International Journal of Medical and Health Research
ISSN: 2454-9142, Impact Factor: RJIF 5.54
www.medicalsciencejournal.com
Volume 3; Issue 8; August 2017; Page No. 28-33

Epidemiology and clinical profiling of constipation predominant irritable bowel syndrome in India

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Abstract
Irritable bowel syndrome (IBS) is regarded as disorder of brain gut axis, with altered central nervous system processing. Limited data is available regarding epidemiology and clinical profiling of constipation predominant IBS (IBS-C) in the general Indian constipated population. Hence the present study was conducted to evaluate the demographics, socio-economic and clinical characteristics in these patients. Patients (≥18 years) satisfying Rome-III criteria for IBS-C were enrolled in this prospective, multicentric, clinico-epidemiological study. Their demographics, socioeconomic status (Kuppuswamy scale), comorbid conditions, concomitant medications, severity of constipation (constipation scoring system [CSS]), constipation-related symptoms (patient assessment of constipation symptoms [PAC-SYM]) and quality of life (PAC-QoL) were assessed. Out of 925 patients of constipation, 226 (24.43 %) patients fulfilled the Rome-III criteria for IBS-C were enrolled; rest of 75.57 % patients had functional constipation. Mean age of study population was 43.8 ± 16.3 years (men: 65.5%; women: 34.5%); higher proportion of patients were from urban population compared to rural (62.0 % vs. 38.1 %). Patients had higher mean scores of education and occupation and belonged to upper socio-economic class. Patients had higher mean scores of PAC-SYM (30.1±4.9) and CSS (11.2±3), leading to poor quality of life (PAC-QoL: 42.2±13.6). Acid peptic disorders (APD; 21.7%) and hypertension (13.7%) were the most common comorbidities reported. Laxatives (50.9%), drugs for APD (40.7%), antihypertensive (14.2%) and antianxiety/antidepressants (12.8%) were the most commonly used concomitant medication. Higher educational/occupational scores point towards increased stress/anxiety, which could be attributed to dysfunctional brain-gut axis in IBS. Patients with IBS-C reported high frequency and severity of constipation-related symptoms, thereby leading to poor QoL. Moreover, these patients had higher prevalence of APDs, thus highlighting the need to identify the presence of upper gastrointestinal comorbidities in IBS patients. This study thus emphasizes the necessity for a multi-faceted approach for holistic management of IBS.

Keywords: IBS, IBS-C, CSS, PAC-SYM, PAC-QoL

Introduction
Irritable bowel syndrome (IBS) is the one of the most common gastrointestinal disorder with a worldwide prevalence of upto 20%.[1] IBS is a chronic, continuous or intermittent illness wherein the patient has frequent and unexplained symptoms that include abdominal pain, bloating and bowel disturbance [1] IBS is today accepted to be a multifactorial disorder, associated with altered central nervous system processing.[1] Many IBS patients also experience comorbid behavioural disorders, such as anxiety or depression. Stress is an important etiological factor associated with development and exacerbation of visceral pain symptoms. Chronic stress modifies central pain circuitry, and it gastrointestinal motility and permeability [1, 2, 3, 4, 5].

IBS has been globally reported to adversely affect a patient's quality of life (QoL), irrespective of their culture or nationality.[5] In spite of an increasing trend in IBS cases across India, limited data is available regarding the epidemiology and clinical profile of IBS-C in Indian patients with constipation. Hence, the present epidemiological study was conducted to evaluate the prevalence of IBS-C in Indian patients along with assessment of their demographics, socioeconomic status, usage of constipation-related medications and comorbid conditions. The present study also aimed to evaluate the relationship between severity of constipation and QoL in IBS-C in Indian patients.

Methods
Study site details
A non-interventional, prospective, cross-sectional, clinico-epidemiological, single visit study was conducted across 20 centres in India (3 centres each at Kolkata, Mumbai, Ahmedabad and Jaipur and 2 centers each at Bangalore Chennai, Delhi and Pune) from November 2014 to March 2015. The study was conducted in accordance with the Declaration of Helsinki, International Conference on Harmonization of Good Clinical Practice guidelines, Indian Council of Medical Research, Indian Good Clinical Practice guidelines and the approved protocol. The study protocol was approved by the respective institutional ethics committee in each centres.

