



## Endoscopic findings in patients with refractory dyspepsia at A Tertiary Care Hospital in Peshawar, KPK Province, Pakistan.

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**ABSTRACT... Objectives:** This study was aimed to describe the endoscopic findings in patients with refractory dyspepsia. **Study Design:** Observational study. **Setting:** Rehman Medical Institute Peshawar. **Period:** March 2017- Feb 2019. **Material & Methods:** All the patients who were referred for endoscopy for refractory dyspepsia were included by consecutive non probability sample technique. Data was entered and analyzed on SPSS version 22. **Results:** Out of 727 patients, 51.6% (n=375) were male. Mean age was 43.09±15. 54.30% (n=395) endoscopies were normal. Antral gastritis, Fundal gastritis and Pangastritis were noted in 14% (n=102), 4.40% (n=32) and 8.50% (n=62) patients respectively. Gastroenteritis was found in 5.40% (n=39) while 3.20% (n=23) patients had duodenitis. Reflux oesophagitis was observed in 2.50% (n=18) patients. 1.20% (n=9) had erosions while 0.80% (n=6) had gastric ulcers, 1.20% (n=9) had carcinoma, 2.30% (n=17) had hiatal hernia and 2.10% (n=15) had other gastric pathologies. Functional dyspepsia was seen in 89.9% patients. It was observed more in young age, female gender, and in patients from Afghanistan, frequency being 66.3%, 63.4% and 59% respectively. **Conclusion:** Most patients with refractory dyspepsia had normal endoscopy, it was common in females, young age and Afghanistan patients. Reflux oesophagitis was common pathological finding with predominance in elderly.

**Key words:** Dyspepsia (MeSH), Endoscopy (MeSH), Gastritis (MeSH).

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### INTRODUCTION

Dyspepsia is symptom based diagnosis. A wide spectrum of definitions exist for dyspepsia, but a reasonable one is “epigastric pain or discomfort for at least three months in a patient who does not report predominant heart burn or regurgitation”.<sup>1</sup> The definitive diagnostic test for evaluation of dyspepsia is flexible oesophagogastroduodenoscopy (OGD), which is an invasive procedure carrying a small risk of perforation.<sup>2</sup>

Refractory dyspepsia is a term used to describe dyspeptic symptoms not relieved by acid suppression therapy.<sup>3</sup> Its prevalence is 7-45% globally and 8-30% in Asian population.<sup>4,5</sup> Oesophagitis, peptic ulcer disease(PUD), pylori infection and carcinomas of stomach and esophagus can present with refractory dyspepsia but they usually make small part in etiology.<sup>1</sup> In 70-

80% of refractory dyspepsia cases OGD is normal; they are classified as having functional dyspepsia (FD).<sup>1</sup> Functional dyspepsia is the commonest reason of dyspepsia worldwide<sup>6</sup> and has been defined by Rome IV criteria as “the presence of worrisome postprandial fullness, early satiety, epigastric pain/burning that is thought to originate from the gastroduodenal region in the absence of any organic, systemic or metabolic disease”.<sup>7</sup> Its prevalence is 11-29% worldwide while in Asia it is 8-23% prevalent.<sup>4,5</sup> Refractory dyspepsia is a common condition being addressed very frequently in clinical practice.<sup>5</sup> It doesn't cause any increase in mortality or morbidity as in 80% cases it is functional.<sup>1</sup> However, it imposes considerable effect on patients life and also burdens health care services.<sup>5</sup>

It is difficult to differentiate between organic and functional disease merely on symptoms<sup>8</sup>, and

even the presence of alarm features are not always helpful.<sup>9</sup> OGD is not mandated in the management of dyspepsia, however it is the only tool to establish the underlying etiology of dyspepsia, and also to clarify the diagnosis of functional dyspepsia in the absence of any organic findings.<sup>1</sup> New emerging psychotropic therapies for functional dyspepsia can help these patients once the diagnosis is confirmed.<sup>10</sup> There are different reviews regarding dyspepsia management and evaluation. Test and treat approach is opted by NICE and American guidelines and OGD is only recommended in patients with ALARM features.<sup>3,11,12</sup> A Dutch study described that initial OGD followed by cause directed therapy caused less economic burden than empiric therapy.<sup>13</sup>

