ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Diagnosis of Functional Dyspepsia on the basis of Rome III clinical diagnostic criteria in a tertiary care hospital: A cross-sectional observational study

[1]Kaushik Biswas, [2]Rajdip Hazra, [3]Sisir Chakraborty, [4]Rajarshi Bose, [5]Swadesh Garain

[1]Post Doctoral Trainee, Department of Cardiology, Nilratan Sircar Medical College and Hospital, Kolkata, [2] Tutor, Department of Anesthesiology, Nilratan Sircar Medical College and Hospital, Kolkata, [3]Assistant Professor, Department of Medicine, College of Medicine and Sagore Dutta Hospital, Kolkata, [4]Assistant Professor, Department of Pediatric Medicine, Nilratan Sircar Medical College and Hospital, Kolkata, [5] Specialist Medical Officer, Department of Gynecology and Obstetrics, Nadia District Hospital, Krisnanagar

Submitted: 08-12-2017 Revised: 20-12-2017 Published: 01-01-2018

ABSTRACT

Background: Though functional dyspepsia (FD) is often a diagnosis of exclusion, whether minor mucosal gut pathology represents organic disease or FD, it still remains controversial. **Aims and Objectives:** The present study has been conducted to determine the accuracy of symptom based diagnosis of FD based on Rome III diagnostic criteria in a tertiary care center. **Materials and Methods:** Total 140 patients aged between 18-55 years of both sexes with upper abdominal symptoms without known or post investigational organic diseases, were included in this study. Patients fulfilling the Rome III criteria were diagnosed as FD and undergone upper GI endoscopy (UGIE). Those devoid of organic lesions were confirmed as 'true FD'. **Results:** Out of 140 study patients, 100 patients fulfilled Rome III criteria (clinical FD) out of which 77 were confirmed as 'true FD' after UGIE with an accuracy of 83.57 %. **Conclusion:** Rome III clinical criteria can be applied to diagnose FD in a tertiary care center with some limitations. The authors suggest some modification of Rome III criteria.

Key words: Functional Dyspepsia, Rome III criteria, Symptom based diagnosis

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v9i1.18716

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Dyspepsia and gastrointestinal reflux diseases (GERD) are very prevalent throughout the world.[1-5] Though they are often overlapping, an well accepted definition of dyspepsia is lacking. It is often vaguely defined as upper abdominal pain or discomfort with or without other gastrointestinal symptoms such as nausea, belching, vomiting etc.[6-8] The most common dyspepsia is the functional dyspepsia (FD).

According to the Rome III criteria, functional gastrointestinal disorder (FGID) has been categorized into the following major groups:

i) Category A (functional esophageal),
ii) Category B (functional gastroduodenal),
iii) Category C (functional bowel),
iv) Category D (functional abdominal pain syndrome),
v) Category E (functional gall bladder and sphincter of Oddi disorder),
vi) Category F (functional anorectal disorder),
vii) Category G (childhood functional GI disorder: Infant/Toddler),
viii) Category H (childhood functional GI disorder: Child/Adolescent).

Out of these categories, functional dyspepsia (FD) falls under the category B (B1 subtype) i.e. functional gastroduodenal disorders subgroup of FGID.

Functional Dyspepsia (FD) is a highly prevalent (20-30%) disorder with large geographic variation. It is defined as persistent or recurrent pain or discomfort centered in the

Address for correspondence:
Dr. Sisir Chakraborty, Department of Medicine, College of Medicine and Sagore Dutta Hospital, Kolkata 700058. **Mobile:** +919433109302
Email: chakrabortysisir2017@yahoo.com

upper abdomen not relieved by defecation or not caused by organic diseases. Most commonly used guideline to diagnose and treat FD is Rome guidelines, Rome III being the latest. According to this, one or more of 4 cardinal symptoms (early satiation, postprandial fullness, epigastric pain and epigastric burning sensation) must be present for the last 3 months with symptom onset at least 6 months prior to diagnosis in absence of any organic, systemic or metabolic diseases. It is more common in women.