Study inclusion and exclusion criteria
Consecutive patients of age ≥18 years who visited their general physician with symptoms of constipation fulfilling Rome III criteria for IBS-C as per physician assessment and willing to sign the patient authorization form were invited to participate in the study. Patients who had intestinal obstruction, acute

abdomen (sudden, severe abdominal pain of unknown etiology), any disease with the potential to precipitate intestinal obstruction, pregnant or lactating females were excluded from the study.

Study variables

The patients were asked questions related to their demographics, socioeconomic status, frequency and severity of constipation symptoms, QoL, treatment and medical history, concomitant medications and co-morbid conditions. The socioeconomic status, frequency of symptoms, severity of constipation and QoL, was assessed by Kuppuswamy socioeconomic status scale [3], Patient Assessment of Constipation symptoms (PAC-SYM), Constipation Scoring System (CSS) and Patient Assessment of Constipation-Quality of Life questionnaire (PAC-QoL) respectively. Since the predominant population for this study was urban, the Kuppuswamy scale (latest version 2014) was used to evaluate data on the socioeconomic status based on occupation, education and family income. These questionnaires were administered to the patients by the investigator or the trained designee, enabling accuracy and confidentiality of the collected data (standard English versions were used).

There was no pre-determined statistical hypothesis tested. Descriptive statistics (generated using Statistical Analysis System® version 9.3 software) was used to summarize the variables; the continuous variables were summarized by counts, mean ± standard deviation, median, range and the categorical variables were summarized by frequency and percentages. The P value for the continuous and categorical data was calculated using 2-sample t-test and chi-square test, respectively, with two-sided significance level $\alpha = 0.05$.

Results

Patient demographics

Out of 925 patients of constipation, 226 (24%) patients who fulfilled the Rome-III criteria for IBS-C were enrolled; rest of the 76% patients had functional constipation. Mean age of study population was 43.8 ± 16.3 years (men: 66%; women: 34%). A higher proportion of patients were from urban population as compared to rural (62% vs. 38%).

Socioeconomic Characteristics

Patients had high mean scores of education and occupation and belonged to upper/upper middle socio-economic class, as assessed by Kuppuswamy scale (Table 2).

Table 1: Prevalence of IBS-C in Different Age Groups

Age group	% prevalence IBS-C
18 – 40 years	114 (50. 44%)
41 – 60 years	71 (31.41%)
61- 80 years	38 (16.81%)

Table 2: Kuppuswamy Socioeconomic Scale

	Mean±SD N = 226
Education [A], mean ± SD	4.7 ± 1.6
Occupation [B], mean ± SD	4.4 ± 3.5
Family income [month [C], mean ± SD	7.1 ± 3.6
Total score [A+B+C], mean ± SD	16.2 ± 7.0
Socio-economic class	
Upper= 26-29	18%
Upper middle = 16-25	34%
Lower middle = 11-15	21%
Upper lower = 5-10	27%
Lower ≤ 5	0

Total score was calculated by adding the mean scores of education, occupation and family income of these patients, based on which the socioeconomic class was determined. Recent (2014) version of Kuppuswamy scale was used.