Dyspepsia can be due to multiple pathologies in the GI tract. A systematic review based on nine studies included 5389 participants with dyspepsia. OGD findings showed erosive oesophagitis in 13% and peptic ulcer disease (PUD) in 8%, cancers of upper Gastrointestinal tract accounted for less than 0.3% of patients with dyspepsia.<sup>14</sup> Oesophagitis was more in West as compared to Asian population (25% vs 3%), where as PUD was more common cause of dyspepsia in Asians as compared to Western people. (3% vs 11%).<sup>14</sup>

Keeping in view the geographic and ethnic difference in endoscopic findings of dyspepsia, the data from Pakistan is insufficient to present our population.<sup>11,15-17</sup> In KPK region only 1 study has been reported in this regard that included only 50 patients, more over they included all patients with dyspepsia and was not specific to refractory dyspepsia.<sup>16</sup>

This study was aimed to note the endoscopic findings in patients with refractory dyspepsia.

## MATERIAL & METHODS

It was an observational study carried out over a period of 2yrs from March 2017- Feb 2019 after approval from Hospital Ethical committee. All the patients who were referred for endoscopy for refractory dyspepsia were included by consecutive nonprobability sample technique. Patient who had other GI symptoms along with

dyspepsia and also those who were taking drugs (NSAIDs, bisphosphonates, calcium channel blockers, corticosteroids and nitrates) were excluded. Written informed consent was taken from patients. Endoscopy was performed by consultant skilled in technique, visualization up till 2<sup>nd</sup> part of duodenum was carried out and endoscopic diagnosis was made. Patient's demographic profile and endoscopic diagnosis was noted in a pre designed pro forma.

Dyspepsia was defined as per ROME IV criteria as 1 or more of the following 3 symptoms for 3 months within the initial 6 months of symptom onset: (1) post-prandial fullness, (2) early satiety, and (3) epigastric pain or burning. Patients who didn't respond to 3months treatment with PPI or patients who have had H pylori eradications were categorized as refractory dyspepsia.<sup>3</sup>

On upper GI endoscopy, oesophagitis/Gastritis/duodenitis/gastroduodenitis was defined as mucosal edema and erythema in esophagus/stomach/duodenum or both. Superficial mucosal defects of <5 mm in diameter with flat edges that could be red, yellow or white were termed gastroduodenal erosions and Mucosal breaks of >5 mm in diameter were termed as gastroduodenal ulcers.<sup>11</sup>

## DATA ANALYSIS

Data was entered and analyzed through SPSS version 22. Descriptive statistic was calculated for both numerical and continuous variables. For numerical variables percentage and frequency were calculated. For continuous variables mean±SD was calculated. Student T test and Chi-square test were used to look for statistical difference where ever indicated. P value ≤ 0.05 was taken statistically significant.

## RESULTS

A total of 727 patients were included in study. Mean age was 43.09±15. of total study population, 51.6% (n= 375) were male while females accounted for 48.4% (n=352).58.7% (n=427) were Pakistani and 41.3% (n=300) belonged to Afghanistan.

Out of a sample of 727 people, the endoscopic

findings of 54.30% (n=395) turned out normal with no pathology picked up on OGD. Other endoscopic findings are described in Figure-1.

Table-I illustrates the frequency of the different endoscopic findings in different age groups of the sample. Age stratification showed that reflux oesophagitis was more commonly seen in older age group (56-70yrs) as compared to other age groups. The difference is statistically significant. (P value 0.01). Gastroduodenitis was significantly more common in patients aged between 41-55yrs. (P value 0.02) Patients belonging to younger age group (<25yrs) had significantly higher number of normal OGDs. (P value <0.05). No other significant age specific finding was observed.

