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Abstract

Background: In this study we determine the response of IBS (C) patient to eradication of *H. pylori*. Irritable bowel syndrome (IBS) is one of the most common gastrointestinal motility disorder leading to poor quality of life. Its symptoms persist for longer time with multitude of presentation including abdominal associated with change in consistency/frequency of stool. It is a multifactorial disorder with mortality, psychiatric disorder and hormones are the most common causes to be blamed for it. Most of IBS patients come as an overlap syndrome with upper and lower gastrointestinal symptoms indicating a possible pathogenic role of *Helicobacter pylori* infestation in causing IBS. With this in mind this study is therefore to observe quality of life of patients with *H. pylori* positive constipation predominant IBS following successful *H. pylori* eradication.

Methods: This descriptive study was conducted at department of gastroenterology in District Headquarter Hospital timergara, Dir Lower, Khyber pakhtoonkhwa from January - 2018 to December - 2019. A total of 112 patients with *H. pylori* positive constipation predominant IBS were recruited after informed consent. Rome # 4 criteria was used for labeling patients as having ibs (c). *H. pylori* infection was diagnosed by serology and LOAD therapy was given for *H. pylori* eradication. Eradication of *H. pylori* was confirmed using stool antigen test conducted 3 months after initial therapy.

Results: Out of 112 patients enrolled 62.5% (n = 70) were male and 37.5% (n = 42) were female. Regarding age wide range of patients population was included with minimum age of 17 years and maximum 65 year and mean of 37 93 years. Out of 112 patients enrolled 83.9% (n = 94) patients were successfully eradicated while 16.1% (n = 18) failed to respond. In successfully eradicated patients quality of life of patients such as abdominal pain and discomfort along with bloating, constipation or its severity, significantly decreased as compared to those in whom eradication was not successful.

Conclusion: Thus, patient with IBS feeling much better after successful *H. pylori* eradication, this subject need further validation to have multi center and randomized controlled studies.

Keywords: Osteosarcoma; Maxillary Sinus; MRI

Introduction

Functional gastrointestinal disorders (FGIDs) account for at least 40% of all referrals to gastroenterologists. Of the 33 recognized adult FGIDs, irritable bowel syndrome (IBS) is the most prevalent, with a worldwide prevalence estimated at 12%, [1]. Which is defined accord-

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ing to Rome # IV Criteria as follows recurrent abdominal pain associated with a change in the frequency of stool, or consistency of stool and this should be fulfilled for the last 3 months with symptoms onset at least 6 months prior to diagnosis [2].

These symptoms occur over a long time, often years [3].

it has been classified into three main types depending on consistency of stool like diarrhea, constipation or mixed type and are named as IBS-D, IBS-C, IBS-M, respectively) [4]. IBS negatively affects quality of life and may result in missed school or work plus increased healthcare cost and reduced health related quality of life [5].

Despite the fact that IBS is a prevalent gastrointestinal disorder, its pathophysiology remains unclear. Anxiety, depression, and chronic fatigue syndrome are common among people with IBS [4]. Also, alteration in gut microbial system and persistent systemic and mucosal subclinical inflammation are common in individuals with IBS [6].

Significant number of patients with IBS also have dyspepsia [7] hinting at a possible pathogenic role of *Helicobacter pylori* (*H. pylori*) in IBS. *H. pylori* is a gram-negative bacterium that infest more than half of the world's population, and it is even more common in developing countries [8]. By infecting the stomach it can either enhanced or dumpen the gastrocolic reflex thus have an active role in causing IBS.

The food ingested by us is digested, absorbed, and excreted by gastrointestinal (GI) tract, and this complex mechanisms is carried by using three distinct centers of control [9]:

- Muscle control: The intrinsic motility rhythm of the intestinal musculature. This rhythm is generated by interstitial cells of Cajal (ICC).
- Hormonal control: This system includes various hormones cholecystokinin, gastrin, and secretin.
- Neural control: This consists of enteric nervous system and the autonomic nervous system [10].

These system work together to properly control motility, secretion, digestion, and absorption by the gastrointestinal system. We in this study primarily focus on hormonal control such as gastro colic reflex either to enhance or slow down the gut motility especially colonic transit.

The gastrocolic reflex is a physiological reflex generated in the stomach after ingestion of meal and affect transit time of colon.