Previously coined as "non-ulcer dyspepsia", FD is not the result of underlying structural disorders of gut rather it is the consequence of several pathophysiological mechanisms such as delayed gastric emptying, impaired gastric accommodation, hypersensitivity to gastric distension and altered duodenal sensitivity to lipids and acids. There may be a relation with H. Pylori infection and mood disorders like anxiety, depression etc. and treatment of these conditions often improve the disease process. Heartburn and IBS (Irritable Bowel Syndromes) can occur concurrently with FD, but their mere presences do not exclude the diagnosis of FD. These make it very difficult to distinguish between organic disease and FD in uninvestigated patients when FD is diagnosed solely on the basis of upper gastrointestinal (GI) symptoms.

Though FD is often a diagnosis of exclusion, whether minor mucosal gut pathology represents organic disease or FD, it still remains controversial. Most patients with organic dyspepsia are proved to have esophagitis, benign esophageal strictures, Barrett's esophagus, peptic ulcer disease (PUD) or upper GI malignancies. Thus the use of only clinical criteria in diagnosis of FD may be controversial. Results of previous studies in this context are highly variable; while some showed reasonable accuracy, others showed lack of effectiveness in clinical evaluation. This situation remains unexplored in eastern part of India. This study aims to evaluate the accuracy of symptom based diagnosis of FD according to Rome III criteria in a tertiary care hospital.

MATERIALS AND METHODS

After approval from institutional ethical committee this study was conducted in Nilratan Sircar Medical College and Hospital, a tertiary care medical college hospital in eastern India. Total 140 patients aged between 18-55 years of both sexes with upper abdominal symptoms without known or post investigational organic diseases, attending the Outpatient Department (OPD) of General Medicine were selected as study population.

Any patient having age > 55 years or < 18 years at symptom onset, endoscopic evidence of structural gastrointestinal diseases, patients with red flag signs like gastrointestinal bleeding, abdominal pain awakening the patients at night, significant weight loss or fever; family history of upper gastrointestinal malignancy, recurrent vomiting, dysphagia or patients with upper gastrointestinal symptoms resulting from some chronic heart, kidney or liver diseases were excluded from this study.

Total 140 patients meeting the inclusion criteria and does not falling into the exclusion criteria at the time of first visit to General Medicine OPD were included in this study. After obtaining written informed consent of the patients, detailed history was taken regarding patient profile and symptoms including bothersome post-prandial fullness, early satiety, epigastric pain, epigastric burning sensation etc. to rule out organic causes and chronic ailments that can produce chronic upper abdominal symptoms. Thorough clinical examinations were done to rule out apparent organic anomalies. They were also given a set of questionnaire which was to be answered promptly. Thus the patients fulfilling the Rome III criteria were diagnosed as FD. Now, these clinical FD patients were advised for various laboratory investigations to exclude chronic diseases and organic causes. These included biochemical parameters, upper abdominal ultrasonography etc. and most importantly, immediate upper GI endoscopy (UGIE) with or without biopsy, the gold standard test to differentiate between FD and organic dyspepsia. At the same time, appropriate treatment for organic dyspepsia (Proton Pump Inhibitors or PPIs) was given to all the patients of study population (i.e., both FD and organic dyspepsia) for at least 8 weeks and observed whether the symptoms of either FD patients or organic disease patients persist or not. There would be persistence of symptoms if organic dyspepsia was coexistent with FD.

Statstical analysis

Data were entered in Microsoft Excel spread sheet and analyzed using SPSS software version 18.0 (SPSS Inc., Chicago, Illinois, USA) with appropriate statistical techniques. Numerical data were presented as percentages. Categorical data were compared using Chi-square test. A p value of less than 0.05 was considered as statistically 'significant' ($p < 0.05$).

RESULTS

A total of 140 patients aged between 18-55 years of both sexes with upper abdominal symptoms without known or post investigational organic diseases were included in this study. Among these 140 patients, 100 patients who fulfilled the Rome III criteria and thus were clinically diagnosed as FD, undergone upper GI endoscopy (taken as 'Gold

standard' in this study) revealing that only 77 patients truly suffered from FD and the rest 23 patients were actually suffering from organic dyspepsia. Out of these 23 patients, 11 had peptic ulcer disease (PUD), 9 had erosive gastritis (EG), 1 had both PUD and EG,1 had both EG and varix and only 1 had gastric malignancy.

