



CORRELATION BETWEEN HISTOPATHOLOGIC PATTERNS AND
ENDOSCOPIC FINDINGS OF GASTROINTESTINAL LESIONS IN SOUTH-
WEST ETHIOPIA: A 3 YEARS RETROSPECTIVE STUDY

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Abstract

Background: The gastrointestinal tract is a hollow tube consisting of the esophagus, stomach, small intestine, colon, rectum, and anus. Gastrointestinal tract diseases show regional variations. They are broadly categorized as upper and lower gastrointestinal lesions based on site. Gastrointestinal complaints are very common in Ethiopia. Gastrointestinal diseases are known to cause significant morbidity and mortality unless they are diagnosed and treated early. The treatment options and follow up of treatments in general depend on the findings of gastrointestinal endoscopy and histopathologic evaluation. This study will allow a reasonable evaluation of the correlation between histopathologic and endoscopic findings of gastrointestinal tract lesions which will be crucial in bridging the knowledge and research gaps in this area.

Objectives: To assess the correlation between histopathologic and endoscopic findings of gastrointestinal tract lesions in South-West Ethiopia

Methods: A three-year retrospective facility based study was conducted from September 15 to October 30, 2022. Data was collected from 318 eligible gastrointestinal endoscopic mucosal biopsy specimens submitted to pathology department from 11th of September 2020 to 10th of September 2022. After collection of histopathology and endoscopy reports of 318 cases they were retrospectively reviewed. Data was collected through observation of records, and then copied to data collection format prepared for this purpose. Data was cleaned, coded, checked for outliers and missed values and entered into Epidata v4.6 and exported to SPSS version 23 for analysis. Descriptive studies were done. Sensitivities, specificities and diagnostic accuracy of endoscopy were determined by taking histopathologic diagnosis as a gold standard diagnostic test.

Result: 318 endoscopic mucosal biopsies were included in the study. M: F ratio was 1.3:1 with mean age of 49.6. Progressive dysphagia was the most frequent clinical indication for endoscopic evaluation which constitutes 121(38%) biopsies. 184(57.9%) biopsies were found to be malignant neoplasms and 106 (33.3%) were benign. Esophageal cancer 122(38.4%) was the most common endoscopic diagnosis. Esophageal squamous cell carcinoma was found in 100(31.4%) cases. Gastric adenocarcinoma and colorectal adenocarcinoma accounted for 24(7.5%) and 39 (12.3%) cases respectively. Endoscopy finding of esophageal carcinoma had a sensitivity of 99.1% and specificity of 80%. Endoscopy finding of gastric carcinoma had a sensitivity of 83.3% and specificity of 79.2%. Endoscopic findings of colorectal cancer showed a sensitivity of 100% and specificity of 97.9%.

Conclusion: Progressive dysphagia is the most frequent clinical indication for upper GI endoscopic evaluation. Malignant neoplasms are the predominant histopathologic entities and esophageal squamous cell carcinoma is the most common malignancy. Endoscopic finding of malignancy in esophagus, stomach and colon has overall diagnostic accuracy of 98.3%, 80.5% and 99.8% respectively. Endoscopy in conjunction with histopathologic evaluation of biopsies is a useful adjunct for diagnosis of gastrointestinal lesions

Keywords: Histopathology, Endoscopy, Correlation, GIT, JUMC, Jimma, South West Ethiopia

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List of abbreviations and acronyms

CRC-Colorectal carcinoma

EGD- Esophagogastroduodenoscopy

GIT - Gastrointestinal tract

IBD- Inflammatory bowel disease

JUMC - Jimma university medical center

MALT - Mucosa associated lymphoid tissue

NUD- Non ulcer dyspepsia

SCC- Squamous cell carcinoma

UGIT – Upper Gastrointestinal tract

SEER- Surveillance, Epidemiology, and End Results

CHAPTER ONE: INTRODUCTION

1.1 Background

The gastrointestinal tract (GIT) is a hollow tube consisting of the esophagus, stomach, small intestine, colon, rectum, and anus. Each region has unique, complementary, and highly integrated functions that together serve to regulate the intake, processing, and absorption of ingested nutrients and the disposal of waste products. The intestines also are the principal site at which the immune system interfaces with a diverse array of antigens present in food and gut microbes. (1) In the GIT, just as there are regional variations in structure and function, so are the diseases. (2) They are broadly categorized as upper and lower GI lesions based on site. (3)

The disorders of gastrointestinal tract (GIT) are responsible for a great deal of morbidity and mortality and are one of the most commonly encountered problems in clinical practice. (4) GIT diseases could be inflammatory, congenital or neoplastic (benign or malignant). In general, inflammatory lesions of the GIT are more common, followed by malignant lesions while benign neoplasms are rare. (2)

Gastrointestinal diseases are known to cause significant morbidity and mortality unless they are diagnosed and treated early. (5) GIT endoscopy along with biopsy is an established procedure for investigating a wide range of gastrointestinal conditions especially inflammatory and malignant diseases. To facilitate diagnosis of different lesions, endoscopy and histology are complementary. (6)

Endoscopy and histopathology are two morphological diagnostic procedures which allow direct examination of organs with optical methods. They can detect abnormalities of the normal anatomy and histology and provide a precise diagnosis. Based on the information derived from these investigations an adequate treatment, either medical or surgical can be proposed. The optical resolution of both methods is different. Classical endoscopy is using essentially the naked eye observation of the tissue which allows a diagnosis of an ulcer or a raised lesion for instance, while histopathology is reaching the cellular and sub-cellular level. The new endoscopic techniques however do increase the optical resolution. (7) Endoscopy is a simple procedure that is safe and tolerated well. The use of versatile endoscopy has resulted in a marked increase in diagnostic procedures involving the upper and lower GI tract visualization and biopsy. (8)

Gastrointestinal biopsies are the major bulk specimens received in the surgical pathology section of tertiary hospital. These include endoscopic biopsies from gastric and duodenal mucosa, appendectomies, colonoscopic biopsies, colectomies, etc.(3) The major contributions of histopathology to endoscopy are situated in inflammatory and neoplastic diseases. Histopathology allows a more precise diagnosis of the type of inflammation and a better classification of tumors.(7)

Histopathological study of biopsy specimens are used to confirm endoscopic diagnosis in suspected malignancy or to rule out in the endoscopically benign appearing lesions and also are performed for monitoring the course, determining the extent of a disease as responses to therapy and for the early detection of complications. (6) A good correlation in diagnosis can be achieved by complementing endoscopic findings with histology of biopsy specimens.(4)

1.2 Statement of the problem

Digestive disorders and diseases significantly affect millions of persons worldwide inducing a highly significant economic impact comprising health care costs and work absenteeism, in addition to patient's decreased quality of life.(9) Worldwide, carcinoma of the stomach is the second most common cancer, and carcinoma esophagus is the sixth leading cause of death. (8) According to the reports of SEER program conducted by National cancer institute, 8% new cancer cases represent colorectal cancer and is the fourth leading cause of death among the other cancers in US. (15) Gastrointestinal complaints are very common in Ethiopia.(5) In developing countries like Ethiopia, where patients present late with chronic diseases and their complications, the treatment options and follow up of treatments of these cases in general depend on the findings of upper GI endoscopy and colonoscopy. It is evident that with clinical symptoms alone, it is impossible to rightly diagnose the pathologies.(10)

Jimma university medical center (JUMC) has an endoscopy unit and which started to regularly perform upper GI endoscopy and colonoscopy since 2020. Since then, patients with GI complaints fulfilling the clinical indications are provided with the service and biopsy specimens are sent to pathology department for histopathological evaluation. So far, no study is done about endoscopic findings and histopathologic patterns of GI mucosal biopsies in JUMC.

The main objective of this study is to assess the correlation between histopathological patterns and endoscopic findings with specific objectives of determination of endoscopic findings and histopathological patterns of GIT lesions and the age and sex distribution of the

predominant lesions at various sites of gastrointestinal tract and common clinical indications for GI endoscopy.

1.3 Significance of the study

There is a relatively high incidence of gastrointestinal diseases requiring endoscopic and histopathologic evaluation in South - West Ethiopia. Despite this fact, data are not available which can show the age, sex and anatomic distribution, histopathological patterns and endoscopic findings of various GIT lesions. The availability of such information not only enables comparisons with other studies addressing the same subject but also allows for a reasonable evaluation of the range of gastrointestinal pathologies across different age and sex groups along with assessment of the correlation between endoscopic findings and histopathological patterns of different GIT lesions. The result of this study will be of great help to the physicians in endoscopy unit and pathology department by providing a baseline objective evidence to assess the quality of their current practice and to point out areas of improvement which will have a direct impact on the quality of care patients get. Additionally crucial in bridging the knowledge and research gaps in this field, this study also serves as a solid foundation for upcoming researchers.