The gastro colic reflex acts to start and controls migrating motor complexes along the whole colon via neurological, muscular and hormonal mediators [11].

Stretch of the stomach by ingestion of food leads to enhanced gastrocolic reflex, which as a results stimulate motility of the colon by heightened amplitude and frequency of migrating motor complexes thus allows room for the consumption of more food.

The gastrocolic reflex initiates cyclical periods of contraction followed by relaxation in sigmoid to propel food distally toward the rectum, resulting in urge to deficate.¹⁰ These contractions are generated in the myenteric plexus and accomplished by the muscularis externa, mediated via hormonal control especially gastrin and motilin.

Enhanced gastrocolic reflex leads to diarrhea predominant IBS whereas poor gastrocolic reflex leads to constipation predominant IBS by lowering the amount of gastrin, motilin and cholecystokinin. One of the example is Diabetic patients where autonomic neuropathy leads to either enhanced or poor gastrocolic reflex which results in either diarrhea or to constipation¹ respectively.

Methods

This descriptive study was conducted at department of gastroenterology and hepatology in District Headquarter Hospital timergara, Dir Lower, Khyber Pakhtunkhwa from January - 2018 to December - 2019. Adult Patients of either gender fulfilling rome #4 criteria were

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included who tested positive for *H. pylori*. Patients with chronic idiopathic constipation, long standing diabetes, thyroid disorders or those taking calcium channel blocker were excluded from this study. The ethical committee of the hospital had given approval to conduct this study. Informed written consent were taken from all enrolled patients. In the included patients complete history and physical was carried out all relevant laboratory investigations imaging like ultrasound were carried out for inclusion and exclusion purposes. Blood sample was taken for Elisa test to diagnose *H. pylori* in the included patients. LOAD therapy consisting of nitazoxanide, levofloxacin, doxycycline and omeprazole was given or ten days. The response was assessed at three month post therapy before conducting stool ELISA test for *H. pylori* to confirm eradication.

We analyzed our data using SPSS version 20. The categorical variable like gender, response to therapy were presented as percentage and frequency while nominal variable like age was presented as mean, minimum, maximum and standard deviation. The analysed data was presented as table, charts and graph.

Result

Out of 112 patients enrolled 62.5% (n = 70) were male and 37.5% (n = 42) were female. Regarding age wide range of patients population was included with minimum age of 17 years and maximum 65 year and mean of 37 93 years. Out of 112 patients enrolled 83.9% (n = 94) patients were successfully eradicated while 16.1% (n = 18) failed to respond. In successfully eradicated patients quality of life of patients such as abdominal pain and discomfort along with bloating, constipation or its severity, significantly decreased as compared to those in whom eradication was not successful.

Response of IBS (c) to H.P eradication

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	94	83.9	83.9	83.9
	No	18	16.1	16.1	100.0
	Total	112	100.0	100.0	



Table 1

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Gender frequency

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Male	70	62.5	62.5	62.5
	Female	42	37.5	37.5	100.0
	Total	112	100	100	





Age distribution of IBS (c) and H.P infection

	Age	Frequency	Percent	Valid Percent	Cumulative Percent
Valid	17	1	0.9	0.9	0.9
	20	6	5.4	5.4	6.3
	22	1	0.9	0.9	7.1
	25	10	8.9	8.9	16.1
	26	1	0.9	0.9	17.0
	27	2	1.8	1.8	18.8
	28	2	1.8	1.8	20.5

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Table 2

30	14	12.5	12.5	33.0
32	2	1.8	1.8	34.8
33	1	0.9	0.9	35.7
35	19	17.0	17.0	52.7
36	1	0.9	0.9	53.6
38	3	2.7	2.7	56.3
40	12	10.7	10.7	67.0
41	1	0.9	0.9	67.9
44	3	2.7	2.7	70.5
45	5	4.5	4.5	75.0
46	1	0.9	0.9	75.9
50	16	14.3	14.3	90.2
52	1	0.9	0.9	91.1
55	2	1.8	1.8	92.9
60	7	6.3	6.3	99.1
65	1	0.9	0.9	100.0
Total	112	100.0	100.0	
50 52 55 60 65 Total	16 1 2 7 1 112	14.3 0.9 1.8 6.3 0.9 100.0	14.3 0.9 1.8 6.3 0.9 100.0	90.2 91.1 92.9 99.1 100.0

Table 3



Discussion

The aim of this study was to determine the association *H. pylori* in the pathogenesis of IBS. As we mentioned IBS is a chronic illness with poly symptomatology that's why its called a syndrome. Different criteria were used to define IBS in different times but currently Rome 4 criteria is used; which define it as recurrent abdominal pain associated with:

- a. Related to defecation.
- Associated with either a change in the frequency or consistency of stool. These symptoms occurs at least 1 day/week in the last 3 months with symptom onset at least 6 months prior to diagnosis [13].

