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Clinicopathological Correlation of Upper Gastro-Intestinal Endoscopy and Biopsy

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Abstract: In this paper, the author has described the clinic pathological correlation of upper gastro -intestinal endoscopy and biopsy. Until about the time of World War II knowledge of Gastrointestinal Pathology was largely based on autopsy studies which were often erroneous because of tissue autolysis. Although the years between the two World Wars saw the beginnings of an increase in the number of surgically resected specimens, after the Second World War there was a huge increase in the number of gastrectomies and intestinal resections. New techniques of gastric biopsy, small bowel biopsy and colonoscopy biopsy followed and added to the abundance of tissue available to pathologists for the diagnosis and the study of the pathogenesis of gastrointestinal disease.

Keywords: Clinic, pathological, Gastro -Intestinal Endoscopy, Biopsy, Gastroenterology.

INTRODUCTION

Today gastrointestinal pathology is accepted as one of the largest sub-specialties within general histopathology. There has been a steady movement away from old style morbid anatomy and histology during the past 50 years to a greater appreciation of cellular pathology.2Although new techniques, in particular immunities to chemistry and molecular analysis have become popular, especially in research, it is remarkable how the old technique of H and E staining remains the standard for diagnostic purposes.

In humans, the gut is divided into four major organs: Oesophagus, stomach, small intestine, and large intestine. These are separated by sphincters that control the passage of contents from one organ to the next. The junctions between organs are identifiable by an abrupt change in the mucosal nature and by the presence of the sphincters.

The different pathologies that affect gut as a whole or a part there of could be easily divided into those that have an inflammatory etiology or a neoplastic condition which could further be divided into benign and malignant lesions. Hence, all lesions will be divided on the basis of their anatomic origin and their etiologic patho-physiology.

MATERIALS AND METHODS

This study is an observational study performed on the gastrointestinal specimen received from Department of Gastroenterology/Surgery from different tertiary care hospital of Cachar District over a period of 13 months from May 2014- June 2015, after the hospital ethical committee clearance. A total of 222 cases were studied. The study material was obtained from patients admitted and who underwent endoscopic examination and also specimens sent from nearby private or government hospitals in and around Cachar, India.

Inclusion Criteria

All gastrointestinal biopsy specimens received from department of surgery/gastroenterology from different tertiary care hospitals of Cachar district, India.

Exclusion Criteria

None

Following the receipt of surgical specimen in 10% formalin at the Department of Pathology, It was subjected to thorough gross examination according to annexure I and then kept for fixation in 10% formalin for 24-48 hours in the ration of 1:10. After adequate fixation of the specimen the sections were processed and paraffin blocks were prepared. Sections were cut and stained with haematoxylin and eosin stain (Appendix 2). The Giemsa stain was also used to confirm the presence of H. Pylori organism for gastric biopsies. Detailed histopathological features were studied and recorded. Microscopic and gross findings were also documented.

Thereafter, various data were collected from the endoscopy and histopathological findings like various indications for performing procedure, type of lesion identified in the histopathological examination, percentage of cases in which the clinical diagnosis were correlated with the histopathological findings, endoscopic findings were correlated with the histopathological findings, frequency of different gastrointestinal pathologies, pattern of occurrence of different lesions in relation to age and mode of presentation Further, the obtained parameters were evaluated using descriptive statistical analysis; Statistical analyses were performed using the IBM SPSS (Statistical package for the Social Sciences v14.0).

DATA ANALYSIS AND RESULTS

The present study is an observational study of 222 cases of all age groups. The cases either presented to the Department of Surgery/Gastroenterology at various tertiary care hospitals of Cachar District with principal complaints of the Gastro-intestinal system or the biopsies were received in the Department of pathology from private consultants. The same had undergone endoscopies followed by biopsies taken from appropriate sites or underwent resections. The specimens were subsequently sent to the Department of Pathology where the histopathological diagnosis was established. The clinical diagnoses, endoscopic findings and the subsequent histopathological diagnoses were then divided into major classifications i.e. inflammation, strictures, premalignant conditions (dysplastic), malignancies and studied for correlation.

The first attempt was made to find out age and gender incidence in the cases with gastrointestinal complaints.

Table 1: Age distribution in the cases (n=222)

Age	Number	Percentage (%)
Child (1-18 yrs)	6	2.7
Young adult(19-35 yrs)	30	13.1
Adult(36-60 yrs)	115	52.1
Elderly (>60 yrs)	71	32.1
Total	222	100.0

In the present study, maximum number of cases were in the adult group (36-60 yrs) followed by elderly age group (>60 yrs), young adult (19-35 yrs) and child (1-18 yrs).