CHAPTER TWO: LITERATURE REVIEW

2.1 Epidemiology, endoscopic findings and histopathologic patterns of upper GIT lesions

Upper Gastrointestinal tract harbors a wide range of neoplastic and non-neoplastic lesions affecting various age groups. Non-neoplastic lesion includes infective, inflammatory, autoimmune, mechanical and other disorders with numerous underlying etiologies. An important being, *Helicobacter pylori* infection associated with gastritis, duodenal ulcer, gastric ulcer, atrophic gastritis, intestinal metaplasia, gastric carcinoma and MALT lymphoma.(11)

Worldwide, carcinoma of the stomach is the second most common cancer, and carcinoma esophagus is the sixth leading cause of death. According to the national cancer registry, esophageal and gastric cancer are most frequently found in men, while esophageal cancer ranks third in women following carcinoma of the cervix. Early malignancy detections greatly enhance patient rate survival. The 5-year survival rate of early esophageal cancer is 83.5 percent and 90 percent or more for early gastric cancer.(8)

A 5 year facility-based retrospective cohort study conducted in Ayder referral hospital evaluated total of 2,486 patients' endoscopic examinations. Upper gastrointestinal endoscopy totaled 1,994 procedures. 58.7% of esophago-gastroduodenoscopies (EGD) were performed on male patients. The mean, minimum and maximum age of the study subjects was 40, 1 and 94 years of age respectively. The common EGD findings were erythema of gastric mucosa in 24.5%, varices in 12.7%, gastric cancer in 9.4%, peptic ulcer disease in 8.8% and gastro esophageal reflux disease in 4.8%.The sensitivity of endoscopic findings for gastritis and gastric cancer was 47.9% and 94.7% respectively. Specificity of endoscopic findings for gastritis and gastric cancer was 92.9% and 76.7% respectively.(5)

A one year prospective study at Gondar University teaching hospital included a total of 500 consecutive patients. The majority of the patients are below 35 years of age. The study showed that the most prevalent endoscopic finding was a non- ulcer dyspepsia (NUD) which accounted for 37.8% followed by active duodenal ulcer and pyloric stenosis or deformity with a feature of gastric outlet obstruction in 21.8% and 15.6% of the cases, respectively. Esophageal varices accounted for 8.2%. There is no significant difference between male and

female ulcer prevalence. Esophageal carcinoma was detected in 3.0% and 1.84% of the patients had gastric cancer.(10)

A 2 year retrospective histopathology-based study carried out in Saudi Arabia showed out of 191 endoscopic biopsies studied 99 were from female patients and 92 were from male patients. An age range of 14 - 97 years was observed. There was a single case from the esophagus, 148 cases from the stomach. Nine biopsies were derived from the small intestine. 167 cases were non-neoplastic, 6 cases were benign neoplasms, three lesions were suspicious for malignancy whereas 15 were malignant neoplasms. Histopathology revealed chronic gastritis in 148 cases (77.5%) as the major histopathological finding in all investigated biopsies.(13)

A retrospective study conducted on 280 benign gastrointestinal lesions in India showed that maximum cases (39%) were observed in the age group of 41-60 years. Male patients outnumbered the females (male to female ratio was 1.4:1). Most common esophageal lesion was nonspecific esophagitis with least common being Barrett's esophagus. Correlating the results of endoscopic and histopathological features of acute and chronic gastritis a positive predictive value of 80% with sensitivity of 44.4% was seen.(4)

A 2 year prospective study carried out in Bangladesh evaluated total of 110 upper GIT endoscopic biopsy samples. M: F ratio is 1.4:1. Of all 22 were esophageal, 73 gastric and 15 duodenal biopsies. Among 110 UGIT biopsies total 51 were malignant. Among all 33 were gastric carcinoma, 16 esophageal carcinoma and 02 duodenal carcinoma. Among esophageal biopsies 18 were histologically neoplastic. Among all the esophageal carcinomas 62.5% were provisionally diagnosed as carcinoma by endoscopists. Among 33 adenocarcinoma of stomach 69.69% were clinically diagnosed or suspected as carcinoma by the endoscopist.(12).

A 3 year retrospective and prospective study of upper GI endoscopic biopsy carried out in India included 396 cases. From these 250 cases were esophageal biopsies, 104 cases were gastric biopsies and 42 cases were duodenal biopsies. The male: female ratio was 1.9:1. The highest number of cases was seen between 61 to 70 years. The most common lesions encountered in the esophagus were carcinomas (67%) followed by esophagitis (16%). The commonly encountered gastric lesion was chronic gastritis in 54.8%. Among the duodenal biopsies, non-neoplastic lesions were most common (59.5%) followed by neoplastic lesions (26%).(8)

2.2 Epidemiology, endoscopic findings and histopathologic patterns of lower GIT lesions

The large intestine and Anal canal are sites for broad array of non- neoplastic and neoplastic diseases, which at times, can lead to serious complications. They can be sites for infections, vascular disorders, ulcers, various inflammatory conditions and neoplasms. Epithelial tumors are major cause of morbidity and mortality.(14)

Colon and rectum cancer is one of the leading causes of cancer related mortality in developed and also in developing countries. According to the reports of SEER program conducted by National cancer institute, 8% new cancer cases represent colorectal cancer and are the fourth leading cause of death among the other cancers in US. The disease is frequently diagnosed in age range 65-74 years and survival rate in US is 66.9%. Developing countries have lower survival rates.(15) Adenocarcinomas are the commonest malignancies arising in the colorectal region, other being carcinoid, anal zone carcinoma & melanoma. Non neoplastic polyps are classified as hyperplastic, hamartomatous, juvenile & PeutzJeghers polyp, inflammatory & lymphoid polyp. Other benign conditions are adenoma, lipoma, neuroma, angioma, etc.(14)

Inflammatory bowel diseases like Crohn's disease and Ulcerative colitis are premalignant conditions, hence their early diagnosis is necessary to avoid further consequences and for proper treatment.(14)

A 5 year hospital based cross-sectional study conducted on medical records of patients who had colonoscopy examination at St. Paul's Hospital Millennium Medical College evaluated 309 subjects. Of these 60.5% were male. The mean age was 43.3 years with range of 15 to 84 years; 37% were older than 50 years.74.1% of the examined subjects had abnormal colonoscopic findings. Hemorrhoidal diseases 28.5% (88), gross mass lesions 14.9% (46), and inflammatory bowel diseases 12.0% (37) was the most common abnormal findings. Moreover, 80 patients (25.9%) had normal colonoscopic studies. Histopathology examination was performed for 114 patients. Analysis of the biopsy result showed that IBD (24) and CRC (20) were the commonest histopathology diagnosis followed by polyps (20), and (11) non-specific chronic inflammation.(18)

A five year facility-based retrospective cohort study conducted in Ayder referral hospital included 492 colonoscopies. Of these 74% of colonoscopies were performed on male

patients. The common colonoscopic findings were colorectal cancer in 114(23.2%), non-specific erythema of colonic mucosa in 78 (15.9%) and internal hemorrhoids in 37(7.5%).Considering histopathology as a gold standard test, GI endoscopy finding of colitis and colorectal cancer had a sensitivity of 75.0% and 87.8% respectively.(5)

A two year retrospective study in India evaluated 196 colonoscopic biopsies. Mean age of patients was 49.7 years with a male to female ratio of 1.6:1. Out of total 196 biopsies, 104 were non-neoplastic lesions, 92 were neoplastic lesions. Most common location of the lesion was rectum. The most common presenting complaint for both non-neoplastic and neoplastic lesions was bleeding per rectum. Non-specific colitis was the commonest followed by non-neoplastic lesion and ulcerative colitis. In the neoplastic lesions, adenocarcinoma was the commonest subtype followed by adenomatous polyps. Colonoscopic diagnosis correlated well with histopathology diagnosis in carcinomas.(16)

A 1 year retrospective histopathology-based study carried out in Saudi Arabia evaluated 191 endoscopic biopsies from which 30(16%) cases were from the colon. Malignant neoplastic lesions constituted 6.3% (12) cases , (non-IBD) inflammatory lesions 3.2% (6) cases, benign neoplastic lesions 2.6% (5) cases, inflammatory polyps 0.5% (1) case, inflammatory bowel diseases (IBDs) 1.6% (3) cases, and suspicious lesions for malignancy 1.6% (3)cases. Adenocarcinoma comprised the most frequently diagnosed malignant lesion.(13)

Another 2 year retrospective study in India included a total 133 cases. Out of 133 patients 86 were males and 47 were females. Patients showed wide age range from 11 years to 80 years. The most common presenting complaint was loose stools in 66 cases. The most common endoscopic finding was erythema in 82 cases. Out of 133 cases, 105 cases were non neoplastic, 08 cases were benign neoplastic and 20 cases were malignant neoplastic on histopathology. There was significant correlation of endoscopic findings like erythema and edema with histopathologic diagnosis.(17)

