findings (6).

In Ethiopia an institution-based cross-sectional study conducted (from July to September 2022), 142 patients were selected, with an average age of 48.35 and 52.1% being male. The presence of the alarm feature was associated with an increase of 6.801 in the odds of developing SEF and an increase of 4.199 in the odds of developing malignancy (72). Of those, 70% had confirmed

cancer of either the stomach or the oesophagus, giving our study subjects an 18.31% prevalence of cancer, which is the same as a study from India (37). This shows a higher prevalence of malignancy compared to the study done at the University of Udayana /SanglahHospital, Denpasar, which shows 5.13 percent prevalence (73). An association was confirmed between the presence of alarm features and malignancy of the UGI tract.

#### **D. LOCAL**

In Ayder, a facility-based retrospective cohort study was conducted, 1,994 endoscopic examinations were included in the study, and 58.7% of esophagogastroduodenoscopies' (EGD) were performed on male patients. The common EGD findings were erythema of gastric mucosa in 489 (24.5%), varices in 253 (12.7%), gastric cancer in 188(9.4%), peptic ulcer disease in 176 (8.8%) and gastroesophageal reflux disease in 96 (4.8%) (5). these finding were lower compared to previous studies in Ethiopia, which reported a prevalence of 7.9 % (20).

### 3. OBJECTIVES OF THE STUDY

#### 3.1 General objective:

- ✓ To investigate the clinical indications of upper GI endoscopy and their predicting value of upper GI malignancies, at GI clinic, in Ayder comprehensive specialized hospital, Mekelle, northern Ethiopia from Jan 2019 to Jun 2024.

#### 3.2 Specific objectives:

- I. To assess socio-demographic profile of patients who underwent UGIE.
- II. To investigate the common clinical indications and its upper GI endoscopy findings
- III. To determine the magnitude of upper GI cancer.
- IV. To identify which indications can strongly suggest upper GI malignancies.
- V. Verifying the correlation of endoscopic findings with the histological findings

## **4. METHODOLOGY**

### **4.1 STUDY AREA**

Ayder Comprehensive Specialized Hospital (ACSH) in Mekelle University, College of Health Sciences (MU-CHS), locates in Mekelle capital of Tigray region, which is around 778 km from capital city, Addis-Ababa. ACSH was established in 2008 as a public hospital and gives service to about 10 million populations within the catchment areas of Tigray, north afar, and northeastern parts of Amhara region. ACSH has 500 inpatient beds, additional outpatient and emergency units, and specialty and subspecialty services.

The Department of Internal Medicine has 116 inpatient beds (ICU and ward) and outpatient services within its different subspecialty units equipped for bronchoscope, spirometry, upper and lower gastrointestinal endoscopy, electroencephalography, echocardiography (ECG), Holter blood pressure, and ECG monitors, resting and stress ECG machines, and a cardiac catheterization laboratory. ACSH is the only hospital in the region where gastrointestinal endoscopy service is provided. ACSH is involved in teaching both undergraduate medical and allied health professionals and postgraduate students.

One of the units in this department is Gastrointestinal unit was established in 2011 and the hospital began to offer endoscopy services in the same year. It has provided endoscopic services for patients with gastrointestinal disorders. The unit currently runs by only one gastroenterologist, trained internists and unit nurses, and other supportive staff. The upper gastrointestinal endoscopy sessions were done three days per week, and on average, four to six patients attended each of endoscopic days. In addition it gives service any time with emergency conditions. It provides multiple consultation services from different units in the department, including ICUs and interdepartmental consultation, mainly from surgery and the obstetrics and gynecology department.

### **4.2 STUDY PERIOD**

- ✓ This study was conducted from Dec 2023 to Sep 2024.

### **4.3. STUDY DESIGN**

A facility based descriptive cross sectional study.

#### 4.4 SOURCE POPULATION

All adult patients who were underwent upper GI endoscopy evaluation at GI unit in Ayder Comprehensive Specialized Hospital.

#### 4.5 STUDY POPULATION

All adult patients were complaining of upper GI symptoms that underwent diagnostic upper GI endoscopy evaluation at gastrointestinal unit during the stated period of from Jan 2019 to Jun 2024 in Ayder Comprehensive Specialized Hospital.

#### 4.6 ELIGIBILITY CRITERIA

##### 4.6.1 Inclusion criteria

- Patient profile that documented in endoscopy registry book
  - ✓ Adults 18 years or older patients who underwent upper endoscopic evaluation at GI unit during the study period .
  - ✓ Referral reports with the diagnosis or reason for referral registered as upper GI complaints by the referring doctor.

##### 4.6.2 Exclusion criteria

- ✓ Reason for referral was reported that did not meet the inclusion criteria.
- ✓ Incomplete upper gastrointestinal endoscopic reports and duplicate records.

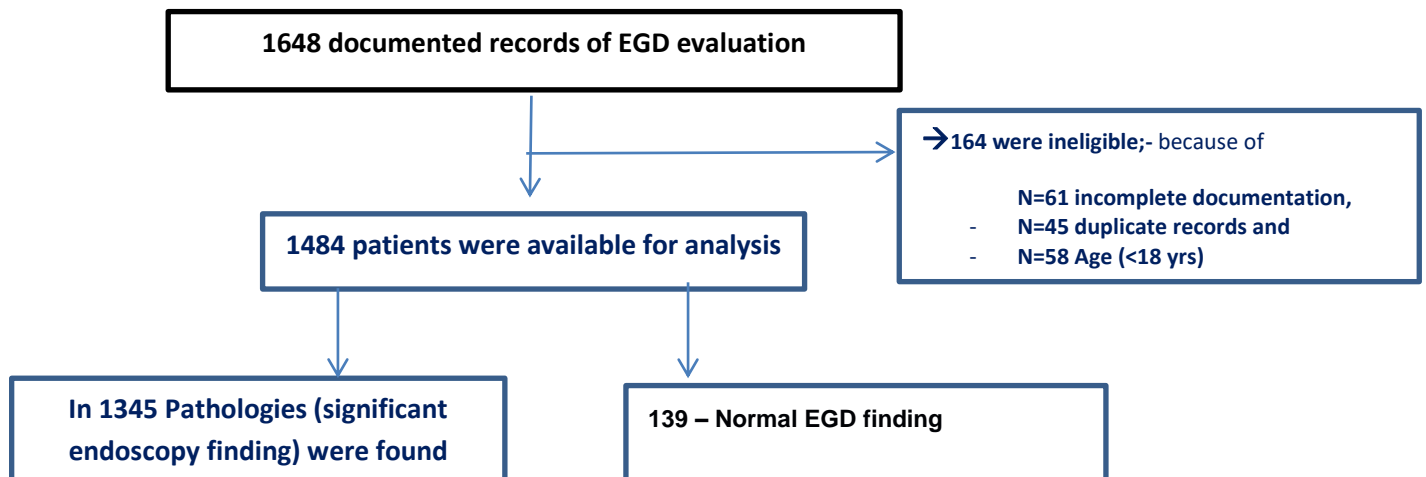


Figure 2 ; -Systematic review flow diagram

## **4.7 SAMPLE SIZE DETERMINATION**

- All adult patients who underwent diagnostic upper GI endoscopy evaluation were included in the study from Jan 2019 to Jun 2024.