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102

Worldwide prevalence of IBS is upto 20% amongst adult population. Male to females ratio is 1:2 and female are more likely than men to visit a doctors [14-16].

Factors such as visceral sensitivity, intestinal dysmotility, psychosocial issues and inflammation [13] are factors consider responsible for symptoms of IBS. Visceral hypersensitivity is the main factor responsible for abdominal discomfort or pain and gastrointestinal motor disturbances leading to either diarrhea or constipation [17,18]. Some studies consider psychological disturbances as the primary factor responsible for symptoms of IBS however, not all patients with IBS have significant psychological issues and referral bias may partly account for the psychological associations [17,18].

Furthermore, in one trial rectal barostat study was conducted to elicit signs symptoms typical of irritable bowel syndrome abdominal in patients with IBS, positive symptoms were mostly seen in IBS patients having positive test for *H. pylori*, suggesting a potential role of *H. pylori* in altering intestinal modality [20] by visceral hypersensitivity. Preclinical and clinical studies have often reported an association between increased visceral hypersensitivity and changes in sensory-motor function [21,22].

As such, *H. pylori* infection may lead to gastric dysmotility and altered visceral hypersensitivity and thus leads to typical IBS symptoms, having said that *H. pylori* my affect the colonic mortality via gastrocolic reflex. Enhanced gastrocolic reflex leads to diarrhea while poor reflex leads to constipation. This causation of different type of gastrocolic reflex is may be because of *H. pylori* infesting different area of the stomach.

For example, if it infect the antral area of the stomach it may leads to enhanced gastro- colic reflex by stimulating excessive secretion of gastrin and motilin. Also, if it infect body and fundus then it will lead to poor gastrocolic reflex by reducing acid production and thus decreased production of gastrin and motilin through negative feed back system. Thus, in this case if we eradicate *H. pylori* it will enhanced the gastro colic reflex and increase the colonic mortality and improvement in IBS symptoms especially with constipation which I observed during my study. Alteration in the gastrocolic reflex has been a suspected etiology in patients with irritable bowel syndrome (IBS). Patients with IBS have demonstrated a stronger colonic response to the gastrocolic reflex. These patients may experience a strong urge to defecate following ingestion of a meal and may experience symptoms like abdominal distension, flatulence, pain, and tenesmus [23]. Some studies suggest that diarrhea predominant IBS are caused by heightened gastrocolic reflex, whereas poor gastrocolic reflex leads to constipation predominant IBS [24].

To diagnose *H. pylori* two methods are used. Invasive methods, such as endoscopy, which is unpleasant but are highly sensitive and specific and have the added advantage of sampling at the exact target location. The Kimberly-Clark CLO- test is a form of the rapid urease test which is highly accurate, convenient and affordable [25].

Second method is non - invasive such as serology to diagnose the *H. pylori*. Because most of the people are using antibiotics and PPI on daily basis which is available as over the counter medicine in our locality so using the gold standard test such as histology and urease tests which is affected by PPI and Antibiotics on the first visit was not possible. So, we used serology to confirm *H. pylori* infection in IBS (C) patients. The serum *H. pylori* antibody test had high sensitivity and specificity and it was a good diagnostic screening tool in one of the study [26]. Then after completing 14 days of LOAD therapy the patients included in this study were counseled not to take antibiotics for 4 weeks and ppi for 2 weeks and stool antigen test for *H. pylori* was repeated to confirm eradication rate. Also, response of the patients having IBS (C) was assessed in those who were successfully eradicated.

Conclusion

From this observational study it come to the surface that the prevalence of h pylori in patients with constipation predominant IBS is a common finding in our population. Also, to be noted that after eradication of *H. pylori* there is significant improvement of constipation. This study can lead to further insight and more attention for validation for permanently ameliorating the misery of this suffering population.

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104

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