



## Original Article

## Treatment Modalities in Irritable Bowel Syndrome in a Tertiary Hospital in North India

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## ARTICLE INFO

## A B S T R A C T

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**Background:** Irritable bowel syndrome (IBS) is a common functional gastrointestinal disorder, affecting 4 to 26% population worldwide. Multiple risk factors are associated in pathophysiology of IBS; accordingly its therapy employs different categories of drugs. **Aim:** The study aimed to monitor the therapy in different types of IBS patients and to identify the most effective mono or combination drugs used. **Patients and Methods:** This prospective, observational study was carried out from January to September 2012 in New Delhi, India. Based on Rome III inclusion/exclusion criteria, 169 patients of IBS were recruited for the study and data on the pertinent parameters was obtained using; patient profile and follow-up proforma, structured questionnaire, ADR form and pathology laboratory test reports. **Results:** The results from a total of 169 IBS patients depict; higher percentage of males (57.39%), non-vegetarian (79.88%), sedentary (68.63%), non-smokers (72.78%), in age group 21- 40 years (72.78%). The treatment modalities in IBS depend upon symptoms, severity and types of IBS. In current study the combinations drugs were commonly prescribed and found to be more effective in controlling IBS symptoms. **Conclusion:** It can be concluded that combination therapy is common and superior to monotherapy. Conventional medicines, like; antispasmodics, bulking agents, and antidepressants etc., were not as much effective to control the symptoms and severity of IBS. A number of emerging therapies with novel mechanisms of action are currently being investigated in IBS; the practitioners may explore their efficacy and safety. **Keywords:** Irritable bowel syndrome, constipation, diarrhea, epidemiology

## 1. INTRODUCTION

Irritable bowel syndrome (IBS) is a common, relapsing, functional gastrointestinal disorder (FGID) encountered in clinical medicine. <sup>1</sup> It affects 4% to over

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26% of the population in different countries; being higher in the developed West, while lower in the developing Asian nations. In India, the prevalence of IBS<sup>2</sup> is 4.2%, reported more often in male than female<sup>3</sup> and more common in the age groups of 20–50 years.<sup>4</sup> In North India it affects 4% of the population.<sup>5</sup> The overall symptom profile of IBS includes chronic abdominal pain or discomfort and alterations in bowel habits<sup>6</sup>, with male patients more commonly reporting diarrhea and females constipation as their predominant bowel pattern.

Irritable bowel syndrome is categorized as diarrhea-predominant (IBS-D), constipation-predominant (IBS-C), or mixed-type (IBS-M). The pathophysiology of IBS is still not well understood but is most probably multifactorial.<sup>7</sup> Several factors such as; motor and sensory dysfunction, neuro-immune mechanisms, psychological factors and changes in the intraluminal milieu appear to play a role. The increased release of serotonin into the circulation and increased serotonin proteases (derived from mast cells) in stools of patients with IBS argue increasingly for the potential role of neurotransmitters in mediating the disorder and the potential of pharmacological agents targeting these mechanisms.<sup>8</sup>

Conventional IBS therapies are mainly of symptomatic approach because the exact mechanism for development of IBS is unknown e.g. antidiarrhoeals for diarrhea, laxatives for constipation or smooth muscle relaxants for pain. These measures help alleviate symptoms but do not cure the condition; also their efficacy is often limited in addressing the overall symptom cascade. Hence, there is a need for a definitive targeted treatment approach for this highly prevalent disease. Increasing knowledge of the pathophysiology and potential mechanistic targets provide the basis for the development of new therapeutic modalities for IBS.<sup>9</sup>

The study was aimed to establish the IBS data and enhance therapeutic outcomes in selected geographical set of population by monitoring the therapy in different types of IBS patients in North Indian tertiary hospital, to identify the most effective mono or combination drugs used.

## 2. METHODOLOGY

This prospective and observational study was carried out from January to September 2012 in the Medicine outpatient department (OPD) of HAH Centenary Hospital, Jamia Hamdard, New Delhi, India to monitor the therapy in different types of IBS patients and to identify the commonly prescribed mono or combination drugs therapy in North Indian population.

### 2.1 Ethical consideration

The study protocol was reviewed and approved by institutional review board of Jamia Hamdard University New Delhi, India. Ethical practice was critically observed with regard to Patients' willingness to participate in the study, informed consent, painless procedures, no additional intervention, etc. The patient details and data were kept confidential and were accessible only to the study personnel and to the Jamia Hamdard Institutional Review Board.