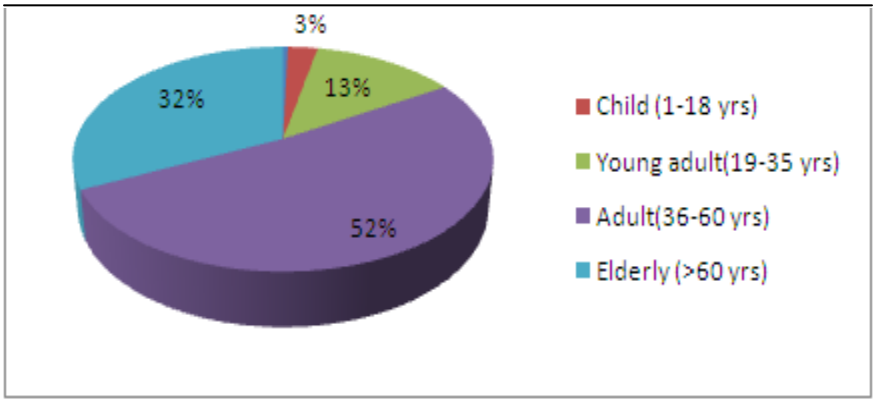

Figure 1: Age Distribution of the cases

Table 2: Gender distribution in the cases (n=222)

Gender	Number	Percentage (%)
Male	135	61.1
Female	87	38.9
Total	222	100.0

A slight male preponderance was observed in the present study with a M:F ratio of 1.6:1.

Table 3: Distribution of Clinical Diagnoses of the cases (n = 222)

Clinical Diagnoses	Number	Percentage (%)
Non specific	4	1.4
Malignancy	98	44.3
Inflammation	117	53.0
Polyp	3	1.4
Total	222	100.0

The commonest (53.0%) clinical diagnosis was Inflammation (117 cases), followed by a substantial number of provisional malignancies (44.3%). 3 cases were deemed to suffering from polyps while a specific clinical diagnosis could not be given in 3 cases.

Table 4: Distribution of Endoscopic findings in the cases (n=222)

Diagnosis	**Number**	**Percentage (%)**
Normal	15	6.3
Malignant	85	39.8
Inflammation	114	50.2
Stricture	8	3.6
Total	222	100.0

Inflammatory changes (50.2%) were the commonest endoscopic finding followed by malignant conditions (39.8%), normal mucosa (6.3%) and stricture (3.6%).

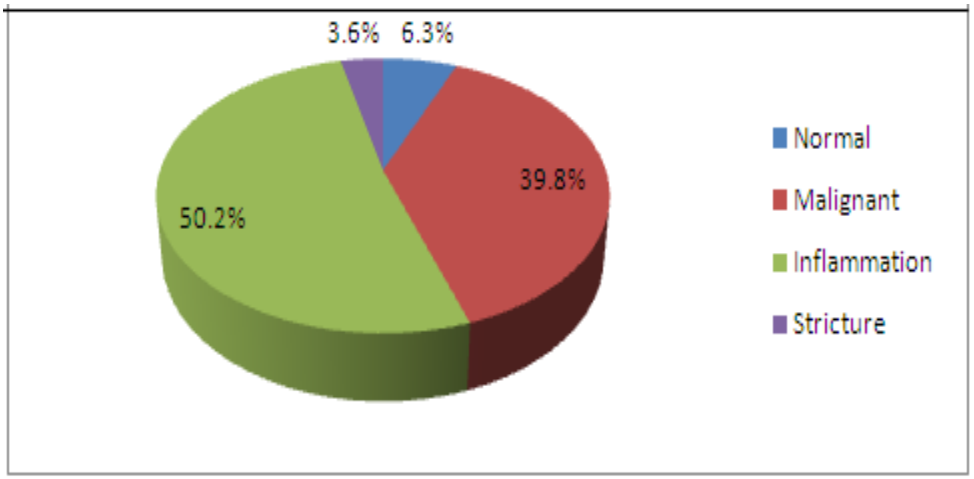

Figure 2: Distribution of Endoscopic Findings (n=222)

Lesions of the Stomach: The commonest pathological diagnoses in the stomach biopsies were gastritis (60 cases) followed by malignant cases.

Intestinal Lesions: Out of the 78 cases that came from the different regions of the intestine, the commonest histopathological diagnosis was that of an inflammatory condition (50 cases) followed by malignancies (19 cases) and premalignant conditions (5 cases). 5 cases were diagnosed without any pathological findings.