## **4.8 STUDY VARIABLES**

### **4.8.1 Dependent variable (outcome)**

- a. Significant endoscopy findings: upper GI malignancies

### **4.8.2 Independent variables**

- a. Socio-demographic characteristics (Age, Sex)
- b. Clinical indications:- dyspepsia, epigastric pain , screening for CLD or EVL follow up dysphagia, upper gastrointestinal bleeding, progressive unintentional weight loss, persistent vomiting or of unknown cause, anemia , abdominal or epigastric mass and others ( trauma ,laceration, dysphonia and foreign body)

## **4.9 DATA COLLECTION PROCEDURE**

The structured checklist was developed from different literature and standard text books. Data on the age and sex of the patients, indications for upper gastrointestinal endoscopy (UGIE) and endoscopic findings were retrieved from electronic database of endoscopy registry and/or from endoscopy report format available at the endoscopy/ GI unit. For those patients who had biopsy & pathologic report; information was extracted from patient chart using MRN or ID card and from the endoscopy evaluation report format or from pathology department registry.

Focused training was given to data collectors for one day to make them familiar with objectives and aims of the study; and how to extract relevant information from the database or patient chart or pathology report registry using systematic tool that entered on the prepared information sheet. A questionnaire completed for each patient.

## **4.10 DATA ANALYSIS**

The data were checked and cleaned by principal investigator on daily bases during data collection for completeness, consistencies, then coded, entered and analyzed using SPSS version 27. Descriptive analysis was used to describe the percentages and number distributions of the variables in the study and the Chi-square test was used for categorical data. The diagnostic values of individual alarm feature, including sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), were calculated. Based on this, area under the

receiver operating characteristic (ROC) curve was used to find out an optimal age for screening of malignancy. In addition, bivariate and multivariate analyses were done in the binary logistic regression to estimate both the crude and adjusted odds ratios. Finally, statistical significance was declared at P-value  $\leq 0.05$ . The result was presented using tables, graphs and texts as based on type of data.

#### 4.11 DATA QUALITY ASSURANCE

To assure the quality of data, the data collection tool was pre-tested on ten selected patient with two different data collector and clarity of the language will also be checked before actual study. Every day the collected data was checked for its completeness and consistency by principal investigator.

#### 4.12 ETHICAL CONSIDERATION

Ethical clearance was obtained from the institutional review board (IRB) of college of health sciences of Mekelle University. An official letter was obtained from department of internal medicine and was submitted to responsible body at endoscopy unit. Information obtained from the records is kept confidential and in closed cabinet in the internal medicine department till publication of the study.

#### 4.13 OPERATIONAL DEFINITION

**Dyspepsia** -is a chronic or recurrent pain or discomfort centered in the upper abdomen, characterized as recurrent upper abdominal discomfort, abdominal fullness and bloating, early satiety, nausea and vomiting, loss of appetite.

**Endoscopic indication:** patient's reason for diagnostic upper GI endoscopy including dyspepsia, epigastric pain, dysphagia, gastrointestinal bleeding, and progressive unintentional weight loss, persistent vomiting or of unknown cause, anaemia or epigastric mass and to rule out malignancies.

**Upper gastrointestinal endoscopy-** A thin, flexible fibro optic tool that allows seeing inside lining of esophagus, stomach, and the first part of small intestine (duodenum), used for diagnostic and therapeutic.

**Alarm symptoms:** - Symptoms, which may have Positive predictive value for an upper gastrointestinal tract malignancy or PUD and include Unintentional weight loss, Progressive dysphagia, Odynophagia, Unexplained iron deficiency anemia, Persistent vomiting, upper GI bleeding, abdominal mass or lymphadenopathy and family history of malignancies.

**Significant endoscopic findings-** as the presence of any of the following findings duodenal ulcer, gastric ulcer, esophagitis, esophageal varices ,esophageal stricture, esophageal ca, gastric ca, duodenal ca gastroesophageal junction ca, mallory weiss tear, GERD ,GOO, achalasia, hiatal hernia and candidiasis, or other findings that required specific therapy and were judged to have contributed to patient's symptoms.

#### **4.14 PLAN FOR DESEMINATION OF RESULTS**

Findings of the study were presented and submitted to the department of internal medicine. The copy of the finding were kept in Ayder comprehensive specialized referral hospital research center and library, this is help as a source of reference for further research. We will also send for national and international journals for publication.

## 5. RESULT

### 5.1 SOCIO –DEMOGRAPHIC CHARACTERISTICS

A total of 1,648 documented records of upper gastrointestinal endoscopic evaluations performed between January 01, 2019 and June 30, 2024 were reviewed. From the total endoscopy evaluation, 164 were excluded due to different reasons such as incomplete documentation (n = 61), duplicate records (n = 45) and age (<18 yrs) (n=58).