CHAPTER THREE: OBJECTIVES OF THE STUDY

3.1 General Objective

To assess the correlation between endoscopic findings and histopathologic patterns of GIT lesions in Jimma, Oromia, South-West Ethiopia, 2022

3.2 Specific objectives

- To determine endoscopic findings of GIT lesions in Jimma, Oromia, South-West Ethiopia, 2022
- To determine the histopathological patterns of endoscopic mucosal biopsies in Jimma, Oromia, South-West Ethiopia, 2022
- To identify common clinical indications for GI endoscopy in Jimma, Oromia, South-West Ethiopia, 2022
- To determine the age, sex and anatomic distribution of GI lesions at various sites of GIT in Jimma, South-West Ethiopia, 2022

CHAPTER FOUR: METHODOLOGY

4.1 Study area and study period

The study was carried out in Pathology department of Jimma University Medical Center (JUMC) from September 15, 2022 to October 30, 2022. Geographically, it is located in the city of Jimma, 352 km southwest of Addis Ababa. Currently it is the only teaching and referral hospital in the southwestern part of the country, providing services for approximately 16,000 inpatient, 220,000 outpatient attendants, 12,000 emergency cases and 4,500 deliveries in a year coming to the hospital from the catchment population of about 15 million people. The pathology department of JUMC has four Pathologists, 10 residents, 4 histopathology technicians and six assistant technicians. Services given by the department include histopathology, cytopathology and hematology with annual average number of cases above 2000, 5000, and 300 each respectively.

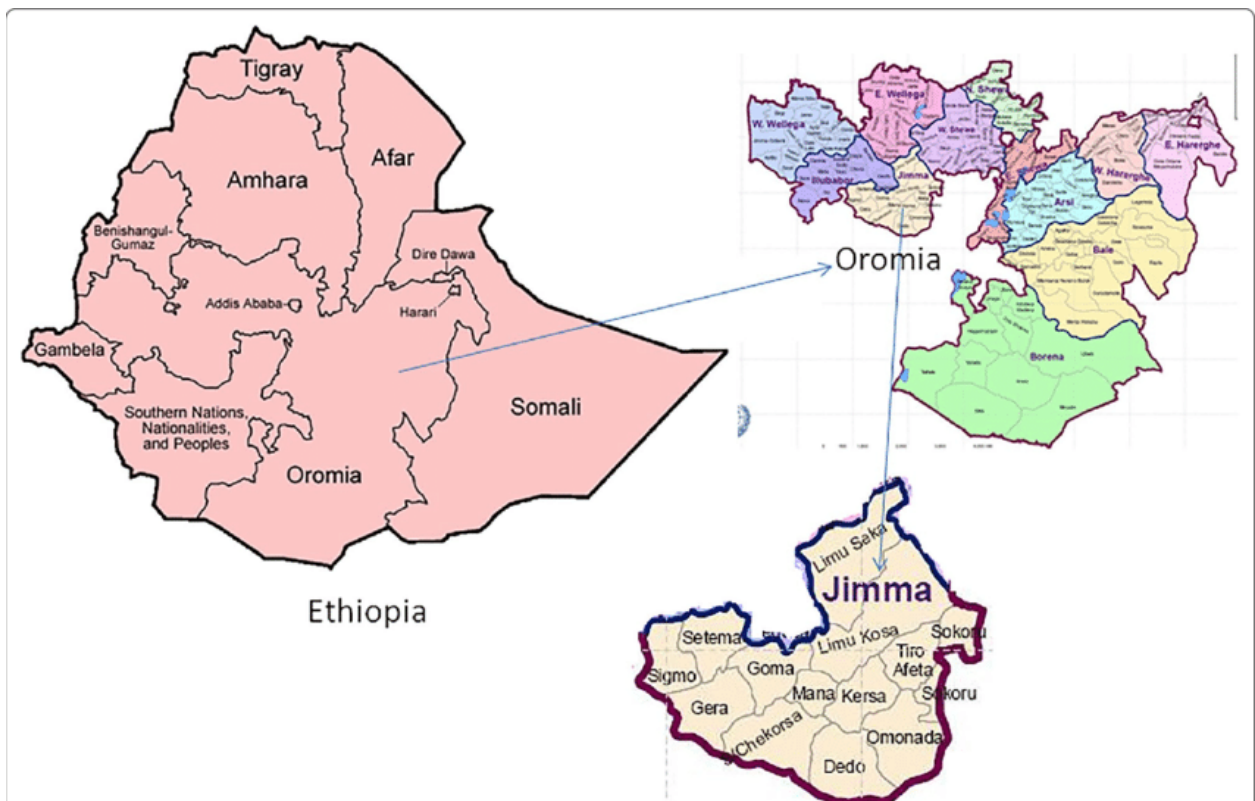


Figure 1: Map of Jimma Zone

4.2 Study Design

A facility-based retrospective cross sectional study was conducted

4.3 Population

4.3.1 Source population

All patients who submitted biopsy specimens to JUMC pathology department for histopathologic diagnosis from September 11, 2020 to September 10, 2022.

4.3.2 Study population

All patients who submitted GI endoscopic mucosal biopsy specimen to pathology department for histopathologic diagnosis from September 11, 2020 to September 10, 2022 fulfilling the inclusion criteria

4.3.3 Target Population

The population of South West Ethiopia

4.4. Inclusion and exclusion criteria

Inclusion criteria

- All GIT endoscopic biopsy requests and corresponding histopathologic reports from September 1, 2020 to September 10, 2022

Exclusion criteria

- Endoscopic biopsies missing one of the following information: sex, age, clinical presentation, endoscopic diagnosis and histopathologic diagnosis

4.5 Sample size and sampling technique

330 histopathology and endoscopy hard copy reports from 11th September 2020 to 10th of September 2022 were retrieved from JUMC pathology department data archive. The reports that fulfilled the inclusion criteria were manually selected and then grouped by year. 12 biopsy reports were excluded using exclusion criteria.

After collection of histopathology and endoscopy reports cases which fulfill the inclusion criteria were selected and retrospectively reviewed. A total of 318 cases with endoscopic findings and histopathologic reports were obtained. The endoscopic finding reports were matched with the original biopsy request papers and correlation with the corresponding histopathology reports was done.

The sensitivity, specificity, diagnostic accuracy, positive predictive value (PPV) and negative predictive value (NPV) of endoscopy in diagnosing GIT lesions were calculated according to the following equation: -

$$\text{Sensitivity (True positive rate)} = \frac{\text{True positive (TP)}}{\text{True positive (TP) + False negative (FN)}}$$

$$\text{Specificity (True negative rate)} = \frac{\text{True negative (TN)}}{\text{True negative (TN) + False positive (FP)}}$$

$$\text{Positive predictive value (PPV)} = \frac{\text{True positive (TP)}}{\text{True positive (TP) + False Positive (FP)}}$$

$$\text{Negative predictive value (PV)} = \frac{\text{True Negative (TN)}}{\text{True negative (TN) + False negative (FN)}}$$

$$\text{False positive rate (FPR)} = \frac{\text{False positive (FP)}}{\text{False positive (FP) + True negative (TN)}}$$

$$\text{False negative rate (FNR)} = \frac{\text{False negative (FN)}}{\text{False negative (FN) + True positive (TP)}}$$

$$\text{Total accuracy} = \frac{\text{True Positive (TP) + True negative (TN)}}{\text{Total number of cases}}$$

4.6 Data collection procedures

Structured checklist was adopted through reviewing of literatures and books to include information that fulfill the objective of the study. One supervisor from junior pathology residents and two data collectors from assistant technicians were enrolled in data collection. Endoscopy and histopathology reports of GIT mucosal biopsies submitted from endoscopy unit and private hospitals to pathology department from 11th September 2020 to 10th of September 2022 were retrieved from pathology department data archive. Eligible 318 reports fulfilling inclusion and exclusion criteria were extracted and recorded into a prepared checklist containing study variables

4.7 Study variables

- Sociodemographic factor
 - Age
 - Sex
-
- Anatomic site
- Endoscopic findings
- Histopathology findings
- Clinical Indication for endoscopic and histopathologic evaluation

4.8 Data processing and analysis

Data collected by checklist was coded, edited and entered into Epidata and then exported to SPSS for analysis. Descriptive statistical analysis was employed to determine frequency and age, sex and site specific distribution of the various GI lesions across the GIT. Sensitivities, specificities, positive predictive values, negative predictive values and diagnostic accuracy of endoscopic diagnosis were determined. The findings are presented using text, tables and charts.