Table 5: Correlation Analysis between histopathological findings and clinical diagnoses (n= 222)

	Provisional Clinical Diagnoses					
Histopathological Diagnoses		**Non specific**	**Malignancy**	**Inflammation**	**Polyp**	**Total**
	Normal	0	7	4	2	13
	Malignancy	2	68	5	0	75
	Inflammation	1	7	105	1	114
	Premalignant	0	16	3	1	20
	Total	4	98	117	3	222

105 cases out of the total 117 cases that were clinically suspected to be an inflammation confirmed the same findings histopathologically. However, 5 clinically suspected as inflammatory cases were that of a malignancy, while 4 cases did not show any significant pathological finding.

Out of the 98 cases that were clinically diagnosed as a malignancy, majority of the cases (68 cases) were confirmed as a malignancy on histopathology. 16 cases, however, had premalignant changes while 7 cases had primarily inflammatory changes without any malignant features. 7 cases did not show any significant pathology amongst the 98 malignant diagnoses.

Hence, the provisional clinical diagnoses correlate strongly with the final histopathological findings. This is proven by the fact that Level of agreement is present by kappa and p value is statistically significant (<0.05).

Root Cause analysis of the Discordances

Twenty discordances were encountered in the current study, out of which, fourteen were false positives while six were false negative incidences. There was an attempt made to understand the reasons behind these discordances. A number of reasons have been stipulated for the false negatives and positives in various studies and literature.

Endoscopy allows clear visualization of the mucosa but it is impossible to determine to what extent the normal appearing is the result of increased salivary and mucous production, local compensatory anti-inflammatory mediators or even of altered motility increasing the clearance and rapidly relieving the organ of its contents. These defence mechanisms may be enough to maintain normal mucosa appearance, but not to block the sensitivity of the organ, thus explaining why highly symptomatic individuals may present with normal endoscopic findings.

There is a great deal of ignorance about the normal macroscopic appearance of the gastric mucosal lining. In all probability many of the appearances which endoscopists interpret as normal are presumably not normal. Endoscopic findings such as erythema are frequently labelled as gastritis despite a long recognized lack of evidence supporting a correlation between endoscopic features and histologic gastritis.

The false negative histopathologic results could be due to sampling error and recent or concurrent therapy with drugs. Despite careful selection of the patients having strong indication for the endoscopic biopsy they show normal mucosa on final histopathologic examination. This could be due to improper sampling where in site and depth may not be representative of the clinically suspicious lesion. This also leads to false negative cases. Sometimes poor bowel preparation does not allow the proper visualization of the gastro-intestinal tract mucosa on endoscopic examination.

While false positive cases can occur, if the equipment used previously for some true positive cases and after that not cleaned properly. So they can have remnants of previous tissues and on histopathological examination they show positive findings due to those remnants.

DISCUSSION

As previously mentioned symptoms originating from the GI tract as heartburn, indigestion, dyspepsia, dysphagia, irregular bowel habits, bleeding from the GI tract are very common in every community and they may indicate the presence of underlying disease process. Endoscopy is recommended as the first line investigation during the workup of a patient with GI symptoms. Endoscopic examination is essential to differentiate between organic and functional causes while histopathological examination of a biopsy can determine the exact diagnosis of lesion. The advantage of combining endoscopy with histopathological study of biopsy has been emphasized by various authors in diagnostic grounds. Its importance in diagnosing GI tract lesion has been established.

Various authors studied endoscopic, histopathological correlation in patients with GI symptoms. The data have been published under various headings including site specific and diagnoses headings.

Present study is of 222 cases in which endoscopic biopsies were done and sent for histopathological examination. Histopathological correlation was done for 222 cases, sensitivity and specificity were calculated and found to be 70.11% and 89.55% respectively with respect to detection of malignancy.

Table 6: Age related incidences in lesion of GI tract

Sr. No.	Study	Year	Total cases	Age range yrs	Mean age
1.	Ali A AL Hamalani et al	2001	100	19-75	41.5
2.	Haryanto Rahardjo et al	2006	79	21-70	45.19
3	Amit Kumar Das et al	2006	100	22-75	40
4	Saeed Afzal et al	2006	787	9-85	--
5	Sandhya Panjeta et al	2010	192	19-75	--
6	Stephen et al	2012	190	>18 yrs	59
7	Present study	2015	222	11-84	--

Various authors reported different age range in their studies. Most of them reported wide ranges that included paediatric; adolescent, adult and elderly population of patients with lesions of GIT, present study had patients from age 11 to 84 years. Also, the commonest age of presentation was the adult group. The findings of the present study correlate with the study of Saeed et al.