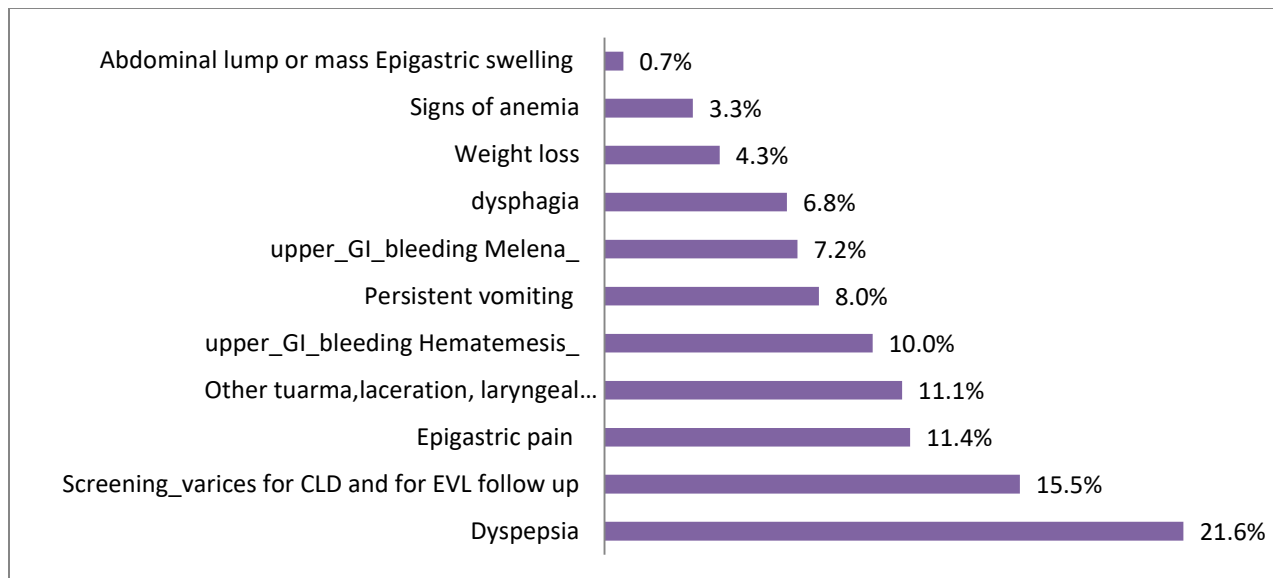
Data from 1,484 patient records were analyzed, yielding a completeness rate of 90.0%. Of the 1484 patients, 1044 (70.4%) were male and 440 (29.6%) were female. The median age was 38 years, with the youngest and oldest patients aged 18 and 90 years, respectively. Most patients were in the age ranges of 25-44 accounting for 44.7 %. Three fourth of the population were in the age groups of <=60 years (Table1).

Table 1:- Age and sex distribution of Patients who underwent upper EGD at ACSR hospital, Tigray, Ethiopia, 2019 to 2024 (N = 1484)

Variables		Sex		Total
		Male, n(%)	Female, n(%)	
25-44Age category	<=24	181 (17.3%)	73 (16.6%)	254 (17.1%)
	25-44	467(44.7%)	156(35.5%)	623(42.0%)
	45-59	217(20.8%)	126(28.6%)	343(23.1%)
	>=60	179(17.1%)	85(19.3%)	264(17.8%)
<b>Total</b>		1044(70.4%)	440(29.6%)	1484(100%)

#### 1. INDICATIONS FOR UPPER GASTROINTESTINAL ENDOSCOPY AND FINDINGS

Dyspepsia, which accounted for 21.6% (n = 468) cases, was the most common indication for undergoing upper gastrointestinal endoscopy, followed by Screening for varices in patients with chronic liver disease (CLD) 15.5% (n = 336) and Epigastric pain or regurgitation 11.4% (n = 248)cases. Less common indications which accounted less than 10 % included persistent vomiting, dysphagia, weight loss, upper GI bleeding (melena), abdominal lump or mass, sign of anemia and weight loss. Figure 3



→Some of the patients had more than one sign and/or symptom as indications for the EGD.

Figure 3;-Indications for upper gastrointestinal endoscopy at ACSR hospital, Tigray, Ethiopia, 2019 to 2024 (N = 1484).

Upper gastrointestinal endoscopic examinations were normal in 9.4% (n = 139) patients, while pathologies were found in 90.6% (n = 1345), with 70.6% (n = 949) being male. Of those, the commonest EGD finding was esophagitis 30.8% (n=792), followed by pan gastropathy 14.4% (n=371).

In patients with dyspepsia, the predominant pathologies identified were esophagitis 48.5 % followed by pan gastropathy 38.2%. Thirteen percent of dyspeptic patients had normal upper gastrointestinal endoscopy.

Among patients Screening for varices, 76 % (n = 252) had esophageal varices, followed by portal hypertensive gastropathy 7.8% (n = 26), esophagitis 5.8% (n = 19), duodenal ulcers 3.57% (n = 12) and gastritis 2.5 % (n = 9). Normal findings were reported in 3.9% (n = 13) of the patients. Table 2

Table 2: Common EGD finding at ACSR hospital, Tigray , Ethiopia, 2019 to 2024 (N = 1484).

EGD finding Frequencies		
EGD finding	Responses	
	N	Percent
Normal EGD Finding	139	4.7%
Significant endoscopy finding	1345	95.3%
Types of significant endoscopy finding (n=1,345)		

Peptic ulcer disease (n=262)		
Duodenal ulcer	229	8.9%
Gastric ulcer	33	1.2%
Inflammatory conditions (n=1166)		
Esophagitis	792	30.8%
Gastritis	233	9.1%
Duodenitis	141	5.5%
EGD suggestive Malignancy finding (n=166)		
Esophageal cancer	39	1.5%
Gastric cancer	107	4.2%
Gastro esophageal Junction cancer	9	0.3%
Duodenal cancer	9	0.3%
Gastro duodenal junction cancer	2	0.1%
OTHERS (n=976)		
Esophageal varices	331	12.8%
Esophageal stricture	28	1.1%
Achalasia	14	0.5%
Pan gastropathy	371	14.4%
GOO	56	2.1%
Hiatal hernia	145	5.6%
polyps	4	0.2%
External compression	1	0.0%
Foreign body	4	0.2%
Others specific	22	0.85%
Total	2570	100.0%

Some of the patients had more than one finding detected during the EGD procedure

The most common lesions identified in individuals with dysphagia (n = 348) were esophagitis 35.5 % followed by pan gastropathy 25 % , esophageal tumors 16.2 % ,tumors achalasia 5.4 % and esophageal stricture 4.05% ,while no pathology was identified in 14.2% of them.