4.9 Data quality management

Checklist was adopted after reviewing different literatures and it was pretested on 32 (10% of total sample size) GI endoscopic biopsy hard copy reports done in the year 2022 which were not included in the current study.

Then the checklist was revised with some modification of the variable and the final checklist was used for data collection. Two days of training was given to the data collectors on how to locate, retrieve, categorize and record the data and initial data collection was accompanied by the principal investigator. The principal investigator subsequently followed and supervised while the data collectors were retrieving and recording the biopsy results from pathology department data archive using check lists. Consultation by senior pathologist was sought at time of technical difficulties. After the checklist was checked for completeness, data was entered into Epi data v4.6 on password protected computer and exported to SPSS version 23 for analysis.

4.10 Ethical considerations

Ethical clearance was obtained from Institutional Review Board of Jimma University and was submitted to the responsible authorities of JUMC department of Pathology before proceeding to data collection. All the information collected from the study was handled confidentially by omitting their personal identification.

4.11 Limitation of the study

Histopathology reports are not fully computerized which resulted in inability to find the biopsy result reports of some patients. Some of the biopsy request papers did not have the clinical information, age of the patient and endoscopic findings which led to the exclusion of the cases from the study. Only morphologic diagnosis of the cases is practiced and other molecular and immunohistochemical (IHC) markers are not available for confirmatory diagnosis at times of diagnostic difficulty.

4.12 Dissemination plan

The result of this study will be forwarded to Jimma University, Institute of health sciences, and department of Pathology. An attempt will be made to present the findings in different conferences and workshops and will be sent to publication in a scientific journal.

CHAPTER FIVE: RESULT

5.1 Age, sex and anatomic site distribution

A total of 7250 biopsies were received by the department and processed for histopathologic diagnosis in the three years period between 2020 and 2022. Out of these, 330 (4.5%) were GI endoscopic mucosal biopsy specimens. Male patients constituted for 179 (56.3%) of the total cases with a male to female ratio of 1.3:1. The age distributions had minimum value of 7 years and maximum value of 85 years with mean age of 49.6 and the standard deviation of 15.1. The most commonly affected age group with GI lesions was between ages 40 and 59 (48.1%). The age and sex distribution of the cases is shown in table 1.

Table 1: Table showing distribution of GIT lesions across different age groups, 2020–2022, JUMC, Jimma, Oromia, South West Ethiopia , N=318

Age group	Sex		Total
	Male	Female	
0-19	5	9	14
20-39	46	44	90
40-59	87	66	153
60-79	40	20	60
80-99	1	0	1
Total	179	139	318

From a total of 318 cases esophageal biopsy specimens were the most common accounting for 41.8%(133) followed by colon 29.9%(95), stomach 26.4%(84), duodenum 0.9%(3) and ileum 0.9%(3). Specimens taken from upper gastrointestinal tract sum up to be 220 (69.2%) and those from ileum and colon are 98(30.8%).

Esophageal, duodenal and ileal lesion were more frequent in females whereas gastric and colonic lesions are more prevalent in males.

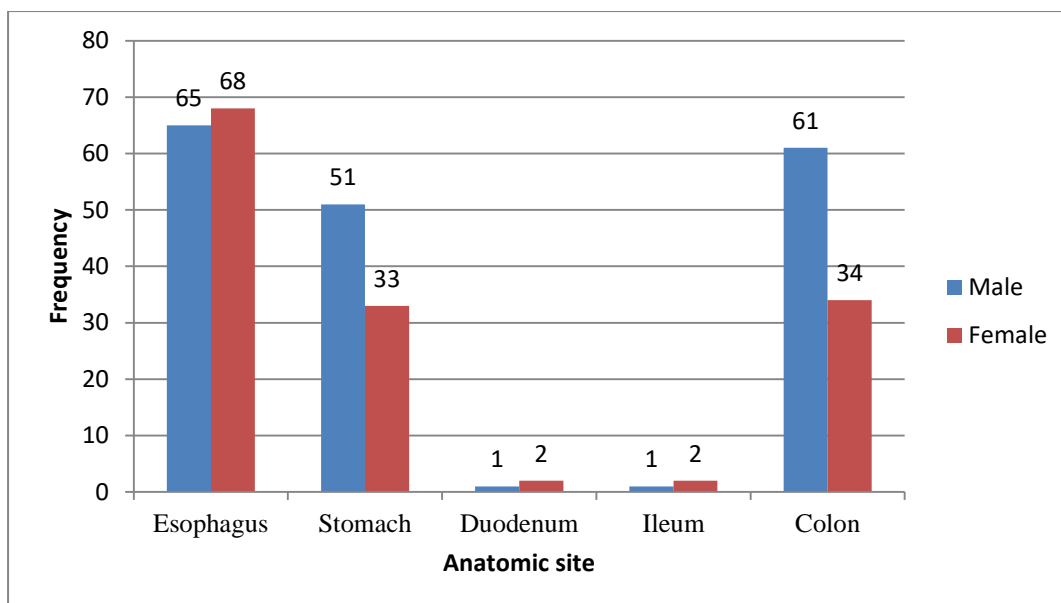


Figure 1: Bar chart showing distribution of GIT lesions across different anatomic sites , 2020–2022, JUMC, Jimma, Oromia, South West Ethiopia , N=318

5.2 Clinical Indication for endoscopic evaluation

Progressive dysphagia was the most frequent clinical indication for endoscopic evaluation which constitutes 121(38%) cases followed by dyspepsia 58(18.2%), rectal bleeding 39(12.3%), abdominal pain 24(7.5%), weight loss 23(7.2%), constipation 13(5.3%) and persistent vomiting 10(3.1%).

Table 2: Clinical indication for endoscopic evaluation of GIT lesions, 2020-2022, JUMC, Jimma, Oromia South West Ethiopia, N=318

Patient complaint at presentation	Frequency	Percent
Dysphagia	121	38.1
Weight loss	23	7.2
Constipation	17	5.3
Persistent vomiting	10	3.1
Symptoms of anemia	3	0.9
Odynophagia	1	0.3
Dyspepsia	58	18.2
Hematemesis	6	1.9
Diarrhea	6	1.9
Abdominal pain	24	7.5
Rectal bleeding	39	12.3
Abdominal swelling	2	0.6
Others	8	2.5
Total	318	100

5.3 Endoscopic findings of GIT lesions

From 133 esophageal lesions esophageal cancer was the most common endoscopic diagnosis which accounts for 97.7% (130) cases followed by esophageal stenosis 2(1.5%) and esophageal ulcer 1(0.8%). Endoscopic diagnosis of esophageal lesions is shown in Table 3.

Table 3: Table showing frequency of endoscopic findings of esophageal lesions, 2020–2022, JUMC, Jimma, Oromia, South West Ethiopia , N=318

Endoscopic diagnosis	Frequency	Percent
Esophageal stenosis	2	1.5
Esophageal ulcer	1	0.8
Esophageal cancer	130	97.7
Total	133	100

Gastric cancer was the predominant endoscopic finding seen in 36 stomach lesions. Peptic ulcer disease, chronic gastritis, gastric outlet obstruction, acute gastritis and were found in 14, 12, 10 and 8 cases respectively. Endoscopic diagnosis of gastric lesions is shown in figure 2.

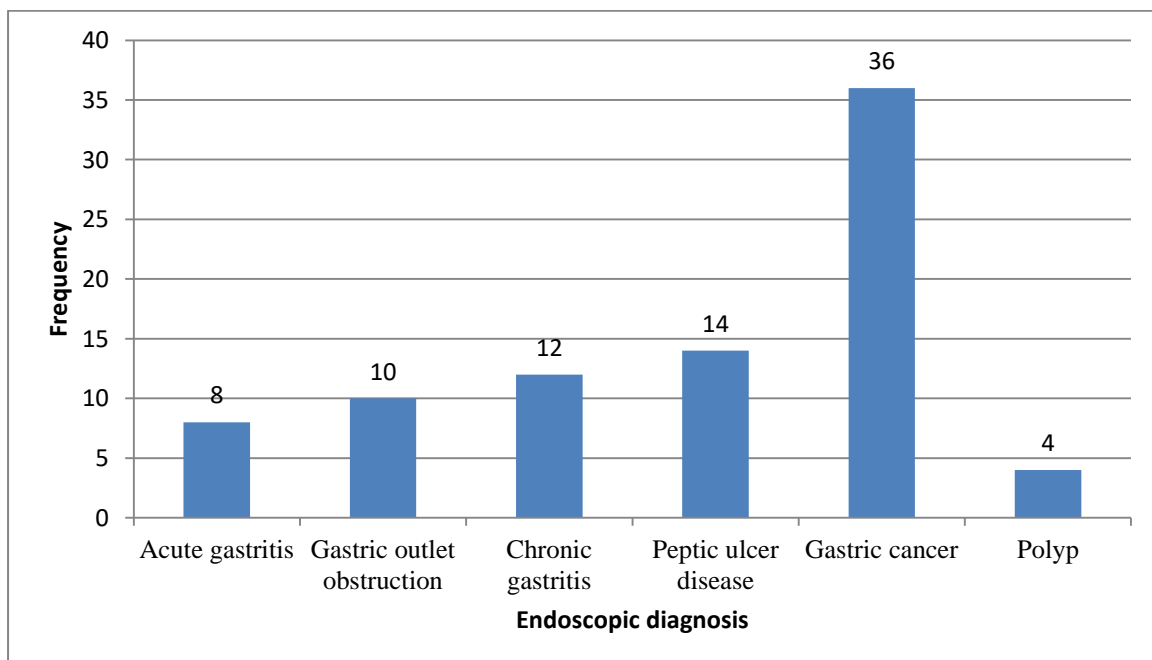


Figure 2: Bar chart showing endoscopic findings of stomach lesions , 2020–2022, JUMC, Jimma, Oromia, South West Ethiopia , N=318