Table 3: Clinical Parameters

Class	Mean±SD N = 226
Patient Assessment of Constipation Symptoms[a] (mean ± SD)	
Discomfort in your abdomen	2.5 ± 1.0
Pain in your abdomen	2.4 ± 0.8
Bloating in your abdomen	2.6 ± 1.1
Stomach cramps	1.8 ± 0.9
Painful bowel movements	1.9 ± 1.0
Rectal burning during or after a bowel movement	1.7 ± 0.9
Rectal bleeding or tearing during or after a bowel movement	1.2 ± 0.5
Incomplete bowel movement, like you didn't "finish"	3.5 ± 0.9
Bowel movements that were too hard	3.3 ± 1.0
Bowel movements that were too small	3.3 ± 0.9
Straining or squeezing to try to pass bowel movements	3.7 ± 1.1

Feeling like you had to pass a bowel movement but you couldn't (false alarm)	2.2 ± 1.2
Composite mean score of PAC-SYM	30.1 ± 4.9
Constipation ScoringSystem[b] (mean±SD)	
Frequency of bowel movements	0.1 ± 0.3
Difficulty: painful evacuation effort	1.4 ± 1.4
Completeness: feeling incomplete evacuation	3.1 ± 1.1
Pain: Abdominal pain	2.4 ± 1.4
Time: minutes in lavatory per attempt	1.6 ± 0.9
Assistance: type of assistance	0.4 ± 0.5
Failure: unsuccessful attempts for evacuation per 24 hours	0.5 ± 0.6
History: duration of constipation (years)	1.6 ± 1.1
Total mean CSS score	11.2 ± 3.0

a: Items were scored on a 4-point Likert scale, with 4 indicating the worst symptom severity (0: absent; 1: mild; 2: moderate; 3: severe; 4: very severe). Total score for the PAC-SYM ranges from 0 to 48. [b] Individuals provided rating to the 8 variables selected by the CSS. A global score is obtained by adding each individual score. The total score ranges from 0 (normal) to 30 (severe constipation).

Table 4: Patient Assessment of Constipation Quality of Life

Parameters*	**Mean ±SD N = 226**
Have you felt bloated to the point of bursting?	1.6 ± 1.1
Have you felt heavy because of your constipation?	2.1 ± 1.0
Have you felt any physical discomfort?	1.9 ± 1.0
Have you felt the need to open your bowel but not been able to?	1.8 ± 1.1
Have you been embarrassed to be with other people?	1.2 ± 1.0
Have you been eating less and less because of not being able to have bowel movements?	1.7 ± 1.2
Have you had to be careful about what you eat?	1.6 ± 1.2
Have you had a decreased appetite?	1.5 ± 1.3
Have you been worried about not being able to choose what you eat (for example, at a friend's)?	1.2 ± 1.1
Have you been embarrassed about staying in the toilet for so long when you were away from home?	1.1 ± 1.1
Have you been embarrassed about having to go to the toilet so often when you were away from home?	0.9 ± 1.0
Have you been worried about having to change your daily routine (for example, travelling, being away from home)?	1.3 ± 1.1
Have you felt irritable because of your condition?	1.8 ± 0.9
Have you been upset by your condition?	1.8 ± 1.0
Have you felt obsessed by your condition?	1.7 ± 1.1
Have you felt stressed by your condition?	1.8 ± 1.0
Have you been less self-confident because of your condition?	1.7 ± 1.0
Have you felt in control of your situation?	1.7 ± 1.0
Have you been worried about not knowing when you are going to be able to have a bowel movement?	1.5 ± 0.9
Have you been worried about not being able to open your bowels when you needed to?	1.6 ± 1.1
Have you been more and more bothered by not being able to open your bowels?	1.7 ± 1.0
Have you been afraid that your condition will get worse?	1.6 ± 0.9
Have you been felt that your body was not working properly?	1.8 ± 1.0
Have you had fewer bowel movements than you would like?	2.1 ± 1.1
Have you been satisfied with how often you open your bowels?	0.8 ± 0.8
Have you been satisfied with the regularity with which you open your bowels?	0.7 ± 0.8
Have you been satisfied with your bowel function?	0.6 ± 0.8
Have you been satisfied with your treatment?	1.5 ± 1.0
Composite score based on PAC-QOL questionnaire	**42.2 ± 13.6**

Severity of Constipation Symptoms and Quality of Life

Patients had high mean scores of PAC-SYM (30.1±4.9) and CSS (11.2±3), indicating the high frequency and severity of constipation in these patients (Table 3), leading to poor quality of life (PAC-QoL: 42.2±13.6) (Table 4).