Fourty-one percent (n=609) of the patients with upper GI symptoms had at least one alarming symptoms. As shown in the figure below, upper GI bleeding and persistent vomiting were the two most prevalent alarming symptoms most patients presented. Figure 1

Biopsies were obtained for 166 (12.3%) patients with a presumed endoscopic diagnosis to rule out malignancy or inflammatory or infectious conditions. Out of those, 118 (8.8%) were confirmed to have upper GI malignancy of the stomach, esophagus, duodenum and GEJ. Figure-4

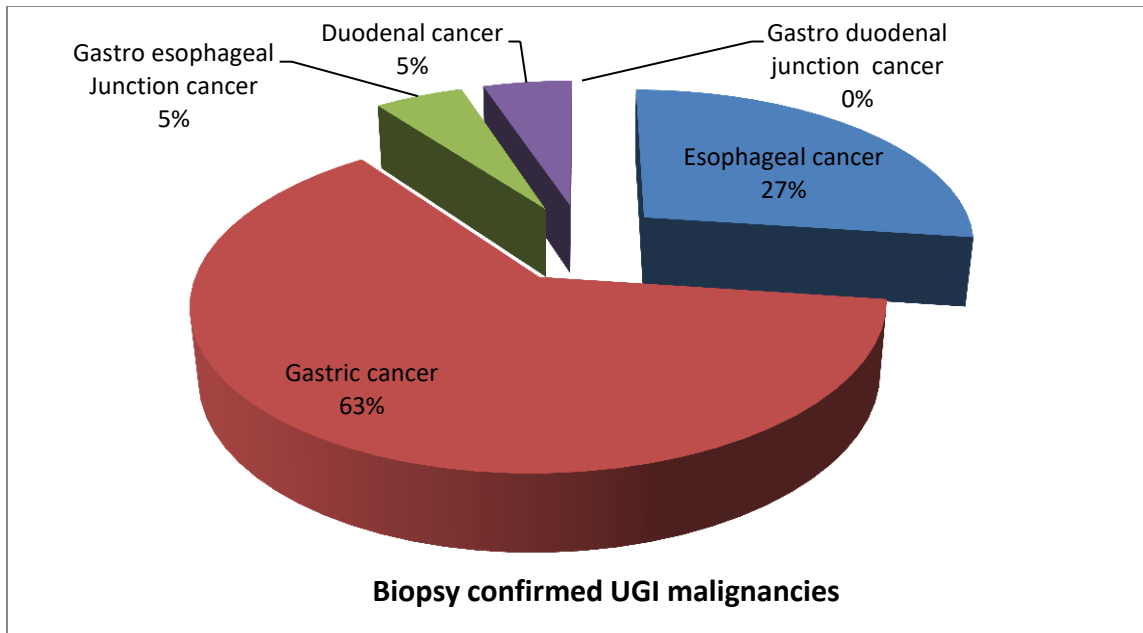


Figure 4:-Distribution of biopsy confirmed upper GI malignancies at ACSR hospital, Tigray, Ethiopia, 2019 to 2024 (N = 1484).

Of the 118 patients with cancer, 74(62.7%) were diagnosed with gastric cancer, 32 (27.1%) with esophageal cancer, 6(5.08 %) with duodenal cancer, and 6 (5.08%) gastro esophageal junction cancer. The majority of gastric cancers were adenocarcinomas (77 %), and esophageal cancers were consisted of 38.7% adenocarcinomas and 61.3% squamous cell types. Figure 5

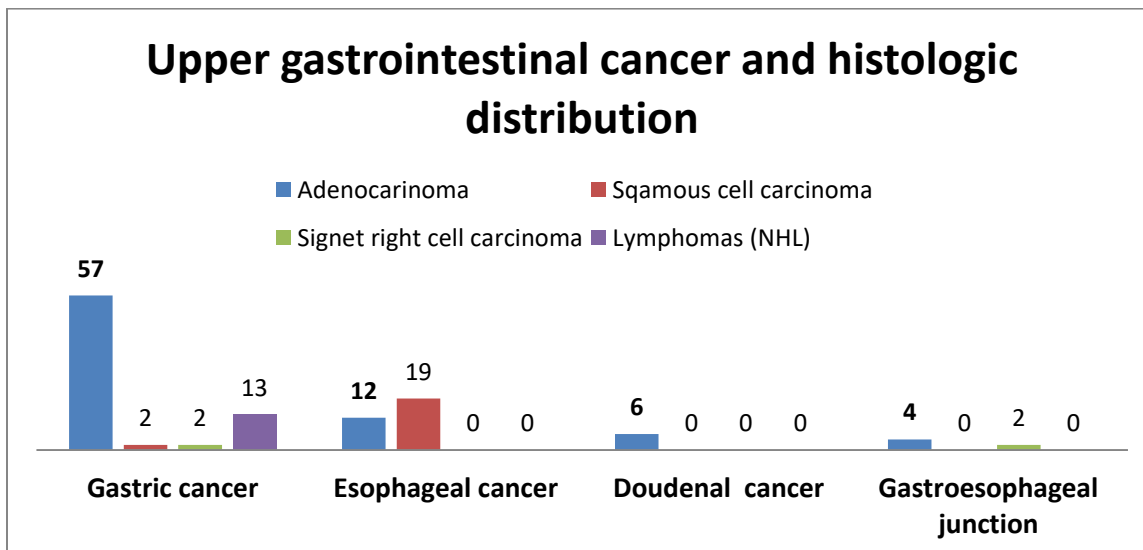


Figure 5:- Histopathology distribution of upper gastrointestinal malignancies at ACSR hospital, Tigray, Ethiopia, 2019 to 2024 (N = 1484).

Patients reporting at least one of the alarm symptoms constituted 77.1 % of patients with UGI malignancies compared to 38.1 % in patients without cancer ( normal ) (p < 0.001).

The majority 91(77.1%) of them had one or more alarm features. The patients with esophageal cancers and gastric cancers had the highest prevalence rate of at least one alarm feature (87.5% and 73.9%), and the most prevalent alarm feature in patients with esophageal cancers and gastric cancers were dysphagia (75%) and repeated vomiting (46%) respectively. Patients with alarm features had a higher prevalence of UGI malignancy (OR 5.5, 95% CI 3.540 -8.616; p<0.001).

### A. Cancer type by age distribution

In our study stomach, esophagus, duodenum and GEJ cancers, were more common in age group more than >= 60 yrs while ALL cancers was less common in < =24 years of age. (Table 3)

The prevalence of UGI malignancy significantly increased from 41.1 % in patients aged 45–49 years to 96.1% in patients aged ≥60 years (p<0.001), and 28 patients with UGI malignancy were younger than 45 years. Table-3

### B. Cancer type by sex distribution

In our finding, Gastric ca (62.7%, n= 74) was the most frequent type, was common among male patients. Female were commonly presented with duodenal ca (66.7%, n=4).