Colorectal cancer was by far the most common endoscopic finding in colonic lesions which accounts for 47.3% (45) of all colonic cases. Inflammatory bowel disease 10.5% (10), proctocolitis 4.2% (4), non specific colitis 3.2 % (3) and diverticulum 1.1% (1) were also seen. Endoscopic diagnosis of colonic lesions is shown in Table 4.

Table 4: Endoscopic diagnosis of colonic lesions, 2020-2022, JUMC, Jimma, Oromia South West Ethiopia, N=318

Endoscopic diagnosis	Frequency	Percent
Non specific colitis	3	3.2
Inflammatory bowel disease	10	10.5
Proctocolitis	4	4.2
Colorectal cancer	45	47.3
Diverticulum	1	1.1
Polyp	32	33.7
Total	95	100

Polypoid lesions were seen in different segments of the gastrointestinal tract. Colon showed 32 cases with polyps whereas 4 cases showed polyps in stomach and only 1 in ileum.

Hamartoma and angioectasia were diagnosed in 2 different patients. Variation in rate of malignancy was seen across segments of the GIT. Endoscopic evaluation of esophageal lesions diagnosed cancer in 97.7% of cases while cancer was diagnosed in 40.5% of stomach lesions and 47.4% of colonic lesions.

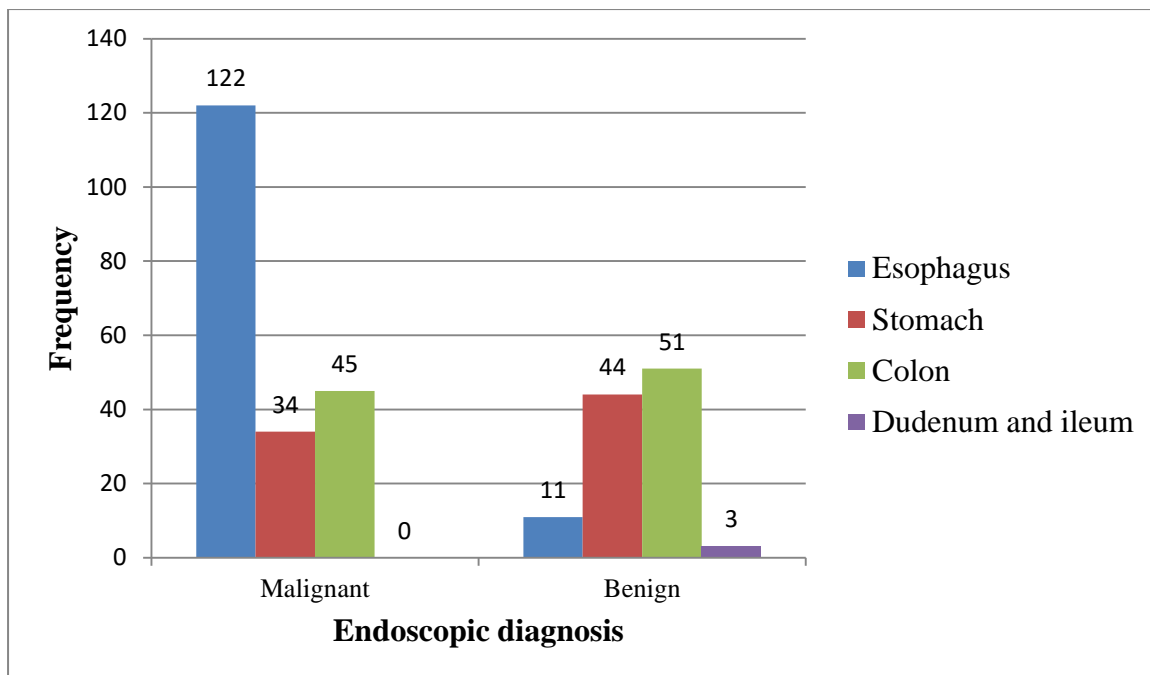


Figure 3: Bar chart showing anatomic distribution of malignancy in GI endoscopic diagnosis, 2020–2022, JUMC, Jimma, Oromia, South West Ethiopia , N=318

5.4 Histopathologic patterns of GIT lesions

Histologic evaluation of the biopsy specimens showed malignant neoplasms in 184(57.9 %) and benign diseases in 106(33.3%) cases. Cases signed out as inconclusive constituted 28(8.8%).

Malignancy was the predominant pathologic entity among esophageal lesions which accounts for about 88 %(117) of all esophageal lesions. Squamous cell carcinoma (75.2 %) was the most commonly diagnosed histopathologic entity followed by adenocarcinoma (12.8 %). Esophageal dysplasia and acute esophagitis were seen in 4 and 1 patients respectively. 11(8.25%) esophageal biopsies were signed out as inconclusive for which better representative sampling was recommended. Age group between 40 and 59 were mostly affected by malignant neoplasms than the other age groups.

Table 5: Histopathologic patterns of esophageal lesions, 2020-2022, JUMC, Jimma, Oromia, South West Ethiopia, N=318

Histopathologic diagnosis	Frequency		Total	Percentage
	Male	Female		
Squamous cell carcinoma	47	53	100	75.2
Adenocarcinoma	11	6	17	12.8
Dysplasia	2	2	4	3
Acute esophagitis	1	0	1	0.75
Inconclusive	4	7	11	8.25
Total	65	68	133	100

Table 6: Table showing histopathologic patterns of esophageal lesions across different age groups, JUMC, Jimma, Oromia, South West Ethiopia , 2020–2022 N=318

Histopathologic pattern	Age group					Total
	0-19	20-39	40-59	60-79	80-99	
Squamous cell carcinoma	2	20	44	31	3	100
Adenocarcinoma	0	1	9	5	2	17
Dysplasia	0	0	4	0	0	4
Acute esophagitis	0	1	0	0	0	1
Inconclusive	1	3	3	2	2	11
Total	3	25	60	38	7	133

Out of 84 stomach biopsies chronic gastritis 43(51.2 %) was the most frequent histopathologic entity. Gastric adenocarcinoma accounted for 24(28.6%), adenomatous polyps for 1(1.2%) and fundic gland polyp 1(1.2%).

Table 7: Histopathologic patterns of gastric lesions, 2020-2022, JUMC, Jimma, Oromia South West Ethiopia, N=318

Histopathologic diagnosis	Frequency			Percentage
	Male	Female	Total	
Chronic gastritis	25	18	43	51.2
Acute gastritis	1	0	1	1.2
Adenocarcinoma	17	7	24	28.6
Adenomatous polyp	1	0	1	1.2
Fundic gland polyp	2	0	2	2.4
Normal	0	1	1	1.2
Inconclusive	5	7	12	14.2
Total	51	33	84	100 %