Among 77 'true FD' patients, 31 patients were male (40.26 %) and 46 patients were female (59.74 %). On further enquiry of these true FD patients, we found that total 62 patients were married (80.52 %) and total 54 patients were literate (70.13 %). Occupation wise, 27 patients were housewives, 25 office workers, 15 farmers and the rest 10 had other occupations. Most of the patients were in 30-39 years age group (33 patients, i.e., 42.86 %) followed by 40-49 years (21 patients, 27.27 %), 18-29 years (16 patients, 20.78 %) and 50-55 years (7 patients, 9.09 %). On subjective severity scoring, 36 patients had mild FD (46.75 %), 27 had moderate FD (35.07 %) and only 14 had severe FD (18.18 %). As per Rome III criteria, epigastric pain was found to be the most common symptom associated (59 out of 77 patients, i.e. 76.62 %). Other common symptoms were bothersome post-prandial fullness (35 patients, 45.45 %), early satiety (30 patients, 38.96 %) and epigastric burnig sensation (24 patients, 31.17 %). When male-female difference of symptom pattern was analyzed, only epigastric pain showed statistically significant male-female difference with a *p* value of 0.009 (Table 1). After 8 weeks of treatment with PPIs, bothersome post-prandial fullness was present in 13 patients (16.88 %), early satiety in 6 patients (7.79 %), epigastric pain in 2 patients (2.6 %) and epigastric burning sensation in 6 patients (7.79 %). This pattern of response to treatment was statistically significant with a *p* value of 0.009 (Table 2). On subjective severity scoring after treatment, 48 patients were found normal (62.34 %) and the rest 29 had only mild symptoms (37.66 %).

Table 1: Different symptoms among male-female FD patients

Symptoms (n)	Male	Female	*p* value
EP (59)	19	40	0.009
BPPF (35)	17	18	0.175
ES (30)	14	16	0.058
EBS (24)	8	16	0.404

EP: Epigastric pain; BPPF: Bothersome post-prandial fullness; ES: Early satiety; EBS: Epigastric burning sensation

Table 2: Response pattern after treatment in FD patients

Symptoms	EP	BPPF	ES	EBS
Before treatment	59	35	30	24
After treatmen	2	13	6	6

EP: Epigastric pain; BPPF: Bothersome post-prandial fullness; ES: Early satiety; EBS: Epigastric burning sensation

When we divided FD patients into EPS (Epigastric Pain Syndrome) and PDS (Post-prandial Distress Syndrome) subgroups according to Rome III criteria, we found 34 EPS patients (44.16 %), 36 PDS patients (46.75 %) and the rest 7 patients showed features of both EPS and PDS (9.09 %).

Analysis: Accuracy of Rome III in FD diagnosis

In this study, total study population = 140, number of patients fulfilling Rome III criteria (clinically FD) = 100, 'true FD' (after upper GI endoscopy) = 77 and organic dyspepsia = 23. So, True Positive (TP) = 77, False Positive (FP) = 23, True Negative (TN) = 40 and False Negative (FN) = 0.

Therefore, accuracy of Rome III clinical diagnostic criteria is-

$(TP + TN / TP + TN + FP + FN) \times 100 =$ (77+40/77+40+23+0) X 100 = 83.57 %.

Sensitivity of the Rome III criteria = 100% with 95 % CI: 95.28-100.00 % (CI = Confidence Interval).

Specificity of the Rome III criteria = 63.49 % with 95 % CI: 50.40-75.26 %.

Positive Likelihood ratio = 2.74 with 95 % CI: 1.98-3.79.

Negative Likelihood ratio = 0.

Positive Predictive value (PPV) = 77.00 % with 95 % CI: 67.51-84.82 %.

Negative Predictive value (NPV) = 100% with 95% CI: 91.11-100.00 %.

However, as the sample sizes in positive and negative groups do not reflect the real prevalence of the disease, PPV and NPV should be ignored.

So, it can be said that Rome III criteria is a valid clinical criteria to diagnose FD with an accuracy of 83.57 %.