Table 3:- Age and Sex Distribution of Patients with Upper gastrointestinal malignancy at ACSR hospital, Tigray, Ethiopia, 2019 to 2024 (N = 1484)

Age ,Sex * Malignancy						
		Gastric cancer N (%)	Esophageal cancer N (%)	Duodena l cacancer N (%)	Gastroesophag eal junction cancer N (%)	Total N (%)
Age categ ory	<=24	1(1.35%)	0(0%)	0(0%)	0(0%)	1(1.35%)
	25-44	18(24.7 %)	5(16.1%)	1(16.7%)	2(33.3%)	26(22%)
	45-59	26(35.6 %)	13(38.7%)	3(50%)	1(16.7%)	43(36.4%)
	>=60	29(38.6 %)	14(45.5%)	2(33.3%)	3(50%)	48(40.6%)
Sex	Male	40(54.1%)	13(40.6 %)	2(33.3%)	5(83.3%)	61(51.7%)
	Female	34(45.9%)	19(59.3 %)	4(66.7%)	1(16.7%)	57(48.3%)
Total		74	32	6	6	118

## 2. Upper GI endoscopy clinical indications associated with UGI malignancy

Logistic regression was performed to determine how the presence of individual indications and alarming features affects a patient's probability of developing GI malignancy. In bivariate logistic regression analysis, the presence of UGI malignancy on upper endoscopy was significantly associated with age ( $p < 0.001$ ), female sex ( $p < 0.001$ ), dysphagia ( $p < 0.001$ ), unexplained weight loss ( $p < 0.001$ ), persistent vomiting ( $p < 0.001$ ), GI bleeding/anemia ( $p < 0.001$ ), abdominal mass and suspected any cancer ( $p < 0.03$ ) and epigastria pain ( $p < 0.001$ ). In multivariate analysis age together with epigastria pain, having any alarm symptoms and individual alarm symptoms were analyzed.

In multivariate analysis, age, female sex, having any alarm symptoms, specific three-alarm features remained independent predictors of UGI malignancy: As shown in table 4

Table 4. Regression analysis; factors associated with upper GI malignancy at ACSR hospital, Tigray, Ethiopia, 2019 to 2024 (N = 1484).

Variables		Upper GI Cancer		Curde (OR)	P-VALUE	AOR	P-VALUE
		Yes, n(%)	No, n(%)				
SEX	Male	61(51.7%)	888(72.3%)	reference			
	Female	57(48.3%)	341(27.7%)	2.356 (1.6-3.4)	<0.001	1.962(1.307-2.946)	0.001
AGE	≤24	1(0.8%)	210(17.1%)	Reference		Ref.	
	25-44	27(22.9%)	546(44.5%)	10.4 (1.4-76.9)	0.022	10.313(1.4-76.7)	0.023
	45-59	42(35.6%)	273(22.2%)	32.4 (4.4-236.7)	0.001	27.676(3.76-203.8)	0.001
	≥60	48(40.7%)	198(16.1%)	50.909(6.96-372.34)	<0.001	37.257(5.1-274.3)	<0.001
Alarm symptoms	yes	91(77.1%)	465(37.9%)	5.523( 3.54 - 8.62)	<0.001	4.250(2.69-6.72)	<0.001
	No	27(22.9%)	762(62.1%)	Reference			
Dysphagia	Yes	33(27.9%)	94(7.6%)	4.679(2.97-7.36)	0.001	0.27(0.16-0.45)	<0.001
	No	85(72%)	1133(92.3%)	Reference			
Persistent vomiting	Yes	40(33.9%)	127(10.4%)	5.85(3.56-9.56)	0.001	0.33(0.16-0.45)	<0.001
	No	78(66.1%)	1100(89.6%)	Reference			
Weight loss	Yes	28(23.7%)	62(5.1%)	0.23(0.15-0.34)	0.001	2.41(1.35-4.32)	0.003
	No	90(76.2%)	1165(94.9%)	Reference			

### 3. Diagnostic performance of individual alarm features of UGI cancer.

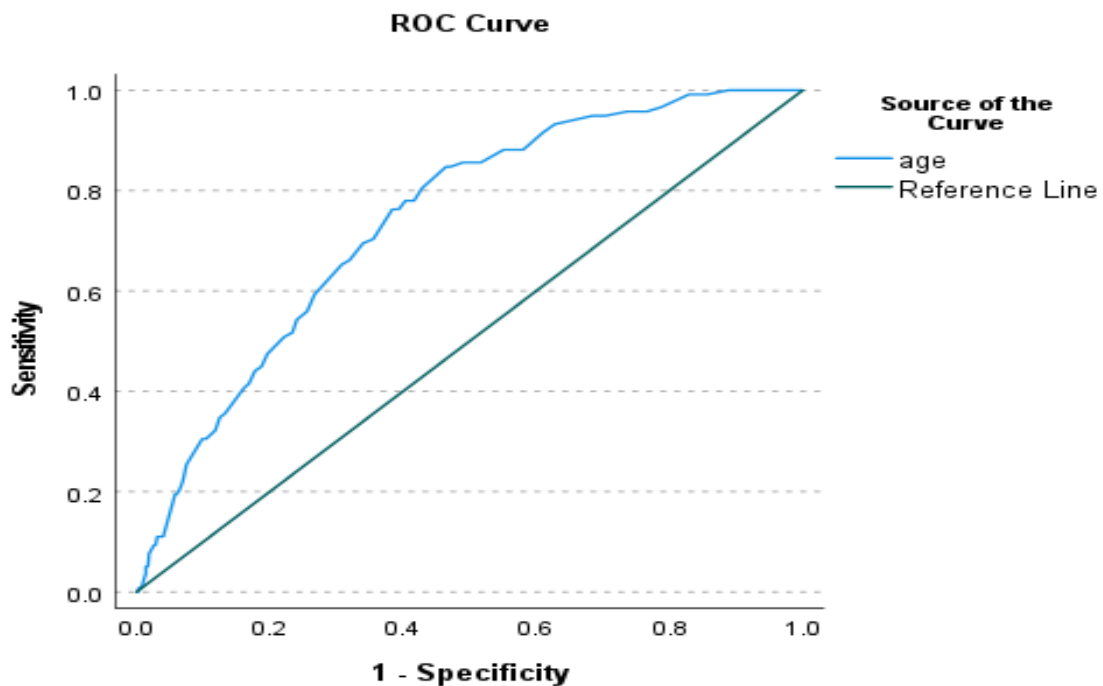
Among 609 (41%) patients with alarm features, 91 (77.1%) were found to have UGI cancer. Using histology as the gold standard for diagnosis of UGI malignancies. The sensitivity, specificity, PPV and NPV of having any alarm features for predicting malignancy were 77.1%, 62.1%, 16.4% and 96.6%, respectively (table 5). Among the three-alarm features, persistent vomiting had the highest sensitivity (33.9%) and the lowest PPV (24%), whereas unexplained weight loss had the lowest sensitivity (23.7%) and a high PPV (31.1%). All of the three- alarm features had high specificity (range: 89.6% to 95%) and highest NPV (range: 92.8%–93.4%).