### 2.2 Study sample

All Irritable bowel syndrome patients visiting the medicine OPD of the HAH hospital were considered for enrollment in the study if they had 3 months history of IBS symptoms diagnosed using the Rome III criteria, administered questionnaire based on the world gastroenterology organization, and are willing to participate. Exclusion criteria for the study included if patients were mentally challenged, unconscious, patients with diarrhea that was of non-IBS etiology, drug addicts, refuse or unable to comply and age less than 10 years. Based on the inclusion and exclusion criteria a total of 169 IBS patients were recruited for the study. The objectives, duration and protocol of the

study were explained and a signed informed consent form was obtained from 169 IBS patients who agreed to participate in the study. All the participants were ensured confidentiality.

**Table 1: Socio-demographic characteristics of IBS patients (N=169)**

Characteristic	Frequency (percent)		Total number (%)	Chi square P- value
	Male	Female		
<b>Gender</b>	97 (57.39)	72 (42.60)	169 (100)	-
<b>Age group (years)</b>				
11-20	8 (8.25)	6 (8.33)	14 (8.28)	0.349
21-30	33 (34.02)	19 (26.39)	52(30.77)	
31-40	38 (39.17)	23(31.94)	61 (36.1)	
41-50	14 (14.43)	16 (22.22)	30 (17.75)	
51-60	2 (2.06)	5 (6.94)	7 (4.14)	
61-70	2 (2.06)	3 (4.17)	5 (2.96)	
Mean age (years) ±SD	32.92±10.13	36.06±12.2	34.47±10.89	
<b>Dietary habit</b>				
Vegetarian	14 (14.43)	17 (23.61)	31 (18.34)	0.304
Non vegetarian	81(83.51)	54 (75)	135 (79.88)	
Eggetarian	2 (2.06)	1 (1.39)	3 (1.77)	
<b>Type of food</b>				
Home made	41(42.27)	52 (72.22)	93 (55.03)	0.0001*
Marketed	56 (57.73)	20 (27.78)	76 (44.97)	
<b>Smoking</b>				
Smoker	33 (34.02)	13 (10.06)	46 (27.22)	0.021*
Non smoker	64 (65.98)	59 (81.94)	123 (72.78)	
<b>Alcohol</b>				
Alcoholic	37 (38.14)	10 (13.89)	47 (27.81)	0.0005*
Non alcoholic	60 (61.86)	62 (86.11)	122 (72.19)	
<b>Life style</b>				
Sedentary	70 (72.16)	46 (63.89)	116 (68.63)	0.251
Locomotive	27 (27.84)	26 (36.11)	53 (31.36)	
<b>Socio-economic Class</b>				
Upper I	11(11.34)	6 (8.33)	17 (10.05))	0.718
Upper-middle II	23(23.71)	14 (19.44))	37 (21.89)	
Middle/ Lower III	36 (37.11)	26 (36.11)	62 (36.68)	
Lower/ Upper lower IV	18 (18.56)	15 (20.83)	33 (19.52)	
Lower V	9 (9.28)	11(15.28)	20 (11.83)	

**2.3 Data collection**

IBS Data were collected using the Physicians prescribing records, patient’s medical profile, structured questionnaire, and adverse drug reaction proforma and pathology laboratory test reports. Following parameters were recorded:

- i. Sex distribution
- ii. Age distribution
- iii. Type of Diets Vegetarian and Non-Vegetarian

- iv. Types of food eg, homemade and junk food
- v. Habits eg, Smoker and Non-smoker
- vi. Alcoholic and Non-alcoholic
- vii. Socioeconomic Class
- viii. Type of IBS (IBS-C/ IBS-D/ IBS-M)
- ix. Number and categories of drug prescribed
- x. Change in dose and frequency of drug
- xi. Recurrent condition of the disease, if any
- xii. Adverse drug reactions

**2.4 Statistical Analysis**

Data were analyzed using SPSS v. 13.0. Categorical data are described using frequency distribution and percentages. Chi square test was used to check the statistical significance and P value < 0.05 was considered as significant.