Table 7: Gender related incidences in lesion of GI tract

S. No	Study	Year	Total cases	Male	Female	M:F ratio
1	Ali A Al Hamlani et al	2001	100	53	47	1.13:1
2	Marioc Vjeira et al	2004	167	88	79	1.11:1
4	Amit Kumar Das et al	2006	100	71	29	2.5:1
5	Sandhya panjetal et al	2010	192	122	70	1.74:1
6	Zaim et al	2011	58	35	23	1.5:1
7	Stephen lewis et al	2012	190	101	89	1.13:1
8	Poudel et al	2013	43	29	14	2.07:1
9	Sherif et al	2014	150	91	59	1.78:1
10	Present study	2015	222	135	87	1.57:1

Male preponderance was observed in the present study, which correlated well with other studies. Few studies observed a higher female preponderance.

Technique

Endoscopy was performed after local anaesthesia of the oropharynx, and occasionally after I.V. injection of diazepam. An endoscopic evaluation of the oesophagus, stomach, intestine was performed as per the clinical complains of the patients and biopsies were taken. The staining quality of the present study was satisfactory. Haematoxylin and eosin stain was use for staining in the present study. The Giemsa stain also used to confirm the presence of H. Pylori organism for gastric biopsies. Z. N. stain for acid fast bacilli was used in case of suspicion of tuberculosis.

Oesophageal cases

Out of the total 222 cases, 61 (27.2%) cases were of oesophagus. The most common lesions were malignant 40 (66.67%) followed by premalignant 14 (23.3%), inflammatory 4 (6.7%) and normal 3 (4.9%). The most common malignancy was SCC (squamous cell carcinoma) of the middle one third of the oesophagus 23/40 (57.5%), followed by lower one third of the oesophagus 10/40, upper one third of the oesophagus 4/40 and adenocarcinoma of the lower one third of the oesophagus 3/40 (7.5%). This finding was similar to that of the study by Krishnappa Rashmi et al[34] Their study showed that most common malignancy was SCC in the middle one third of the oesophagus (73%).

In present study, according to endoscopic findings, out of 61 cases of oesophagus, 45 (75%) cases had malignancy, 8 (13.3%) had inflammation, 6 (10%) had thickening or stricture suggestive of chronic inflammatory process or premalignant lesion and 1 (1.7%) had normal mucosa. Of the 45 cases diagnosed as malignant on endoscopy, 40 were diagnosed as malignant on histopathology. Other 14 cases were diagnosed as premalignant, 4 had inflammation and 3 were normal. 89% of the cases diagnosed endoscopically as malignant correlated with the histopathological diagnosis, while only 50% of the cases diagnosed as inflammatory on endoscopic examination correlated with the histopathological findings. Also 50% correlation was observed in case of normal appearing mucosa.

Mario C Vietra et al41 studied total 167 cases. In that, upper gastrointestinal endoscopy was abnormal in 71 (42.5%) cases, and when these findings were compared with histopathological features, 63 cases showed microscopic abnormalities and 8 cases were normal. Oesophagitis was seen in 76 (79.2%) of the 96 patients with normal endoscopy. Sensitivity of this study was 45% and specificity was 71%, a positive predictive value of 89% and a negative predictive value of 21%. They concluded that endoscopy alone is not acceptable without biopsy, as many true cases of oesophagitis would not be detected and the presence of oesophagitis at endoscopy did not increase the value of the test in predicting the histological abnormality.

Sherif Monier Mohamed et al40 in a study of total 150 cases showed that 99 (66%) patients were diagnosed as non-erosive reflux disease (NERD), 46 (30.7%) patients as ERD and 5 (3.3%) patients as Barrett's oesophagus on the CWL endoscopy, while NBI endoscopy showed NERD in 81 (54%) patients, ERD in 61 (40.6%) patients and BE in 8 (5.4%) patients. Regarding histopathology, 30 (20%) patients were diagnosed as normal mucosa, 102 (68%) patients were diagnosed as erosive oesophagitis, 11 (7.3%) were as BE and 7 (4.7%) were other diagnoses. This study again reaffirms that histopathology remains the gold standard for diagnosis.

The present study concur the findings of the Calabrese et al study which was done on 50 patients and found poor correlation of endoscopy and histopathology in GERD.

The present study presents a good concordance with the study by Kasap et al39, which concluded that histopathological findings were more prevalent then endoscopic changes diagnosed by CWL and NBI endoscopy.