DISCUSSION

Functional dyspepsia (FD) is one of the common health problems due its high prevalence in the general population. Rome III consensus divided it into meal related symptoms and meal unrelated symptoms which were named as post-prandial distress syndrome (PDS) and epigastric pain syndrome (EPS) respectively. The applicability of this subdivision in the diagnosis and management of FD in a tertiary care hospital were our clinical research area. In this study, we found that Rome III clinical criteria were

applicable in 77% cases to diagnose FD truly with an accuracy of 83.57 %.

Rome III criteria are the latest criteria for the diagnosis of functional gastrointestinal disorder (FGID) including functional dyspepsia (FD) which was described in the year 2006. After that, there were several studies in different population including Asian population to define its validity in the diagnosis of FD. Though a number of studies have been done in India on different parameters of FD, but study on the applicability of Rome III diagnostic criteria is really lacking.

In a study by Manabe N et al on 364 Japanese patients with upper gastrointestinal symptoms showed that there was considerable overlap between the groups of EPS, PDS, chronic idiopathic nausea symptoms (109/198 i.e., 55.1%) and non-erosive reflux disease (103/198 i.e. 52 %).[9] Rome III criteria could not be applied on 62.7% of PDS and 61.3% of EPS patients as the onset of symptoms were within 6 months of diagnosis (4.6 ± 0.4 months for PDS and 4.6 ± 0.5 months for EPS patients). They concluded that Rome III criteria is unable to identify a large group of patients of FD because of earlier presentation for medical care and emphasized the need to reduce the duration of symptom onset from 6 months to a lesser value, at least for the Japanese population.[9] However, Reisswitz PSV et al showed the validity of Rome III diagnostic questionnaire in adequately evaluating FD in Portuguese population with 5.3 % of control population and 91.2 % of dyspeptic patients having FD.[10]

Abid S et al tried to evaluate Rome III questionnaires for diagnosis of FD and to clarify whether it can differentiate between EPS and PDS.[11] 70 % (191 out of 272) of the study population fulfilled the definition of FD as per Rome III criteria with 57 % having EPS, 9 % having PDS, 29 % having overlap between EPS and PDS and the rest 5 % being indeterminate. Subsequent upper GI endoscopy revealed that only 71 % (136/191) of these clinical FD patients were 'true FD' (77 % in present study). So, roughly one third of patients fulfilling Rome III criteria had organic diseases and one third of confirmed FD patients did not fall into either of EPS or PDS categories.[11] Documented literature has also provided evidence of significant overlap between presenting symptoms of FD. In fact, considerable portion of patients may not be classifiable at all.[12] Therefore, there is a need for further redefining of Rome III subgroups.

Park JM et al evaluated the pattern of FGIDs both in primary care clinics and tertiary care hospitals and assessed problems in diagnosing the FGIDs by Rome III criteria on Korean population.[13] In primary clinics, 44.9 % patients were diagnosed as having FGIDs with 1: 3 male-female ratio, but it was 53.5 % in tertiary hospitals with 1: 2 male-female ratio. The most common FGID was FD (46 %) followed by IBS (40.2 %) both in primary and tertiary care centre which was same as obtained previously using Rome II criteria[14] and the most common subtype of FD was PDS (same as present study) which was different from previous study using Rome II criteria[14] (again, similar to present study). Park JM et al also showed presence of more than one FGID in 51 % patients and the most common overlap was FD with IBS which was in concordance with previous studies.[15, 16]

Lee YY et al surveyed Rome III criteria among ethnic Malays in a primary care center and found 84.2 % of clinical FD patients having 'true FD' with EPS being most common symptom (68.8 %) and rest having overlapping symptoms with PDS (31.2 %).[17]

In the present study, along with the applicability of Rome III criteria in diagnosis of FD, we have also tried to evaluate the effect of some other parameters like age, gender, occupation, marital status, education etc. on FD. Out of 77 true FD patients 40.26 % were male and 59.74 % were female, so, male-female ratio was 2: 3. Though most population based studies showed that frequency of uninvestigated dyspepsia (UD) was not related to gender, several studies in different population have noted a consistent female predominance with dyspepsia.[18-22] Female gender was found to be the only independent risk factor of FD among 2865 Taiwanese health check attendees.[21] In one population based study in Australia, female adults significantly outnumbered males in most GI disorders including FD.[23] One exception with male preponderance (M: F = 2:1) of UD was found in one Japanese study by Kawamura A et al.[24]