**Table 2: Prevalence of subtypes of IBS in study population**

Type of IBS	Total (n=169) N (%)	Male (n=97) N (%)	Female (n=72) N (%)	Chi square P-value
IBS-D	73 (43.19)	50 (51.55)	23 (31.94)	
IBS-C	41 (24.26)	14 (14.43)	27 (37.5)	
IBS-M	46 (27.22)	28 (28.86)	18 (25)	0.004682*
IBS-U	9 (5.32)	5 (5.15)	4 (5.56)	

IBS: Irritable bowel syndrome; IBS-D: IBS diarrhea predominant; IBS-C:IBS constipation predominant;IBS-M : IBS mixed; IBS-U : IBS unsubtype. \*There is a highly significant difference in the prevalence of IBS in study population.

**3. RESULTS AND DISCUSSION**

Of the 169 IBS patients recruited for the study, 97 (57.39%) were males and 72 (42.6%) were females, indicating that IBS is slightly more prevalent in the male gender (male: female ratio, 1.35:1), an observation in confirmation to the report by Ghoshal et al., (2008)<sup>3</sup>. It could be because of the predominance of certain risk factors for IBS in male as compared to that in females, such as psychological factor or unhygienic dietary habits. The mean age of male and female participants was 32.92±10.13 and 36.06±12.2 years respectively. Age distribution in the sample showed that the disease was more prevalent in young adulthood as 72.78% of the patients were between 21 to 40 years of age. The similar finding was also reported in another study.<sup>10</sup> The maximum number of male and female

IBS patients belonged to the age group of 31 to 40 years. However, many previous studies conducted across the globe concluded that prevalence of IBS is higher in the younger age group than the older age groups (Table 1).

It is a well established fact that low prevalence of IBS is associated with high intake of vegetables or fiber rich diet and very often fiber-free processed foods is attributed as the cause of IBS. Our study results are in consistent with the above mentioned fact and as expected, majority (79.88%) of our patients were non-vegetarians, where as vegetarian and eggetarian patients accounted for only 18.34 and 1.77 % respectively. Approximately 55% of study population preferred homemade food over marketed food.

Among 169 participants, two third (68.63%) had sedentary life style and approximately one third (31.36%) had locomotive life style, showing that IBS is more common in sedentary life style patients. The role of smoking and alcoholism in IBS patients is not fully understood, however, a study by Burns<sup>11</sup> reported that the prevalence of IBS were more in non-smoker patients and they suggested that the effect of smoking may be mediated through psychosomatic factors or other factors affecting gut motility. In our study a significant number of participants were non smokers (72.78%,  $p=0.0211$ ) and non alcoholics (72.19%,  $p=0.00051$ ) respectively.

In an attempt to draw a correlation between IBS and quality of life, we recorded distribution of patients in respective socioeconomic scale. It was observed that majority of the study participants (36.68%) were from middle /lower middle-socioeconomic class (III) and least number of IBS patients belonged to upper I socioeconomic class. The data given in the table 1 suggest that the most common affected group is below the upper level socioeconomic class and it is evident that IBS is more common in lower socioeconomic

group. A Similar study also reported that IBS is more common in lower socioeconomic groups.<sup>12</sup>

IBS subtypes summarized in Table 2 illustrates that the predominant IBS subgroup in study population and among male participants was IBS diarrhea predominant (IBS-D), to which 43.19% and 51.55% respectively belonged. However, IBS- constipation predominant (IBS-C) subtype was more prevalent in females (37.5%), a finding consistent with the previous studies that women have more symptoms of non-pain related gastrointestinal symptoms such as nausea, constipation and bloating, whereas men report more diarrhea.<sup>13</sup> A significant difference was observed in the prevalence of subtypes of IBS between male and female participants ( $p=0.0047$ ). Several physiological factors may play a role in these gender-related differences in self reported bowel habits, including differences in central autonomic control, in enteric nervous system physiology and smooth muscle physiology.<sup>14</sup>

Treatment modalities for IBS, in general, depend on symptoms pattern (e.g., constipation versus diarrhea predominance) and severity (e.g., mild to severe, as characterized by symptom intensity and functional impairment). As severity worsens, pain, other gastrointestinal discomforts (e.g., bloating), and perceptions of bowel dysfunction often become dominant. Conventional medicine such as antispasmodics, bulking agents, and antidepressants are frequently prescribed for IBS. But, they are rarely efficacious in patients with advanced symptoms. Also due to the complexity of IBS, it is very difficult to identify a single drug that can ameliorate all the associated symptoms, therefore, patients are often dissatisfied with the efficacy and adverse effect profiles of conventional therapies. This leads to multiple doctor visits and frequent medication switching or augmentation – factors that often lead to increased medical costs.