Co-morbid conditions

Acid Peptic Disorders (APD) (22%), hypertension (14%) and diabetes (6%) were the commonly reported comorbid conditions reported among the IBS-C patients. (Figure1)

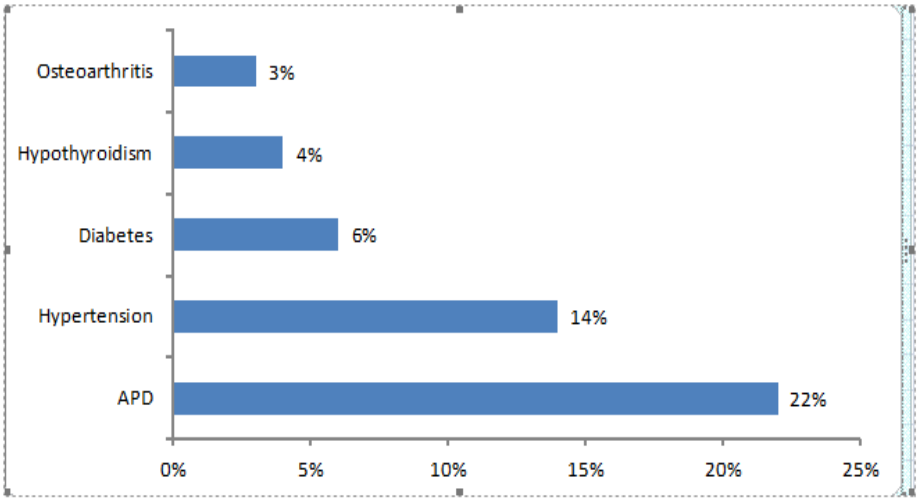

Fig 1: Comorbid Conditions in IBS-C Concomitant medications

Concomitant medications

Laxatives (51%), drugs for acid peptic disorders (APD; 41%), antihypertensives (14%) and antianxiety/antidepressants (13%) were the most commonly used concomitant medications. The commonest laxatives used were osmotic (41%) and bulk laxatives (37%) (Figure 2)