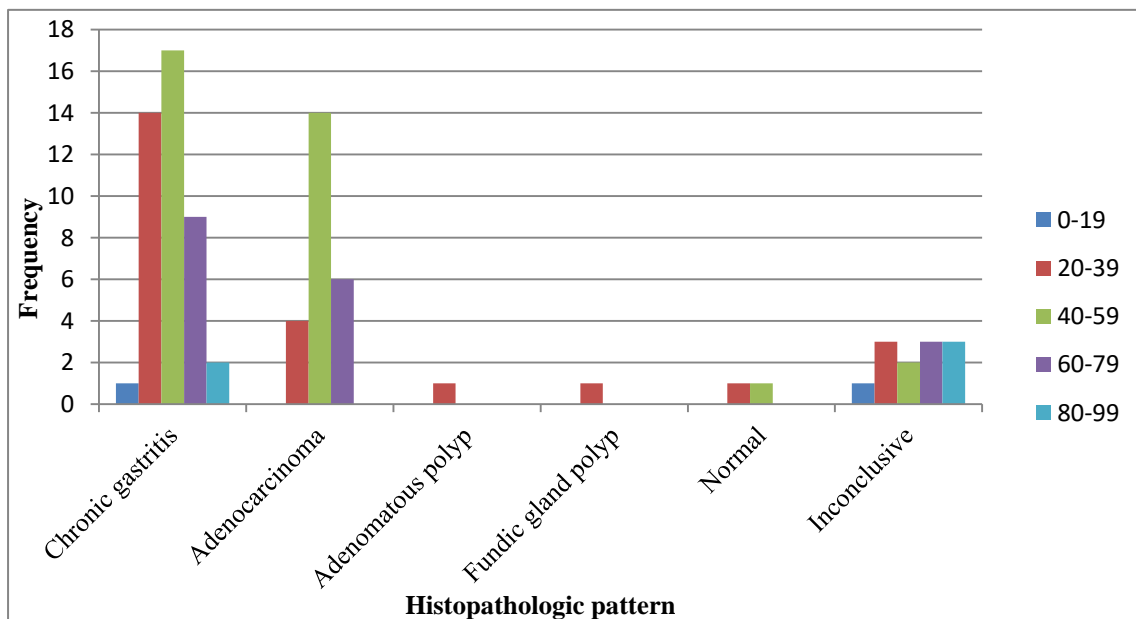


Figure 4: Bar Chart showing histopathologic patterns of stomach lesions across different age groups, JUMC, Jimma, Oromia, South West Ethiopia , 2020–2022 N=318

Small intestinal lesions were the least commonly biopsied of all GIT lesions in this study. A total of 6 biopsies were received from duodenum (3) and ileum (3). Histopathologic evaluation of duodenal biopsies revealed duodenitis (2) and duodenal adenocarcinoma (1). Crohns disease (1), non specific ileitis (1) and inflammatory polyp were seen in ileal biopsy specimens.

Table 8: Histopathologic patterns of duodenal and ileal lesions, 2020-2022, JUMC, Jimma, Oromia South West Ethiopia, N=318

Anatomic site	Histopathologic diagnosis	Frequency	Total
Doudenum	Duodenitis	2	3
	Adenocarcinoma	1	
Ileum	Crhons disease	1	3
	Inflammatory polyp	1	
	Non specific Ileitis	1	

From a total of 95 colonic biopsies histopathologic evaluation showed adenocarcinoma be to the most common morphologic diagnosis made in 39(41.1%) biopsies followed by hyperplastic polyp 16(16.8%), adenomatous polyps 14(14.7%) and chronic non specific colitis 11(11.6%). Ulcerative colitis (3), anorectal squamous cell carcinoma (3), Schistsoma colitis (2), juvenile polyp (1) and hamartoma (1) were also seen. All morphologic patterns were more common in males. Five colonic biopsies were signed out as inconclusive with recommendation to take adequate representative sample. Frequency of different histopathologic patterns of colonic lesions is seen in table 9.

The age group between 40 and 59 was mostly affected by malignancy. Adenocarcinoma was seen in 13 out of 34 biopsies in this age group.

Table 9: Histopathologic patterns of colonic lesions across different age groups, 2020-2022, JUMC, Jimma, Oromia South West Ethiopia, N=318

Histopathologic patterns	Age group					Total
	0-19	20-39	40-59	60-79	80-99	
Adenocarcinoma	1	11	13	12	2	39
Chronic nonspecific colitis	0	2	6	3	0	11
Schistosoma colitis	2	0	0	0	0	2
Ulcerative colitis	0	3	0	0	0	3
Adenomatous polyp	0	1	4	6	3	14
Juvenile polyp	1	0	0	0	0	1
Hamartoma	0	0	1	0	0	1
Hyperplastic polyp	1	1	8	6	0	16
Anorectal squamous cell carcinoma	0	1	1	1	0	3
Inconclusive	0	2	1	1	1	5
Total	5	21	34	29	6	95

5.5 Correlation of endoscopic and histopathologic findings

A total of 318 GI endoscopic mucosal biopsy requests with endoscopy findings were retrieved and correlated with the corresponding final histopathologic diagnosis. They were grouped based on anatomic site of origin into five groups. Each group was further subdivided according to the histopathologic findings. There were 28 cases signed out as inconclusive. There were 179 male and 139 female patients with male to female ratio of 1.3:1 and mean age of 49.6.

Among 133 esophageal lesions esophageal cancer was the most common endoscopic diagnosis which constituted 122 biopsies. From these 11 cases were inconclusive on histologic evaluation. There was 1 false positive case which turned out to be acute esophagitis. The true positive and negative cases were 116 and 4 respectively.

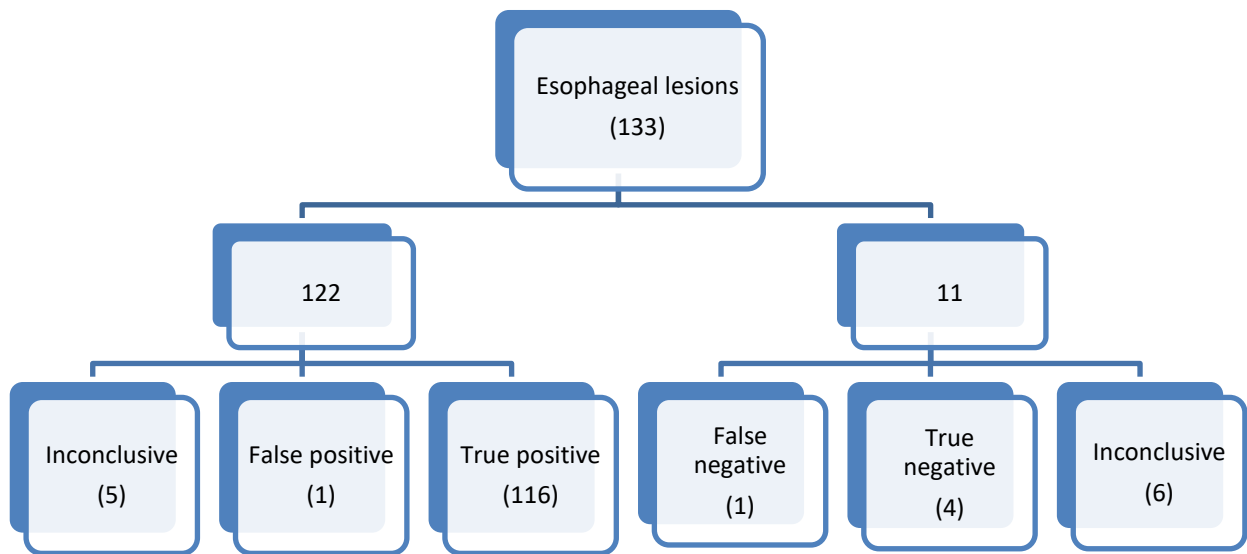


Figure 5: Diagram showing correlation of endoscopic and histopathologic findings of esophageal carcinoma in 133 esophageal lesions, 2020–2022, JUMC, Jimma, Oromia, South West Ethiopia , N=318

Considering histopathology as a gold standard test, GI endoscopy finding of esophageal carcinoma had a sensitivity of 99.1% and specificity of 80%. The positive and negative predictive values are 99.1% and 80%. The overall diagnostic accuracy was 98.3%.

Gastric cancer was the predominant endoscopic finding seen in 36 stomach lesions. From these 12 cases were inconclusive on histologic evaluation. There were 10 false positive cases and the false negative cases were 4. The true positive and negative cases were 20 and 38 respectively. Considering histopathology as a gold standard test, GI endoscopy finding of gastric carcinoma had a sensitivity of 83.3% and specificity of 79.2%. The positive and negative predictive values are 66.6% and 90.5%. The diagnostic accuracy was 80.5%.