Table-II illustrates the gender wise endoscopic findings in patients with refractory dyspepsia. The number of patients with normal OGD was significantly higher in females (P value <0.05). There was no significant difference between two genders in terms of other OGD findings.

Table-II. Frequency of the different endoscopic findings in different genders

Table-III describes the endoscopic findings in Pakistani and patients from Afghanistan separately. The frequency of normal OGD was significantly higher in patients from Afghanistan as compared to Pakistani. (P value 0.03). There was no significant difference in other OGD findings in both nations.

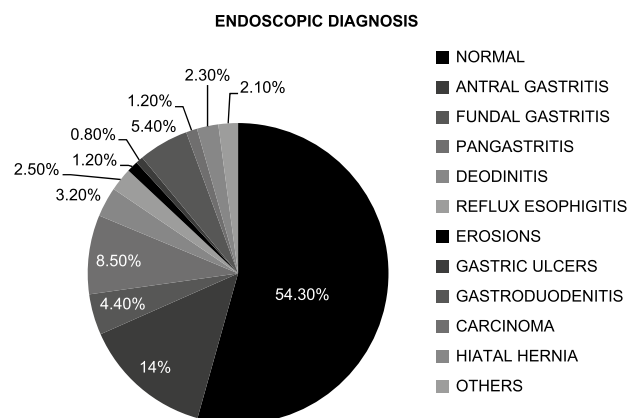


Figure-1. Endoscopic findings of study population

## DISCUSSION

Mean age of our patients was  $43.09 \pm 15$ . Studies conducted in Asia showed relatively younger patients presenting with dyspepsia as compared to Europe.<sup>19,20</sup> In a study conducted in India mean age of patients with refractory dyspepsia was  $41.45 \pm 15.343$ .<sup>19</sup> The mean age of 105 participants was  $36.51 \pm 7.26$  year in a study conducted in Bangladesh.<sup>20</sup> A Study from the US noted average age of patients with dyspepsia as  $48.4 \pm 12.6$ .<sup>21</sup> The mean age of patients was  $58 \pm 16.1$  years in a study from UK.<sup>2</sup>

Male predominance was noted in our study. Most of the other similar studies conducted in different parts of the world observed female preponderance in patients with dyspepsia.

Endoscopic Finding	<25 Years n=86	26-40 Years n=271	41-55 Years n=218	56-70 Years n=118	71 < Years n=34	P-Value
Antral Gastritis	11 (12.8%)	38 (14%)	26 (11.9%)	21 (17.8%)	6 (17.6%)	0.61
Fundal Gastritis	2 (2.3%)	13 (4.8%)	8 (3.7%)	8 (6.8%)	1 (2.9%)	0.55
Pangastritis	6 (7%)	24 (8.9%)	14 (6.4%)	13 (11.0%)	5 (14.7%)	0.38
Gastroduodenitis	1 (1.2%)	11 (4.1%)	16 (7.3%)	6 (5.1%)	5 (14.7%)	0.02
Duodenitis	3 (3.5%)	7 (2.6%)	7 (3.2%)	6 (5.1%)	0 (0.0%)	0.58
Reflux Oesophagitis	0 (0.0%)	5 (1.8%)	4 (1.8%)	8 (6.8%)	1 (2.9%)	0.01
Hiatal Hernia	2 (2.3%)	6 (2.2%)	2 (0.9%)	5 (4.2%)	2 (5.9%)	0.22
Erosions	1 (1.2%)	6 (2.2%)	1 (0.5%)	1 (0.8%)	0 (0.0%)	0.43
Gastric Ulcers	0 (0.0%)	2 (0.7%)	2 (0.9%)	2 (1.7%)	0 (0.0%)	0.71
Carcinoma	0 (0.0%)	3 (1.1%)	4 (1.8%)	2 (1.7%)	0 (0.0%)	0.66
Others	3 (3.5%)	6 (2.2%)	4 (1.8%)	2 (1.7%)	0 (0.0%)	0.78
Normal	57 (66.3%)	150 (55.4%)	130 (59.6%)	44 (37.3%)	14 (41.2%)	<0.05