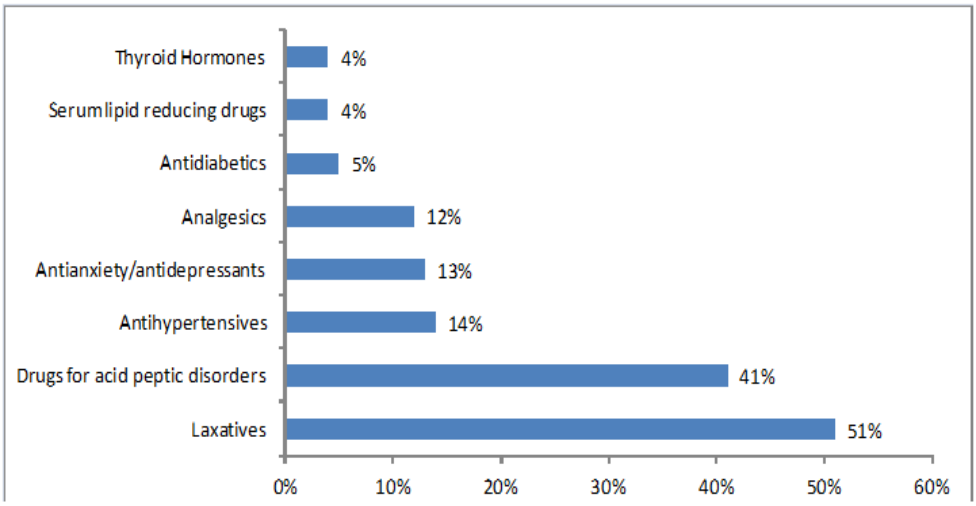

Fig 2: Concomitant Medications taken by IBS-C Patients

Discussion

The understanding of IBS has evolved over the past decades. The evolution of IBS can be traced back to 1948, when Collins described irritable colon as a hyperirritable, neuromuscular imbalance of the colon responsible for the abdominal pain to the current times when IBS is considered to be a functional gastrointestinal disorder which can be explained by the biopsychosocial model. In this biopsychosocial model, the brain-gut axis is considered to play a key role and is associated with complex interplay between the environment, genes, and physical and psychosocial factors [1, 4, 5]. The biopsychosocial model postulates that psychosocial factors interacting with biological mechanisms such as peripheral/central neuroendocrine and immune changes may induce and increase symptoms of IBS, affecting the symptom severity and persistence, treatment response and outcome, finally impacting the quality of life [5]. Multiple studies conducted across the globe have shown that higher socioeconomic status and education, affluent childhood social class, morbid anxiety and emotional stress may contribute to IBS risk [6, 7, 8, 9, 10, 11].

There is a scarcity of robust Indian data on the community population suffering from IBS-C. The true prevalence of IBS-C is difficult to estimate as it is known to change depending on the criteria used for diagnosis. In the present study, prevalence of IBS-C was found to be 24%; the rest of the population had FC (76%). This was consistent with the results of a US population-based survey where the symptoms, care seeking, and disease burden of IBS-C and FC were evaluated as per Rome III criteria; 37.3% with IBS-C and 62.7% patients were diagnosed with FC [12].

Gender differences have been observed in Indians which are diametrically opposite to those observed in Western population with a female-to-male ratio close to 2[13]. A male preponderance is observed in Indians whereas in the Western population a female preponderance has been observed which is largely due to sociocultural differences between the two population [13, 14]. These findings are in concordance with the findings of the Minnesota study which demonstrated that the age-adjusted prevalence of IBS using the Rome II criteria was higher in men than in women. Interestingly, diagnostic criteria

of IBS could also be other contributory factors for the gender differences. It has been postulated that the Manning criteria may be more sensitive in diagnosing IBS in women than in men and the Rome criteria may be less sensitive in men as well, probably due to the fact that men report fewer non-painful IBS symptoms than women [14]. Moreover in India, especially in the rural areas, access to health care facilities may be a deterrent, while in urban areas, the demands of work and family may deter women from seeking medical opinion.

In our study, the highest prevalence of IBS (50.44%) was observed in the age group of 18 to 40 years. IBS has been reported to occur in all age groups, including children and the elderly. No difference has been observed in the frequency of subtypes by age. But, about 50% of patients with IBS have been known to report having first had symptoms before the age of 35 years, and the prevalence of IBS drops in patients aged over 50 years. Patients aged over 50 years with IBS have milder pain, but their overall quality of life is worse. Patients >65 years report significantly shorter duration of symptoms [15].

In the current study the highest prevalence of IBS has been reported in the upper and upper middle socioeconomic class (52%) with high scores of education and occupation. Published literature suggest that a higher socioeconomic class with higher education and occupation level is associated with higher prevalence of IBS, which may be due to higher level of stress experienced by people working in professional and managerial roles. This supports the hypothesis that IBS is a disease of industrialization and urbanization. This could probably be the reasons for the currently reported higher prevalence rates of IBS in Asia, South America, and Africa [15]. Moreover, according to Roohafza *et al*. the prevalence and risk of IBS was higher in people with post-secondary education than in less-educated people. Educational concerns are an important group of life stressors, which along with job-related stressors could significantly predict IBS occurrence. Further, efforts to find suitable jobs and perhaps a lack of sufficient income can make people with postsecondary education prone to anxiety.[16]

IBS patients have difficulties in carrying out activities of daily life. They also exhibit complicated body tensions, and stress patterns. Many IBS patients have been exposed to traumatic events and may have low self-esteem and hypersensitivity. Hence, IBS patients may be in a state of chronic distress, thereby affecting the work productivity [13].Further, the general health status of both young and elderly individuals with IBS is poor as compared to that of the general population [17]. Moreover, patients with IBS seem to have worse health-related quality of life (HRQoL) than patients with gastroesophageal reflux disease, diabetes, and end-stage renal disease[17]As expected, patients with worse bowel symptoms have a lower QoL as compared to patients with milder symptoms. Current evidence indicates that HRQoL in patients with IBS is affected by sex and psychological conditions. Hence careful consideration of these factors may help to individualize a therapeutic regimen to optimize long-term outcomes [17].