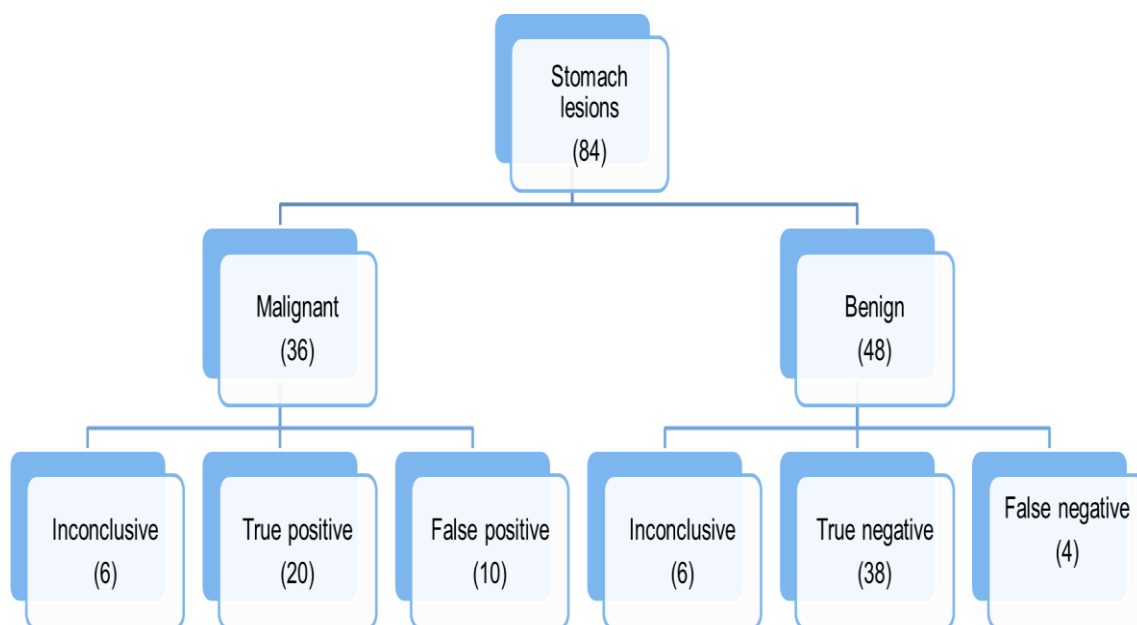


Figure 6: Diagram showing correlation of endoscopic and histopathologic findings of gastric carcinoma in 84 stomach lesions, , 2020–2022, JUMC, Jimma, Oromia, South West Ethiopia , N=318

Colorectal cancer was the most common endoscopic finding in colonic lesions which accounts for 47.3% (45) of all colonic biopsies. 3 cases were inconclusive on histologic evaluation. There was 1 false positive case and there was no false negative case. The true positive and negative cases were 41 and 48 respectively. Endoscopic findings of colorectal cancer showed a sensitivity of 100% and specificity of 97.9%. Positive and negative predictive values were 97.6% and 100% respectively. Diagnostic accuracy was 98.8%

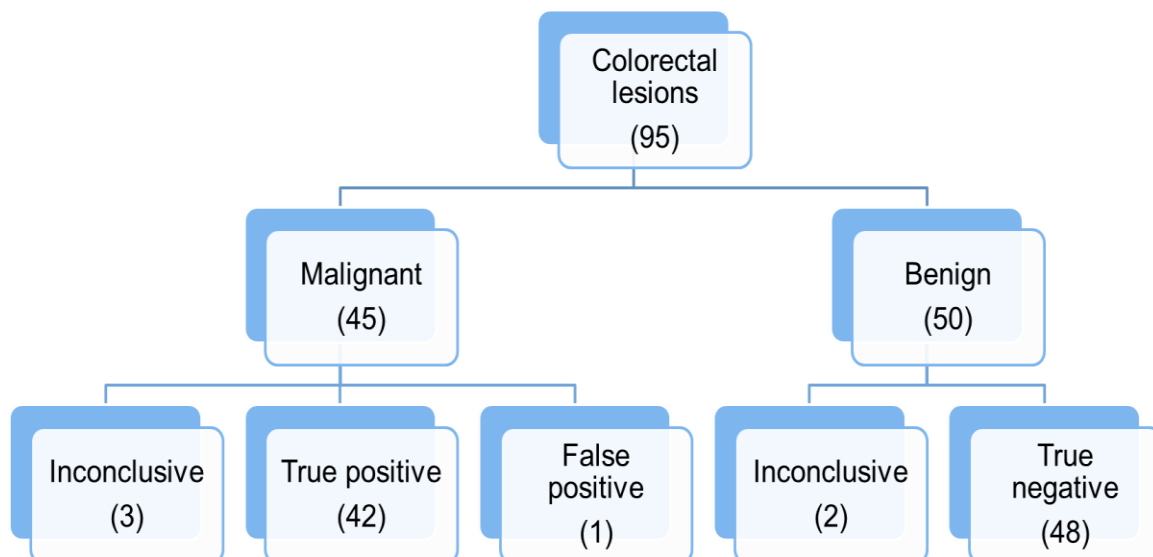


Figure 7: Diagram showing correlation of endoscopic and histopathologic findings of colorectal carcinoma in 95 colorectal lesions , 2020–2022, JUMC, Jimma, Oromia, South West Ethiopia , N=318

Table 10: Sensitivity and specificity of endoscopy taking histopathology as a gold standard diagnostic tool, 2020-2022, JUMC, Jimma, Oromia South West Ethiopia, N=318

Endoscopic diagnosis	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Diagnostic accuracy
Esophageal cancer	99.1%	80%.	99.1%	80%.	98.3%
Gastric cancer	83.3%	79.2%.	66.6%	90.5%.	80.5%
Colorectal cancer	100%	97.9%.	97.6%	100%	98.8%

6. Discussion

The age group commonly affected with gastrointestinal lesions in this study is 40-59 which accounts for 48.1% of the cases with average age of 49.6. This is comparable with a study done in Gondar University where 41% of the patients with gastrointestinal lesion fall under this age group. (10) The ratio of male to female patients for whom the endoscopic mucosal biopsies were taken was 1.3:1. This is in agreement with study done in Ayder referral hospital (1.6:1), Gondar University hospital (1.3:1), India (1.3:1) and Nepal (1.3:1). (4, 5, 6, 10)

Histologic evaluation of all biopsy specimens showed malignant neoplasms in 184(57.9 %) cases and benign diagnosis in 106(33.3%) cases. The overall incidence of malignancy in one Indian study was 51.5%. (8)

Esophageal biopsy specimens were the most common accounting for 41.8 % (133) of all biopsies. This is comparable with study done in India where 49.5% of endoscopic biopsies were from esophagus. (19) Progressive dysphagia was the most frequent clinical indication for endoscopic evaluation which constitutes about 121(38%) patients. This is consistent with a similar Indian study which showed dysphagia to be the commonest indication for endoscopic examination. (19)

Esophageal cancer was the predominant endoscopic diagnosis which accounted for 38.4 % of all gastrointestinal lesions followed by gastric cancer (11.3%). This is in contrast with study done Black lion hospital where the commonest abnormal findings include duodenal ulcer (41%), esophageal varices (9%), acute gastritis (6%), duodenitis (3.4%), and reflux esophagitis (2.3%). The endoscopy diagnosis of cancer in the esophagus and stomach was 2.8% and 1.3 respectively. (21) Colorectal cancer was the most common endoscopic diagnosis among patients with colonic lesions (47.3%). This goes against the finding of a study done in SPMMC (Addis Ababa) where hemorrhoidal diseases (28.5%), gross mass lesions (14.9%), and inflammatory bowel diseases (12.0%) were the most common abnormal findings. (18) This is probably due to selection bias where patients with high likelihood of malignancy get biopsied more frequently than those with suspected benign diseases.

Malignancy was the predominant pathologic entity among esophageal lesions which accounts for about 88 % of all esophageal lesions. This is in agreement with study done in black lion hospital which showed 91.7% malignant lesions. (22) Another Indian study found

malignancy as the most common lesion. (11) Malignant esophageal lesions were slightly more common in a female with F: M of 1.02: 1 which is comparable to the finding of study in black lion hospital (1.3:1). (22) Morphologic classification of malignant lesions revealed Squamous cell carcinoma (75.2 %) as the most frequent morphology followed by adenocarcinoma (12.8 %). This is consistent with study done in black lion hospital in which squamous cell carcinoma was seen in 78.7% and adenocarcinoma was found in 19.8% esophageal biopsy specimens. (22) Studies done in Ghana also showed similar findings in which Squamous cell carcinoma accounted for 78.7% and adenocarcinoma 21.3%. (24) Kenyan study showed 81.1% squamous cell carcinoma and 18.9% adenocarcinoma. (23)

Considering histopathology as a gold standard test, GI endoscopy finding of esophageal carcinoma had a sensitivity of 99.1% and specificity of 80%. A study in Japan showed sensitivity of 90.9% and specificity of 100%. (26) %. The overall diagnostic accuracy was 98.3%. A study in Ethiopia found that upper GI endoscopy had a 90% correlation with the histological diagnosis. (28) One study from India revealed endoscopy had 76.0% agreement with histopathological findings. (19)

Out of 84 stomach biopsies chronic gastritis was the most frequent entity constituting 51.2 %. Gastric adenocarcinoma accounted for 28.6% while adenomatous polyps and fundic gland polyps were seen in 1.2% each. This is in agreement with Ayder referral hospital study finding where chronic gastritis and adenocarcinoma were seen in 46.2% and 28.2% of gastric biopsy specimens respectively. (5) In study which evaluated 396 upper gastrointestinal biopsies chronic gastritis comprised of 54.8% of the cases and adenocarcinoma was seen in 22.1%. (8) Similar findings were noted in two studies from Nepal and Bangladesh. (6,12) In a large study conducted in Addis Ababa involving 10,000 participants showed only 1.3% had gastric adenocarcinoma which is far a lower figure when compared to finding of this study.(21)