Table-I. Frequency of the different endoscopic findings in different age groups

Endoscopic Finding	Gender				P-Value
	Male		Female		
	n=375	(%)	n=352	(%)	
Antral Gastritis	58	15.5%	44	12.5%	0.61
Fundal Gastritis	25	6.7%	7	2%	0.55
Pangastritis	36	9.6%	25	7.4%	0.38
Gastroduodenitis	23	6.1%	17	4.5%	0.06
Duodenitis	17	4.5%	6	1.7%	0.58
Reflux Oesophagitis	12	3.2%	6	1.7%	0.17
Hiatal Hernia	5	1.3%	12	3.4%	0.22
Erosions	6	1.6%	3	0.9%	0.43
Gastric Ulcers	5	1.3%	1	0.3%	0.71
Carcinoma	7	1.9%	2	0.6%	0.66
Others	9	2.4%	6	1.7%	0.78
Normal	172	45.9%	223	63.4%	<0.05

**Table-II. Frequency of the different endoscopic findings in different genders**

Endoscopic Findings	Country of Origin				P-Value
	Afghanistan		Pakistan		
	n=300	%	n=427	%	
Antral Gastritis	40	13.3%	62	14.5%	0.65
Fundal Gastritis	14	4.7%	18	4.2%	0.70
Pangastritis	19	6.3%	43	10.1%	0.07
Gastroduodenitis	11	3.7%	28	6.6%	0.08
Duodenitis	10	3.3%	13	3.0%	0.82
Reflux Oesophagitis	4	1.3%	14	3.3%	0.09
Hiatal Hernia	5	1.7%	12	2.8%	0.31
Erosions	4	1.3%	5	1.2%	0.84
Gastric Ulcers	4	1.3%	2	0.5%	0.20
Carcinoma	5	1.7%	4	0.9%	0.38
Others	7	2.3%	8	1.9%	0.66
Normal	177	59.0%	218	51.1%	0.03

**Table-III. Frequency of the different endoscopic findings in different countries of origin**

61.2% of patients were females in a study conducted in the UK,<sup>2</sup> female preponderance at 72.38% was also noted in Bangladesh.<sup>20</sup> Studies from Iran, Italy and India also showed female preponderance in dyspepsia. The reason for this difference can be that Pakhtun females are less likely to get medical attention or not willing to undergo procedure as compared to males.<sup>24</sup> Regarding endoscopic findings, almost half of our patients had normal endoscopic study. This finding is supported by a study carried out in Rawalpindi, Pakistan that reported 58.8% normal endoscopies with patients with refractory dyspepsia.<sup>11</sup> A study from USA also reported 50% normal OGDs in patients with dyspepsia<sup>21</sup>, while in a study carried out in two hospitals in UK showed that 24.4% patients with dyspepsia had

normal OGD.<sup>2</sup> The lower number of normal OGDs in UK may be explained by the fact that the mean age of study participants in the UK was higher as compared to our study population. (58 vs. 43 years.).

Gastritis was the most common abnormality observed by us in our patients; this finding was supported by a study conducted in Rawalpindi and Bangladesh.<sup>11,20</sup>

It has been shown by a meta analysis that reflux esophagitis is less common cause of dyspepsia in Asia as compared to western countries.<sup>1</sup> In our study only 2.5% of our patients suffered from reflux oesophagitis. This finding is also supported by studies conducted in India, Bangladesh and

Pakistan.<sup>11,19,20</sup>

Hiatus hernia was observed in only 2.3% patients. A study carried out in India showed this finding in only 1% of dyspeptic patients undergoing OGD.<sup>19</sup> On the other hand a study from UK stated 35.6% population with dyspepsia had hiatus hernia on endoscopy.<sup>2</sup> The reason for this difference is the well documented fact that prevalence of hiatus hernia is markedly less in Asia as compared to western countries.<sup>25</sup>