Dyspepsia does not appear to be related to any particular age group. Most of the studies being done in patients above 18 years of age, significant data about dyspepsia among children is lacking and it is a common disorder when it is considered as upper abdominal pain.[25] In spite of this, different studies have showed a particular trend of FD among different age group. Peak FD was found to be 41-50 years among Chinese population.[26, 27] It is > 40 years in Indian population.[28] Peak prevalence of UD has been found to be 45-54 years in Canadian survey.[29] Britain[18] and Taiwan[19] show a decreasing trend of FD with age. In this study, most of the patients were in 30-39 years age group (42.86 %) followed by 40-49 years (27.27 %).

In some studies, relations of FD with socioeconomic condition have been found. Drossman DA et al showed

a strong relationship between lower household income and larger household membership with increased FGID including FD.[30] Similarly in a British study, Moayyedi P et al found that rented accommodation without central heating, low income, sharing of same bed with sibling were predictors of UD in adults.[31] We had only included marriage, occupation and literacy as our socioeconomic study parameters. Similar to Lee YY et al,[17] our study showed higher prevalence of FD among married persons (80.52 %). We had demonstrated higher frequency of FD among housewives than office workers or people of other occupation. Total 70.13 % were literate.

In this study, patients diagnosed as 'true FD' after upper GI endoscopy, were prescribed with PPIs for 8 weeks and symptoms were improved in a statistically significant manner (p value = 0.009). Though previous studies have shown that EPS may be alleviated by using PPIs[32, 33] and symptoms of early satiety related to PDS improve using prokinetic drugs,[34, 35] there is no study in the literature that have tested the effect of PPI or prokinetics in Rome III based subgroups of patients with FD. In fact, treatment of a syndrome based solely on symptoms has not yet provided satisfactory results.[34-36]

Limitation of study

Our study suffered from several limitations. Firstly, the study population only included those patients attending tertiary care hospital. So, applicability of this study to general population is questionable. Secondly, preponderance of FD among female patients may be attributed to the fact that most of the patients attending medicine OPD were female. Thirdly, we found epigastric pain as most common symptom but most common FD subgroup was PDS because in most of the cases epigastric pain was associated with post-prandial fullness and early satiety. Fourthly, this single center study with small population may not reflect actual scenario on a larger scale. Fifthly, this study did not show the usefulness of Rome III criteria in the FD management.

CONCLUSION

We conclude that, a Rome III clinical criterion is applicable to diagnose FD in a tertiary care hospital. However, there are limitations as it cannot diagnose 100 % FD patients truly and also a number of FD patients cannot be subcategorized into either of PDS or EPS because of presence of features of both of these. So, a third subgroup of mixed pattern should be included along with EPS and PDS; and if possible, time frame of the diagnostic criteria should be reconsidered for the applicability to all the ethnic groups.

ACKNOWLEDGEMENTS

The authors like to acknowledge Nilratan Sircar Medical College and Hospital, Kolkata, India for providing necessary support during this research work. None of the authors have any conflict of interest.