All three-alarm features had PPVs for predicting malignancy ranging from 24% to 31.1% and remained high NPVs of >93.4%. These data suggested that most alarm symptoms had poor predictive value for UGI cancer.

Table 5:- Clinical indications: Sensitivity, Specificity, PPV and NPV for upper GI malignancy at ACSR hospital, Tigray, Ethiopia, 2019 to 2024 (N = 1484).

Se r.	Tested	Sensitiv y	Specific ity	Positive predictive value	Negative predictive value
1	Dyspepsia	34.7%	68.4%	9.5%	91.5%
2	Epigastric pain	33.9%	84.5%	17.4%	93%
3	Difficulty of swallowing	27.9%	92.3%	26%	93%
4	Persistent vomiting	33.9%	89.6%	24%	93.4%
5	Upper GI bleeding (Hematemesis)	5.9%	83.7%	3.38%	90.2%
6	Upper GI bleeding (Melena )	3.4%	88.3%	2.72%	90.4%
7	Weight loss	23.7%	95%	31.1%	92.8%
8	Anemia	10.2%	96.9%	19.8%	91.7%
9	Abdominal mass/swelling	2.5%	99.4%	30%	91.3%
10	Screening for varices /EVL follow up	0%	73.6%	0%	88.5%
11	Others ( trauma, foreign body, GERD ,GOO)	11%	84.3%	12.3%	90.8%
12	Any Alarm indication	77.1%	62.1%	16.4%	96.6%

**Based on the ROC curve:** - Age and malignancy was determined to be 0.73, 95% CI (0.69 – 0.78), indicating moderate malignancy predictive accuracy for age. The optimal age for screening of malignancy was 39.5 years in this population.



**Figure 6;-Receiver operating characteristic curve for age and malignancy**

## 6. DISCUSSION

This study aimed to document the demographic characteristics, indications and their association with endoscopic findings particularly with upper GI malignancies of patients who underwent UGIE at ACSR hospital in Ethiopia. In resource limited settings, especially when access to endoscopy service is limited, it is very important for clinicians to know common indications of upper EGD.

This study retrospectively investigated the endoscopy results accordingly; we found dyspepsia was common EGD indication. Prevalence of SEFs and upper GI malignancy was 90.6% and 7.9 % respectively. This study also confirms the role of certain alarm symptoms and age  $\geq 45$  in predicting the presence of SEFs, particularly malignancies

In our study, we found the most common primary indication for UGIE was dyspepsia (21.6%) which was lower than similar local studies conducted in Tikur Anbessa teaching hospital, in Addis Ababa, and at University of Gondar, northwestern Ethiopia, in which it accounted for 59.4% and 53.8%, respectively (58,6) and in Nigeria also (80.5%) (46).

On the contrary, higher than previous local studies conducted in ACSR hospital, in which it accounted for (13.2%) (5). Generally, our findings are consistent with the concept that dyspepsia is a common indication, and marker for various upper gastrointestinal pathologies that can only be differentiated by upper gastrointestinal endoscopy among other sophisticated and expensive tests (45).

Screening of CLD patients for varices and for therapeutic EVL (15.5 %) was the next common indication of UGI endoscopy in this study. which was much higher than similar Ethiopian studies from Addis Ababa (14.8 %) and Mekelle (10%) (20, 5). These report can due to the combination of two screening and therapeutic EVL used as single indication of UGIE in this study.

Alarm symptoms (unexplained weight loss, persistent vomiting, anemia, dysphagia, upper GI bleeding, and abdominal mass) are generally accepted as an indication for direct endoscopy. This is reflected in several guidelines for treatment of patients with upper GI symptoms and in the exclusion criteria for patient selection of most trials (46-49).

The predictive value of alarm features in detecting major endoscopic findings is controversial (30). In our study, patients presenting with having any alarm symptoms was 41%, and the prevalence of alarm symptoms was significantly higher among patients in the abnormal endoscopic group (91.3%) and upper GI malignancy group (77.1%) than in the normal endoscopic group (8.7%), (P; 0.001). This finding was compatible with the outcome of the study conducted in Ghana (74). These findings are important because it demonstrates that the relative importance of alarm features can differ between Ayder hospital and other settings. The high prevalence of alarm features in our study may be attributed to late presentation and poor health seeking behavior. This may be due to a lack of affordable health care in the country particularly in the Tigray region, with many patients resorting to the use of traditional or herbal mixtures, and over-the-counter drugs (OTC) for their health complaints. Thus, many patients may delay seeking medical care until complications occur, and these may manifest as any of the alarm features.

In the present study we found that there was a high prevalence of significant endoscopic findings (90.6%), based on the fact that 8.7% of patients exhibited normal endoscopic results. Similar reports have been made from Gondar (83.4%), AAU (73.9%) and Uganda (73.4%) with significant endoscopic findings (6, 20, 75). In contrast, a study from the United Kingdom where the endoscopy was normal in (73%). This difference may be because the investigators included the findings of gastritis and duodenitis as normal (76). In addition to this is different a study from the Pakistan, where 48% of endoscopies were found to be normal. Reason for carrying out an endoscopy can be to offer patient satisfaction and comfort, even with vague symptoms or without specific relevant indications as per guidelines for having an endoscopy may have had an impact on that study's findings (77).