There was a departure from concordance with respect to the findings of Zuberi BF et al wherein where they found significant correlation between the clinical severity of epigastric pain with the endoscopic findings (P= 0.002) and reflux (P= 0.0) but no correlation was observed with the histological findings (P= 0.19)in the 196 patients studied. Out of 109 (55.6%) patients who had normal mucosa on endoscopy but on histopathology 70 (35.7%) of them had inflammation.

Stomach cases

In the present study, 83 (37.8%) cases were of stomach, the most common histopathological diagnoses being inflammatory 60 (72.3%) followed by malignant 16(19.3%), normal 6 (7.2%) and 1 (1.2%) was premalignant.

In the present study, according to endoscopic findings, out of 83 cases of stomach, 56 (67.5%) cases had inflammation, 18 (21.6%) cases had malignancy, 7 (8.4%) had normal and 1 (1.2%) case had stricture. Of the 56 cases diagnosed as

inflammatory on endoscopy, 60 were diagnosed as inflammatory on histopathology. Other 16 cases were diagnosed as malignant, 6 cases were normal and 1 case was premalignant. 93% of the cases diagnosed endoscopically as inflammatory correlated with the histopathological diagnosis, while 89% of the cases diagnosed as malignant on endoscopic examination correlated with the histopathological findings. Also 86% correlation was observed in case of normal appearing mucosa. There is strong correlation between endoscopic and histopathologic findings for the stomach lesions in the present study.

In contrast to present study Podel et al in a study of 43 cases observed that, the correlation of the endoscopic and histopathological findings of the gastric lesions was only 34.88%. So, it concluded that endoscopic diagnoses of gastric lesions poorly correlated with those of histopathological findings.

Abdel M et al90 in a study of 92 cases observed that, according to endoscopic findings 15 (16.3%) cases had normal mucosa, 26 (28.2%) cases had gastritis, 43 (46.7%) cases had duodenal ulcer and 8 (8.7%) cases had peptic ulcer. On histopathological examination, chronic gastritis seen in 12 (80%) cases of normal mucosa, chronic gastritis was present in 42 (97.7%) cases of duodenal ulcer. So there was also poor correlation between endoscopic and histopathological findings.

Intestinal Cases

In the present study, total 221 cases were studied. Out of them, total 78 (35.3%) cases were of intestine, the most common lesions being inflammatory 50 (64.1%) followed by malignant 19 (24.4%), 5 (6.4%) were premalignant and 4 (5.1%) cases were normal.

In present study, according to endoscopic findings, out of 78 cases of intestine, 47 (59%) cases had inflammation, 24 (30.7%) cases had malignancy, 6 (7.7%) had normal and 1 (13%) case had stricture. Of the 47 cases diagnosed as inflammatory on endoscopy, 50 were diagnosed as inflammatory on histopathology. Other 19 cases were diagnosed as malignant, 5 cases were premalignant and 4 cases were normal. 79% of the cases diagnosed as malignant on endoscopic examination correlated with the histopathological findings. There is strong correlation between endoscopic and histopathological findings for the intestinal lesions in the present study.

In contrast to present study Mashako et al observed that, in a study of 31 children suspected of having Crohn's disease were systematically examined to identify upper GI lesions. They all underwent barium transit endoscopy with multiple-level biopsies. Clinical symptoms suggestive of upper GI tract involvement were found in 5 children (16%), radiological signs in only one child (3%), endoscopic lesions in 13 children (42%), and specific granulomas in 12 children (39%).

In eight of these 12 children, the biopsies were taken from grossly normal areas of the oesophago-gastro-duodenal mucosa. One of the 31 children had no abnormal radiological and endoscopic features suggestive of CD on the distal small bowel and the colon. They found no correlation between the clinical, radiological, and histopathological data. Endoscopy plus biopsy provided a positive diagnosis in 39% of cases and a confirmation of the diagnosis in 87% of cases. Endoscopic and histopathological evidence of CD of the upper GI tract is often present despite an absence of clinical symptoms or radiological changes. Upper GI tract endoscopy with multiple biopsies may be important in the evaluation of exact condition and to make final diagnosis.

CONCLUSION

In our study we found that, similar level of sedation was achieved by both dexmedetomidine and midazolam. At comparable sedation levels, dexmedetomidine-treated patients were aroused easily with adequate sedation and required less propofol. The most notable adverse effect of dexmedetomidine was bradycardia which was in acceptable limit.

In conclusion, the data obtained from the study, seems to validate BIS monitoring for ICU sedation. BIS monitoring can be useful in definingan appropriate sedation level in ICU patients while still maintaining the use of the score systems for care for ICU patient.

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