**Table 3: Single drug therapy prescribing pattern in subtypes of IBS in study population.**

Drug category	Single drug therapy	No. of Patients		
		IBS-D	IBS-C	IBS-M
Antispasmodic	Mebeverine HCl	09	05	-
	Hyoscine butylbromide	07	-	-
Antidepressant	Amitriptyline	07	-	-
	Escitalopram	08	10	13
	Dothiepin	11	-	07
	Livosulpride	-	05	-
Proton pump inhibitor	Pantoprazole	08	08	07
	Rabeprazole	07	05	05
Laxative	Ispagula husk	-	11	-
	Ispagula husk with curd	08	-	09
Anthelmintic	Mebendazole	06	05	05
	Ivermectine	07	04	04
	Albendazole	07	05	04
	Metronidazole	08	-	-
Others	Alprazolam	06	07	-
	Clonazepam	08	05	09

**Table 4: Combined therapy prescribing pattern in subtypes of IBS in study population**

Category	Combination therapy	No. of Patients		
		IBS-D	IBS-C	IBS-M
Antispasmodic	Chlordiazepoxide + Dicyclomine + Clinidinium bromide + Ranitidine	14	03	14
	Chlordiazepoxide + Dicyclomine + Clinidinium bromide	08	06	07
Proton pump inhibitor	Pantoprazole + Domperidone	18	06	10
	Rabeprazole + Domperidone	07	05	04
	Pantoprazole + Levosulpride	-	03	03
Laxative	Lactilol monohydrate + Ispagula husk	-	05	-
Probiotic	Lactobacillus acidophilus + Bifidobacterium longam	26	11	12
Nitroimidazole	Ofloxacin + Ornidazole	15	-	10
Others	Vitamin B complex	09	-	-
	Sucralfate + Oxetacaine	-	05	-

In the current study the commonly prescribed single drug therapy in IBS – D are; Mebeverine hydrochloride (Antispasmodic), Dothiepin (Antidepressant), Pantoprazole (Proton pump inhibitor), Ispagula husk with curd (Laxative), Metronidazole (Anti-amoebic), Clonazepam (Anti-depressant or Anti-anxiety) (Table 3). Whereas, in combined drug therapy for IBS-D the preferred prescribed combinations are; {Chlordiazepoxide+ Dicyclomine+ Clinidinium bromide+ Ranitidine}, {Pantoprazole+ Domperidone,

Lactobacillus acidophilus+ Bifidobacterium longam}, {Ofloxacin+ Ornidazole} and Vitamin B complex (Table 4).

In case of IBS-C, most common single drug therapy is Mebeverine hydrochloride (Antispasmodic), Pantoprazole (proton pump inhibitor), Escitalopram (Antidepressant), Isbagol husk (Laxative) and Alprazolam (anti-anxiety) (Table 3). Whereas, in combined drug therapy the commonly prescribed combinations are; {Chlordiazepoxide+ Dicyclomine+ Clinidinium bromide}, {Pantoprazole+ Domperidone}, {Lactilol monohydrate+ Isbagol husk}, {Lactobacillus acidophilus+ Bifidobacterium longam}, {Sucralfate+ Oxetacaine} (Table 4).

In case of IBS-M the combinations were commonly prescribed; {Chlordiazepoxide+ Dicyclomine+ Clinidinium bromide+ Ranitidine}, {Pantoprazole+ Domperidone}, {Lactobacillus acidophilus+ Bifidobacterium longam} and {Ofloxacin+ Ornidazole} (Table 4). Escitalopram Ispagula husk with curd, and Clonazepam were observed to be the most commonly used mono therapy (Table 3).

#### 4. CONCLUSION

Many scientific published reports have confirmed the efficacy of antidepressants in IBS and other functional gastrointestinal disorders but adjunctive treatment is required for management of other IBS symptoms.<sup>15</sup> Our study results clearly show that prescriber prefer combination therapy over mono therapy to manage IBS. Antidepressants were the most commonly prescribed monotherapy in IBS- C and M while in IBS-D, antihelmintics were frequently prescribed followed by antidepressants. The results of the current study also showed that majority of the patients who came regularly for the follow up were on combination therapy and were satisfied with the treatment outcome. Thus it can be concluded that in this geographical set of population combination therapy suits better than

mono therapy and the choice of medicine is based on the most troublesome symptom of patients (Table 3&4).

A number of emerging therapies with novel mechanisms of action are currently being investigated in IBS, hence practitioner should search which emerging therapies have more efficacy and less side effects.

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