The commonest endoscopic finding of this study (30.8%) was Esophagitis, occurred at a higher rate in our study compared to western and other African countries. It affected almost twice males (68.5%) than females (31.5%). the higher frequency in males however could not be explained by the current study and requires further investigations. Several possible explanations for high frequency of esophagitis in our study, such as infection and GERD can be attributed due to changes in lifestyle and/or a high fat diet with lack of exercise, leading to obesity, misuse analgesics and psychological distress. This may be also due to the high prevalence of inadequate PPI use before of endoscopy (6,48).

Pan-gastropathy (14.4%) was also next common serious endoscopic abnormality in our patients. The frequency of pan-gastropathy may be related to the high prevalence of *Helicobacter pylori* in the nation, which was estimated to be 52.2% (79).

With regard to upper gastrointestinal malignancies, the prevalence of upper GI malignancy recorded in overall endoscopy cases was 11.2% and biopsies been done to rule out cancer, inflammatory, or infectious conditions. Of those, 71.1 % had confirmed cancer of the stomach, the esophagus and the duodenum. It was statistically significant giving our study subjects a 7.9% prevalence of cancer, (P; 0.001). Which was the same to previous studies in Ethiopia, which reported a prevalence upper GI malignancy of 7.9 % (6). But these were higher than that recorded in some previous studies in Thailand (1.2%) and Chinese (1.5%), (65, 38). These differences observed with studies from other countries could be from population's difference in lifestyle, socioeconomic status, dietary factors and genetics.

In this study, Gastric cancer was slightly predominant than esophageal and duodenal cancer (4.9 % vs 2.5%, 0.4 %), similar to a study in an Indian, with comparable prevalence higher proportion of gastric tumor (5%) than of esophageal tumor (5% vs 1.3%). but in contrast to our study the higher proportion of esophageal tumor than of gastric tumor (4.3% vs 3.6%) was found in Gonder, Ethiopia and Zambia (5% vs 3%) (6,74) and lower prevalence of gastric tumor (2.1%) in Ghana (51). Our findings are consistent with the concept Africa had the highest rate of *H. pylori* infection with a prevalence of 70.1% as major risk factor of gastric cancer (78,79,80). Moreover Infection with *H. pylori* causes chronic inflammation and significantly increases the risk of developing duodenal and gastric ulcer disease, and gastric cancer (81).

The most common stomach histopathology in our study was adenocarcinoma accounting for 77.2%. Adenocarcinoma was the most common malignancy in other studies as well 91% (71). The most common malignancy found from esophagus biopsy was squamous cell carcinoma (SCC) accounting for 61%. Similar findings, most common were noted in previous local studies from Ayder 41.7% (5).

This study has found that most common upper GI pathologies affected men (70.6%) compared to females, which is consistent with studies from Gondar, Ethiopia, Lagos, Nigeria, Jammu, Gadag, and Gizan ( 6,82,83,84).

In our study, alarm features were associated with significant endoscopic findings (91.3%) and UGI malignancies (77.1%).(p=0.001) The same is true of Chinese and Iranian studies (33,63). Reports from Nigeria contrast to our findings (46). The presence of alarm features has been a major determinant in prioritizing the initial endoscopic evaluation of patients presenting with upper GI symptoms because it is generally believed that these factors indicate a higher probability of malignancy (18). This investigation, which likely offers a more reliable picture of the problem, reported a prevalence of alarm symptoms of 41.0% (609/1484) and of 77.1% (91/118) in patients with gastro-intestinal cancer. This resulted in a sensitivity of 77.1%, a specificity of 62.1%, a positive predictive value of 16.1%, and a negative predictive value of 16.6 % when the parameter “having any alarm symptom” was used to diagnose the presence of cancer. Also, a patient presenting with an alarm symptom was 5.5 times more likely to yield a positive UGI cancer compared to one without an alarm symptom. In this study, alarm features in the patients with upper GI symptoms were significantly associated with upper GI malignancy (OR 5.5, P <0.001). Supporting our finding, local study that report an association between alarm features and malignancy of the UGI tracts (72) and similar reports were from other in countries (51, 57,20,85). And also another retrospective study reviewing 3926 patients who underwent endoscopy for symptoms of dyspepsia, there was a positive correlation between alarm features and advanced stages of gastric cancers (33).

Interestingly, none of each individual alarm symptom was able to identify more than 31.1% of patients with cancer. However, the predictive value of individual alarm features for cancer varies widely. The individual alarm symptoms such as an unexplained loss of weight, persistent vomiting and dysphagia were statistically significant correlation with a UGI malignancy in our study (P: - 0.001). In support of this, a cross-sectional study of 4664 dyspeptic patients who underwent endoscopy found that persistent vomiting and UGIB are strong predictors for upper gastrointestinal malignancy (65).

Among the three alarm features, persistent vomiting had the highest sensitivity, though it was only (33.9%), and unexplained weightless had the lowest sensitivity (23.7%). In contrast, the specificity and negative predictive value in our study were very high, ranging from (92.3%-95%) and (92.8% to 96.6%) respectively, for individual alarm features as well as for at least one alarm feature, these shows that there is little chance of missing a malignancy in patients without these alarm symptoms, although this partially caused by the low prevalence of upper GI malignancy.

All of those alarm features had very high specificity and NPVs. These results may reflect the low prevalence of cancer in our study, but not any specific attribute of any alarm feature for excluding malignancy. On the contrary, the PPV is relatively low, ranging from (16.4%-31.1%); indicating that only a small proportion of the patients with these individual symptoms do have cancer. However, in most western countries the prevalence of upper GI malignancy is below 0.5%. Therefore, in the general population, both the sensitivity and the PPV of alarm symptoms will be worse, although the NPV will remain high (16, 18).

The positive predictive value of dysphagia (75%) was somewhat better than those of the other alarm features, especially in patients with esophageal cancers. Moreover, the prevalence of alarm symptoms did not differ between young (< 45 years) and elderly (> 45 years) patients (304/609, 49.9% vs 305/609, 50.1%). In contrast to other study, we found epigastric pain was statistical association with upper GI malignancies, despite that alarm symptoms were predominant.

In the multivariate regression analysis age >60 years (P<0.001, OR 37.257) was found more significantly associated with UGI malignancy than young age of 45years (P 0.023, OR 10.313). Only one patient with malignancy was found in patients aged <24 years. We also found a positive correlation between cancer frequency and increasing age, which was similarly found in a Chinese and a Singaporean study (1, 18). Accordingly, The American College of Gastroenterology (ACG) and the Canadian Association of Gastroenterology (CAG) guidelines on dyspepsia have raised this age threshold to 60 years (45). This recommendation was made based on the results of a cost-effectiveness analysis. However, it remains controversial whether these guidelines can be applied to other parts of the world where the disease patterns, the prevalence of malignancy, and the healthcare systems are different (13, 45).