REFERENCES

1. Lin M and Triadafilopoulos G. Belching: dyspepsia or gastroesophageal reflux disease? Am J Gastroenterol 2003; 98(10):2139-2145.
2. Lembo A, Zaman M, Jones M and Talley NJ. Influence of genetics on irritable bowel syndrome, gastro-oesophageal reflux and dyspepsia: a twin study. Aliment Pharmacol Ther 2007; 25(11):1343-1350.
3. Talley NJ, Lam SK, Goh KL and Fock KM. Management guidelines for uninvestigated and functional dyspepsia in the Asia-Pacific region: First Asian Pacific Working Party on Functional Dyspepsia. J Gastroenterol Hepatol 1998; 13(4):335-353.
4. Talley NJ, Zinsmeister AR, Schleck CD and Melton LJ. Dyspepsia and dyspepsia subgroups: a population-based study. Gastroenterology 1992; 102(4 Pt 1):1259-1268.
5. Keohane J and Quigley EM. Functional dyspepsia and nonerosive reflux disease: clinical interactions and their implications. Med Gen Med 2007; 9(3):31.
6. Drossman DA, Thompson WG, Talley NJ, Funch-Jensen P, Janssens J and Whitehead WE. Identification of sub-groups of functional gastrointestinal disorders. Gastroenterol Int 1990; 3(4):159-172.
7. Talley NJ, Stanghellini V, Heading RC, Koch KL, Malagelada JR and Tytgat GN. Functional gastroduodenal disorders. Gut 1999; 45(suppl 2):1137-1142.
8. Bytzer P and Talley NJ. Dyspepsia. Ann Intern Med 2001; 134:815-822.
9. Manabe N, Haruma K, Hata J, Imamura H, Kamada T, Kusunoki H, et al. Clinical characteristics of Japanese dyspeptic patients: is the Rome III classification applicable? Scand J Gastroenterol 2010; 45(5):567-572.
10. Reisswitz PSV, Mazzoleni LE and Sander GB. Portuguese validation of the Rome III diagnostic questionnaire for functional dyspepsia. Arq Gastroenterol 2010; 47(4):354-360.
11. Abid S, Siddiqui S and Jafri W. Discriminant value of Rome III questionnaire in dyspeptic patients. Saudi J Gastroenterol 2011; 17(2):129-133.
12. van Kerkhoven LA, Laheij RJ, Meineche-Schmidt V, Veldhuyzen-van Zanten SJ, de Wit NJ and Jansen JB. Functional dyspepsia: not all roads seem to lead to Rome. J Clin Gastroenterol 2009; 43(2):118-122.
13. Park JM, Choi MG, Cho YK, Lee IS, Kim JI, Kim SW, et al. Functional gastrointestinal disorders diagnosed by Rome III questionnaire in Korea. J Neurogastroenterol Motil 2011; 17(3):279-286.
14. Choi H, Choi MG, Kim SW, Moon SB, Kim BK, Kim BW, et al. Functional gastrointestinal disorders in patients with gastrointestinal symptoms. Korean J Gastroenterol 1999; 33(6):741-748.
15. Corsetti M, Caenepeel P, Fischler B, Janssens J and Tack J. Impact of coexisting irritable bowel syndrome on symptoms and pathophysiological mechanisms in functional dyspepsia. Am J Gastroenterol 2004; 99(6):1152-1159.
16. Wang A, Liao X, Xiong L, Peng S, Xiao Y, Liu S, et al. The

clinical overlap between functional dyspepsia and irritable bowel syndrome based on Rome III criteria. BMC Gastroenterol 2008; 8:43.