Our study shows that IBS-C patients had high mean scores of PAC-SYM and CSS, indicating the high frequency and severity of constipation in these patients, leading to poor quality of life our results were in concordance to the earlier reported literature wherein patients with IBS-C demonstrated high frequency and severity of constipation symptoms which is associated with high PAC-QoL score [12].

IBS is known to be associated with various GI and non-GI comorbid conditions.[18,19] In our study, about 22% of the IBS-C patients had the history of acid peptic disorders, leading to higher consumption of drugs for APDs (41% patients). These results are in line with previously reported literature where patients with IBS were much more likely to report gastroesophageal reflux disorder.[18] Other comorbid diseases reported in our study include hypertension (14%), diabetes (6%) and osteoarthritis (3%) leading to use of respective class of drugs for the same. It is interesting to note that, only 51% patients of IBS-C were on laxatives for management of constipation, this demonstrates inadequate treatment of constipation leading to which might have contributed to high frequency and severity of constipation thereby the poor QoL.

Our study has several strengths. Firstly, this was a first of its kind pan India study to evaluate the epidemiology and clinical profiling of IBS-C including both rural and urban population. Further, all the parameters, including constipation related symptoms, severity of symptoms and QoL has been assessed by very well-defined, validated and reliable tools. Third, all the questionnaires used in the study were administered to the patients by a physician or a designee, which enabled to capture information with greater accuracy and confidentiality. The study has few limitations as well. Firstly, this study was only limited to adult population and has not been studied in children and elderly population. Secondly, it was a single visit study and lacked long-term outcome data. Being a non-interventional study; no data was collected regarding the effect of changes in the management.

Conclusion

IBS is indeed a bio-psychosocial disorder. Biological, social, and psychological components affect disease perception, symptom generation, and healthcare seeking behaviour. Higher educational/occupational scores point towards increased stress/anxiety, which could be attributed to dysfunctional brain-gut axis in IBS. Patients with IBS-C reported high frequency and severity of constipation-related symptoms, thereby leading to poor QoL. Moreover, these patients also had higher prevalence of APDs, thus highlighting the need to identify the presence of upper gastrointestinal comorbidities in IBS patients. Drugs for APD, antihypertensives and antianxiety/antidepressants were the most commonly used concomitant medications to treat respective comorbidities. Only half of the patients were on laxatives, indicating inadequate treatment of constipation in these patients, further substantiating poor QoL. This study thus emphasizes the necessity for a multi-faceted approach for holistic management of IBS and can be the cornerstone in directing the attention towards identifying the risk factors of IBS, addressing these risk factors and thereby improving the quality of life of IBS patients in addition to symptomatic treatment.

Acknowledgement

Dr. Manjusha assisted in the overall development of this manuscript. The authors thank the study participants as well as the following investigators for their participation in this study (listed in alphabetical order): Dr. Ashwani Aggarwal, Dr. Umesh Aalegaonkar, Dr. Bhattacharya, Dr. Sanmay Choudhari, Debasis Datta, Dr. Kamlesh Fatania, Dr. Amit Goyal, Dr. Deepak Kumar Jha, Dr. Mandhir Kumar, Dr.

Parimal Lawate, Dr. Mahesh Jagdish Maheshwari, Dr. Chetan Nayak, Dr. Sandeep Nijhawan, Dr. Swami Pawar, Dr. Ravindra BS, Dr. Shanthi V and Dr. Jayanthi. V.

Funding
Funding sources from Abbott India Ltd.

Conflict of interest
Dr. Rooprai, Dr. Bhat and Dr. Sainani have received research funding from Abbott India. Ltd. Dr. Hegde is an employee of Abbott India Ltd.

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