Carcinoma was observed only in 1.2% patients. This finding is supported by studies carried out in UK, Brazil and US.<sup>2,12,21</sup> Moreover our patients belonged to middle age group in which gastric Cancers are rarely seen.<sup>26</sup>

Although peptic ulcer disease is prevalent in Asia as compare to the Western countries<sup>1</sup> yet we observed very less number (0.8%) of patients who had ulcers on OGD. Other studies from south Asia have documented relatively larger number of patients with ulcers. 2.3% in a study from Pakistan<sup>11</sup>, 3% from India<sup>19</sup>, 3.8% from Bangladesh<sup>20</sup>, 5.1% from Kashmir.<sup>27</sup> Our this finding is supported by a study from Pakistan and North Kashmir.<sup>11,27</sup> The reason may be that patients with large peptic ulcers usually presents with upper GI bleeding and secondly we included patients with refractory dyspepsia i.e. those who have taken PPI &/or H Pylori eradication therapy for adequate time to heal ulcers.

Functional dyspepsia (FD) is more commonly seen in Asia as compared to Europe.<sup>1</sup> Our study showed that 89.8% of our patients had FD, only 10.2% had organic dyspepsia. In a study from Pakistan FD was seen in 73.1% patients<sup>11</sup>, where as a study from Bangladesh documented 68% of patient suffering from FD.<sup>20</sup> In India, frequency of FD was shown as 39.1% and 70.1% in two different studies.<sup>19,28</sup>

Our study demonstrated significantly higher frequency of functional dyspepsia. This can be explained keeping in view the relationship of functional dyspepsia to psychological stress.<sup>1,29,30</sup> Prevalence of psychological illnesses in KPK is

higher as compared to other areas of Pakistan<sup>31</sup>, especially in young adults.<sup>32</sup> Similarly, it has been documented that there is high prevalence of depressive illness in Afghan population possibly due to the conflict persisting in their country.<sup>33</sup>

FD was more significantly observed in the female gender, amongst Afghan population and in the younger age group (26-40yrs). All these groups are shown to have higher prevalence of depressive illness that can be translated in the form of psychosomatic disorders.<sup>31-33</sup> Among other pathological findings, Reflux esophagitis was significantly more in age group 56-70yrs, finding supported by a study from Pakistan.<sup>11</sup>

Our study represents the 1<sup>st</sup> study from Peshawar, KPK exploring the endoscopic causes of Refractory dyspepsia in a large study population both from KPK and Afghanistan. However, it has some limitations. To begin with, it's a single centered study so the results can't be generalized to the whole population in that area.

Our study highlighted that the major part of refractory dyspepsia is contributed by FD that is more common in young age group, female gender and Afghan population. So these groups should be focused to overcome the disease symptoms as these symptoms usually adversely affect quality of life of patients. Moreover, our study reflects that OGD performed in patients with refractory dyspepsia has not led to the detection of any obvious pathology. Further research is required to promote non invasive investigations/tools that can guide selection of appropriate patients for endoscopic evaluation.

## CONCLUSION

Our study demonstrated that normal OGD finding was the most common pattern seen in patients with refractory dyspepsia, it was found to be more common in females, young age group and patients from Afghanistan. Among pathological findings reflux oesophagitis was more common in elderly patients. Carcinoma, hiatus hernia and peptic ulcer disease were less common findings.



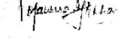
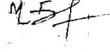

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### AUTHORSHIP AND CONTRIBUTION DECLARATION

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4	M. Fozan Khan	Data acquisition & drafting 2 revising manuscript + final approval	
5	Mohammad Jawad	Data analysis, Interpretation, revising manuscript, Final approval.	
6	Laraib Saeed	Responseve of manuscript	