17. Lee YY, Wahab N, Mustaffa N, Daud N, Noor NM, Shaaban J, et al. A Rome III survey of functional dyspepsia among the ethnic Malays in a primary care setting. BMC Gastroenterol 2013; 13:84.
18. Caballero-Plasencia AM, Sofos-Kontoyannis S, Valenzuela-Barranco M, Martin-Ruiz JL, Casado-Caballero FJ and Lopez-Manas JG. Irritable bowel syndrome in patients with dyspepsia: a community-based study in southern Europe. Eur J Gastroenterol Hepatol 1999; 11(5):517-522.
19. Kwan AC, Bao TN, Chakkaphak S, Chang FY, Ke MY, Law NM, et al. Validation of Rome II criteria for functional gastrointestinal disorders by factor analysis of symptoms in Asian patient sample. J Gastroenterol Hepatol 2003; 18(7):796-802.
20. Shaib Y and El-Serag HB. The prevalence and risk factors of functional dyspepsia in a multiethnic population in the United States. Am J Gastroenterol 2004; 99(11):2210-2216.
21. Lu CL, Lang HC, Chang FY, Chen CY, Luo JC, Wang SS, et al. Prevalence and health/social impacts of functional dyspepsia in Taiwan: a study based on the Rome criteria questionnaire survey assisted by endoscopic exclusion among a physical check-up population. Scand J Gastroenterol 2005; 40(4):402-411.
22. Brun R and Kuo B. Functional dyspepsia. Therap Adv Gastroenterol 2010; 3(3):145-164.
23. Koloski NA, Talley NJ and Boyce PM. Epidemiology and health care seeking in the functional GI disorders: a population-based study. Am J Gastroenterol 2002; 97(9):2290-2299.
24. Kawamura A, Adachi K, Takashima T, Murao M, Katsube T, Yuki M, et al. Prevalence of functional dyspepsia and its relationship with Helicobacter pylori infection in a Japanese population. J Gastroenterol Hepatol 2001; 16(4):384-388.
25. Spiroglou K, Chatziparasidis G, Paroutoglou G, Demertzidou V, Giouleme O, Nikolaides N, et al. Functional Dyspepsia in Children. J Pediatr Gastroenterol Nutr 2001; 33(4):519.
26. Hirakawa K, Adachi K, Amano K, Katsube T, Ishihara S, Fukuda R, et al. Prevalence of non-ulcer dyspepsia in the Japanese population. J Gastroenterol Hepatol 1999; 14(11):1083-1087.
27. Li Y, Nie Y, Sha W and Su H. The link between psychosocial factors and functional dyspepsia: an epidemiological study. Chin Med J 2002; 115(7):1082-1084.
28. Shah SS, Bhatia SJ and Mistry FP. Epidemiology of dyspepsia in the general population in Mumbai. Indian J Gastroenterol 2001; 20(3):103-106.
29. Tougas G, Chen Y, Hwang P, Liu MM and Eggleston A. Prevalence and impact of upper gastrointestinal symptoms in the Canadian population: findings from the DIGEST study. Domestic/International Gastroenterology Surveillance Study. Am J Gastroenterol 1999; 94(10):2845-2854.
30. Drossman DA, Li Z, Andruzzi E, Temple RD, Talley NJ, Thompson WG, et al. U.S. householder survey of functional gastrointestinal disorders. Prevalence, sociodemography, and health impact. Dig Dis Sci 1993; 38(9):1569-1580.
31. Moayyedi P, Forman D, Braunholtz D, Feltbower R, Crocombe W, Liptrott M, et al. The proportion of upper gastrointestinal symptoms in the community associated with Helicobacter pylori, lifestyle factors, and nonsteroidal anti-inflammatory drugs. Leeds HELP Study Group. Am J Gastroenterol 2000; 95(6):1448-1455.
32. Bolling-Sternevald E, Lauritsen K, Aalykke C, Havelund T, Knudsen T, Unge P, et al. Effect of profound acid suppression in functional dyspepsia: a double-blind, randomized, placebo-controlled trial. Scand J Gastroenterol 2002; 37(12):1395-1402.
33. Peura DA, Kovacs TO, Metz DC, Siepman N, Pilmer BL and Talley NJ. Lansoprazole in the treatment of functional dyspepsia: two double-blind, randomized, placebo-controlled trials. Am J Med 2004; 116(11):740-748.
34. Moayyedi P, Soo S, Deeks J, Delaney B, Innes M and Forman D. Pharmacological interventions for non-ulcer dyspepsia. Cochrane Database Syst Rev 2003; (1):CD001960.
35. Tack J, Vos R, Janssens J, Salter J, Jauffret S and Vandeplassche G. Influence of tegaserod on proximal gastric tone and on the perception of gastric distension. Aliment Pharmacol Ther 2003; 18:1031-1037.
36. Eslick GD, Howell SC, Hammer J and Talley NJ. Empirically derived symptom sub-groups correspond poorly with diagnostic criteria for functional dyspepsia and irritable bowel syndrome. A factor and cluster analysis of a patient sample. Aliment Pharmacol Ther 2004; 19(1):133-140.

Authors Contribution:
KB & SC- Plan of study; **KB, SC & RB**- Preparation of the initial draft; **RH & SG**- Contribution to the manuscript; **KB**- Statistical analysis; **RH**- Review and final preparation of the manuscript.

Orcid ID:
Dr. Kaushik Biswas: http://orcid.org/0000-0003-2360-5283
Dr. Rajdip Hazra: http://orcid.org/0000-0001-5480-7457
Dr. Sisir Chakraborty: http://orcid.org/0000-0002-8483-9406
Dr. Rajarshi Bose: http://orcid.org/0000-0002-4299-1979
Dr. Swadesh Garain: http://orcid.org/0000-0002-4949-5652

Source of Support: Nil, **Conflict of Interest:** None declared.