In this study clearly demonstrates statistically significant sex differences in having upper GI malignancy, a patient with female sex was 2.36 times more likely to yield overall a positive UGI cancer compared to one male sex (OR; 2.36(1.6-3.4),P; <0.001). Interestingly, Sex difference was almost negligible per individual type of upper GI malignancies (Gastric cancer (P: 0.77, OR; .88(0.38-2.04), Esophageal cancer (P: 0.149, OR; 5.05(0.56-45.6).

By Contrary, previous studies, Men have higher incidence of gastric cancer than women due to different exposure risk factors (86).and also men have higher incidence of esophageal cancer than women suggests that estrogen may serve as a preventative agent against esophageal cancer (87).

Therefore, in this study, female gender appears to represent a predictor factor for UGI cancer. This is in contrast to the literatures, no statistically significant difference was found in terms of the incidence of malignancy between males and females (87). Equal provision of cancer care is not enough to correct sex difference, but more attention should be paid to female disadvantage in overall upper GI malignancies. These findings call for sex-sensitive health policy to cope with the national upper GI malignancies burden.

Therefore, this study confirms the role of alarm features and cutoff age  $\geq 39.5$  (based on the ROC curve) in predicting the presence of SEFs, particularly malignancies. Patients with alarm features were more likely to have SEF compared to those with no alarm features.

The strength of this study was included all patients who had undergone UGIE irrespective of the indication while other studies analyzed those presented with dyspepsia alone. This study retrospectively evaluated a large number of procedures performed over a long period of time. Therefore, this is a good representation of the study population. In addition, common indications and endoscopic findings were assessed, which helped to identify prevalent upper gastrointestinal pathologies among our patients and characterize them appropriately.

Certain limitations of this study should be considered when interpreting the result. Being the retrospective study and absence of proper cancer registry systems influenced retrieving of important socio-demographic and clinical information such as H. pylori infection, smoking and alcohol history that may relate and add accuracy in diagnosing UGI malignancy.

This study was a single-center study and conducted in a tertiary hospital where severe forms of illnesses are treated; it may have overestimated some results and on the other hand, due to high patient flow some patient has limitation to get access of endoscopy; it may have underestimated some results, for those reason, may not reflect the exact prevalence of upper gastrointestinal pathologies in the community. Another limitation is that we do not know if the symptom was a one-time experience that quickly resolved or an ongoing/persistent symptom. The likelihood of the alarm symptoms being caused by malignancy is likely to be very small if the symptom resolves spontaneously.

## 7. CONCLUSION

Dyspepsia was the most common indication for EGD followed by screening varices of CLD patients. Clinically significant endoscopic findings were common. Esophagitis, pan gastropathy and esophageal varices were the common endoscopic finding. Of those, malignancies gastric CA followed by esophageal CA were common. Alarm symptoms were highly prevalent which was significantly higher among patients in the abnormal endoscopic group, particularly in upper GI malignancy group than in the normal endoscopic group. There were inconsistent in finding between endoscopy and biopsy result. Being age above 39.5 and female, and certain alarm features (persistent vomiting, dysphagia, and unexplained weight loss) were independent predictor of UGI malignancy.

## 8. RECOMMENDATION

- EGD remains a vital tool for the diagnosis and proper characterization of pathologies involving the upper gastrointestinal tract and it should be readily available to assist healthcare professionals in the treatment of patients with upper gastrointestinal diseases.
- Further studies are needed to address the important remaining socio-demographic and clinical information such as H. pylori infection, smoking and alcohol history that may relate and add accuracy in diagnosing UGI malignancy.
- We recommend to do an early endoscopy for any patient with UGI symptoms who has alarm symptoms and to take multiple biopsies from any rudeness or suspicious lesion, especially for age above 39.5 yrs, female gender, and certain alarm features (persistent vomiting, dysphagia, and unexplained weightloss).
- Further studies are required at the community level involving a larger sample size to find out the true prevalence of alarm features in patents with upper GI complaints and to find out the predictive value of alarm features for a significant organic lesion in endoscopy, such as upper GI malignancies.
- Since the epidemiological patterns of cancer prevalence would be important for health policy making to reduce the burden of cancer diseases, more efforts should be made to explore the regional patterns of sex difference in upper GI malignancy of our finding. Equal provision of cancer care is not enough to correct sex difference.

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## 10 .ANNEX

**Research code number** \_\_\_\_\_

**Part: 1- Socio demographic Characteristics** (fill the blank space or circle the right choice)

1-Card number/ code number-----

2-Age of the patient at time of diagnosis (in years) -----

3-Sex of the patient

- a. Male
- b. Female

**Part: 2 -What is the current diagnosis of upper GI endoscopy**

1. Duodenal ulcer
2. Gastric ulcer
3. Esophagitis
4. Esophageal varices
5. Esophageal stricture
6. Mass/polyps
7. Gastritis (erosive, atrophic----specify)-----
8. Gastropathy
9. Mallory Weiss tear
10. GERD
11. GOO
12. Achalasia
13. Esophageal ca/mass
14. Gastric ca/mass
15. Duodenal ca/mass
16. Hiatal hernia
17. External compression
18. Foreign body
19. Include normal finding
20. -Others (specify) \_\_\_\_\_

**Part 3:- Indication for upper GI endoscopy**

1. dyspepsia
2. Epigastric pain

3. Heart burn, regurgitation
4. Difficult of swallowing
5. Persistent Reflux/ vomiting
6. Hematemesis/upper GI bleeding
7. Melena/ upper GI bleeding
8. Signs of anemia
9. Unexplained Weight loss
10. Abdominal lump/Epigastric swelling
11. Others (specify)\_\_\_\_\_

**Part 4:-** Biopsy Report of the patient whose upper GI endoscopy finding showed that (Gastric, esophageal and duodenal malignancy or mass) and specify the type of histology

\_\_\_\_\_

**Name of Data collector**\_\_\_\_\_

**Signature** \_\_\_\_\_

**Date of data collection**\_\_\_\_\_

**Name and signature of the supervisor**\_\_\_\_\_