Considering histopathology as a gold standard test, GI endoscopy finding of gastric cancer had a sensitivity of 83.3% and specificity of 79.2%. The positive and negative predictive values are 66.6% and 90.5%. This is comparable with finding in an Ethiopian study where sensitivity of 94.7% and specificity of 76.7% were reported. The positive and negative predictive values were 57.4% and 97.8%. (5) One study from Nigeria showed an overall association of endoscopic and histopathologic diagnosis of gastric adenocarcinoma to be 79.6%. (27)

Small intestinal lesions were the least commonly biopsied of all GIT lesions in this study. A total of 6 biopsies were received from duodenum (3) and ileum (3). Histopathologic evaluation of duodenal biopsies revealed duodenitis (2) and duodenal adenocarcinoma (1). Crohns disease (1), non specific ileitis (1) and inflammatory polyp were seen in ileal biopsy specimens. A study in Saudi Arabia which included 191 biopsies found 4 duodenal biopsies all of which turned out to be duodenitis and 5 ileal biopsy specimens from which 4 were diagnosed as ileitis and 1 as Crohns disease. (13) A single case of duodenal adenocarcinoma was found in a study done in Gondar university hospital. (10)

From a total of 95 colonic biopsies histopathologic evaluation showed adenocarcinoma be to the most common morphologic diagnosis made in 39(41.1%) biopsies followed by hyperplastic polyp 16(16.8%), adenomatous polyps 14(14.7%) and chronic non specific colitis 11(11.6%). The findings in this study are different from other studies done on colonic biopsies. A study done in SPMMH showed that inflammatory bowel disease 21.1% (24) and colorectal carcinoma 17.5% (20) were the commonest histopathology diagnosis followed by polyps 17.5% (20), and non-specific chronic inflammation 9.6%. (18) Histopathologic findings of Colon biopsy at Ayder referral hospital showed colorectal adenocarcinoma in 27.6% and chronic non-specific colitis in 30.6%. (5) A study done in India involving 124 large bowel specimens found that adenocarcinoma was the commonest finding which accounted for 49.2% followed by acute colitis (11.3%). Hyperplastic and adenomatous polyps were seen only in 3 cases. (14) A review of 196 colonoscopic biopsies showed adenocarcinoma in 32.6%, non specific colitis in 25.5%, adenomatous polyps in 13.6% and hyperplastic polyps in 4.1%. (16)

Endoscopic findings of colorectal cancer showed a sensitivity of 100% and specificity of 97.9%. Positive and negative predictive values were 97.6% and 100% respectively. This is comparable with the finding in Ayder referral hospital study which showed sensitivity of 87.8% and specificity of 88.1%. Positive and predictive values were 63.2% and 96.9% respectively. (5) A study done in SPMMC revealed that diagnostic yield is 86.5% in subjects who presented with bleeding per rectum. (18) One study from Sweden showed similar finding. (25)

7. Conclusion

The M: F ratio is 1:1.3 and peak age of occurrence of gastrointestinal lesions is between 40 and 59. Progressive dysphagia is the most frequent clinical indication for upper GI endoscopic evaluation and rectal bleeding is the commonest indication for colonoscopy.

Esophageal biopsy specimens cover the majority of GI biopsies and esophageal cancer is the most common endoscopic diagnosis of all GI lesions.

Malignant neoplasms are the predominant histopathologic entities among all GI lesions from which esophageal squamous cell carcinoma stands as the most common malignancy overall. Chronic gastritis is the most frequent entity from gastric specimens while colorectal adenocarcinoma is the most common malignancy from colon specimens.

Endoscopic finding of esophageal carcinoma has a sensitivity of 99.1% and specificity of 80% whereas that of gastric carcinoma has a sensitivity of 83.3% and specificity of 79.2%. Endoscopic finding of colorectal cancer has a sensitivity of 100% and specificity of 97.9%.

Diagnostic accuracy of endoscopy in the diagnosis of malignancy is 98.3% in esophagus 80.5% in stomach and 98.8% in colon and rectum respectively.

Endoscopy in conjunction with histopathologic evaluation of biopsies is a useful adjunct for diagnosis of GI lesions and plays an important role in management of patients.

8. Recommendation

The following recommendations are made from this study.

For federal ministry of health

- Overall high incidence of malignancy across all gastrointestinal biopsies points to the need to carry out public health campaigns to raise public awareness about the benefits of early health service seeking behavior.

For JUMC endoscopy unit

- Some request forms do not have the age and sex of the patient and few endoscopic descriptions do not follow standard classification. This should be corrected.
- A significant number of cases are non representative of the actual lesions which leads to in non diagnostic result and repeated biopsies. This can be avoided by taking multiple samples at a different place at the time of initial biopsies.

For JUMC Pathology department

- Data archives of the department should be improved.

For researchers

- Esophageal malignancy which is found to be more prevalent than other neoplasms in this study requires further more extensive studies to reveal the factors behind such figures.

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Data abstraction form

Serial number:

Socio-demographic data			Comments
100.01	Age		
100.02	Sex	1. Male 2. Female	
Clinical data			Comments
200.01	Patients complaints at presentation	1. Dysphagia 2. Odynophagia 3. Dyspepsia 4. Hematemesis 5. Diarrhea 6. Abdominal pain 7. Rectal bleeding 8. Rectal discharge 9. Abdominal swelling 10. Weight loss 11. Incidental finding while on medical check up 12. Other (specify)	
Endoscopic findings			
300.1	Site of the lesion	1. Esophagus 2. Stomach 3. Duodenum 4. Ileum 5. Colon	
300.01	Upper GI Endoscopic diagnosis	1. Normal 2. Chronic Gastritis 3. Signs of Portal HTN 4. Gastric Cancer	

		<ol style="list-style-type: none"> 6. Peptic Ulcer Disease 7. Gastroesophageal Reflux Disease 8. Gastroduodenitis 9. Bile Reflux Disease 10. Gastric Outlet Obstruction 11. Esophageal Cancer 12. Duodenitis 13. Esophagitis 14. Esophageal Candidiasis 15. Post Pyloric Stenosis 16. Acute Gastritis 17. Duodenal Mass 18. Gastroesophagitis 19. Achalasia 20. Esophageal Stricture 21. Esophageal Ulcer 22. Other 	
300.02	Colonoscopy diagnosis	<ol style="list-style-type: none"> 1. Normal 2. Colorectal Cancer 3. Non Specific Colitis 4. Internal Hemorrhoids 5. Inflammatory Bowel Disease 6. Redundant Sigmoid 7. Irritable Bowel Syndrome 8. Other 9. Diverticulitis 	
Histopathologic Findings			Comment

	Upper GI		
400.01	Esophageal Biopsy	<ol style="list-style-type: none"> 1. Squamous Cell Cancer of the Esophagus 2. Adenocarcinoma of the Esophagus 3. Acute Esophagitis 4. Barret's Esophagus 5. Esophageal Dysplasia 6. Undifferentiated Malignant 7. Normal 8. Inconclusive 	
400.02	Stomach Biopsy	<ol style="list-style-type: none"> 1. Chronic Gastritis 2. Adenocarcinoma of the Stomach 3. Signet Ring Cell Cancer 4. Intestinal Metaplasia 5. Undifferentiated Malignant Tumor 6. Dysplasia 7. NHL of the Stomach 8. Acute Gastritis 9. Stomach Mesenchymal Tumor 10. Stomach MALT 11. Normal 12. Inconclusive 	
400.03	Duodenal Biopsy	<ol style="list-style-type: none"> 1. Dysplasia 2. Celiac Sprue 3. Stromal Tumor 4. Duodenitis 5. Carcinoid Tumor 6. Normal 	

400.04	Colon Biopsy	<ol style="list-style-type: none">1. Chronic Non-specific Colitis2. Colorectal Adenocarcinoma3. Dysplasia4. Schistosoma Colitis5. Acute Colitis6. Adenomatous Polyp7. Lymphoma8. Signet ring Cell Cancer9. Anorectal Squamous Cell Carcinoma10. Benign Colonic Ulcer11. Ulcerative Colitis12. Normal	
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CV of the investigator

CURRICULUM VITE (CV) of the principal investigator

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DECLARATION

I, the undersigned, declare that this thesis is my original work, has not been presented for a degree in this or any other university and that all sources of materials used for the thesis have been fully acknowledged.

Name: _____

Signature: _____

Name of the institution: _____

Date of submission: _____

This thesis has been submitted for examination with my approval as University advisor

Name and Signature of the first advisor

Name and Signature of the second advisor

