

Functional Dyspepsia In Patients With Chronic Kidney DiseaseHimanshu Sandeep Baxy¹, Tanuja Manohar²**ABSTRACT**

Background : Prevalence of chronic kidney disease (CKD) is high worldwide. Dyspepsia is a common symptom in CKD patients. Dyspepsia is defined as pain or discomfort in upper abdomen. Owing to uremia, occurrence of gastritis, peptic ulcer disease or mucosal ulcerations at any part of gastrointestinal tract leading to upper abdominal pain, nausea, vomiting or GI bleeding is common. Such varied gastrointestinal symptoms have a significant effect on the health-related quality of life of the patients and increases socioeconomic burden.

Methods : This cross-sectional study was conducted at Lata Mangeshkar Hospital, Nagpur for a period of two months from May 2018 to July 2018. Patients >18 years old and suffering from chronic kidney disease were included in the study. Patients with a known gastric disease, patients not willing for upper GI endoscopy and patients with a disease preventing them to answer questionnaire were excluded from the study. All the patients were interviewed using the ROME III questionnaire. The patients who reported positive for the presence of dyspepsia were further evaluated by endoscopy. Statistical analysis was done by Chi-square test and other methods of data interpretation.

Results : The frequency of functional dyspepsia in CKD patients was found to be 9 out of 40 patients (22.5%). Our sample consisted of 26 (65%) men and 14 (35%) women with mean age of 49.55 ± 12.34 years. Patients had mean BMI of 21.2 ± 2.95 . The laboratory results were hemoglobin of 7.71 ± 1.47 g/dl, total leukocyte count (TLC) of 7405 ± 2611 /ml, platelet count 2.224 ± 0.72 lacs/ml, serum creatinine 9.9 ± 4.95 mg/dl, Serum sodium 133.8 ± 6.3 mEq/L, S potassium 4.6 ± 0.75 mEq/L and blood urea 106.15 ± 61.84 mg/dL. The mean eGFR of dyspeptic subjects is 8.78 ± 4.15 60mL/min/1.73m². Mean eGFR of Non-dyspeptic subjects is 8.42 ± 11.07 60mL/min/1.73m². 39 out of 40 patients were at stage 5 of CKD.

There were no significant differences in the demographic and laboratory variables between patients with and without dyspepsia in CKD. Higher incidence was found in age group of > 60 years. No relation was found between laboratory parameters and functional dyspepsia. CKD patients should be screened for dyspepsia and appropriate treatment and counseling should be done.

Conclusion : Prevalence of dyspepsia among CKD patients obtained in this study was 22.5%. There was no significant relationship found between Functional Dyspepsia and sociodemographic factors like Body mass index, employment and education. Slight relation was found with age. Higher incidence was found in age group of > 60 years.

Key words : Functional dyspepsia, chronic kidney disease, e-GFR

Introduction :

Prevalence of chronic kidney disease (CKD) is high worldwide. It is defined as structural or functional alteration in kidney function for a period of at least 3 months along with health implications¹. The National Kidney Foundation [Kidney Dialysis Outcomes Quality Initiative (KDOQI)] classified CKD into 5 stages depending on the estimated GFR².

Dyspepsia is a common symptom in CKD patients. Dyspepsia literally means poor digestion. It indicates an upper abdominal syndrome triggered by food ingestion. It includes upper abdominal fullness after eating and early satiety and also epigastric pain or burning which may or may not be associated with food ingestion³. It may present as burning pain, nausea, bloating, fullness after meals, a feeling of indigestion or slow digestion. It may be ulcer disease or functional dyspepsia i.e. non-ulcer dyspepsia⁴. Owing to uremia, occurrence of gastritis, peptic ulcer disease or mucosal ulcerations at any part of gastrointestinal tract leading to upper abdominal pain, nausea, vomiting or GI bleeding is common. Increased gastrin levels have also been found in such

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patients. This, along with uremia, inflammation and local circulatory disturbances may lead to injury to mucosa. CKD patients have higher prevalence of gastric mucosal injury than normal population⁵.

Such varied gastrointestinal symptoms have a significant adverse impact on the health-related quality of life of the patients⁶. Identification and proper management of these symptoms can improve their quality of life by lowering hindrance with day-to-day life. Data regarding this issue is lacking in central India. So, this study was undertaken to evaluate prevalence of dyspepsia using ROME III questionnaire, its correlation with severity of CKD as well as to study endoscopic findings in patients with dyspepsia to help treat them better.

Functional dyspepsia is defined as the presence of symptoms which are thought to originate from gastro duodenal region, in the absence of any organic, systemic or metabolic disease that is likely to explain the symptoms³. It is also referred to as “Dyspepsia Symptom Complex” and has been categorized into (Tack et al. 2006):

- i. Postprandial Distress Syndrome (PDS) : which include symptoms such as Postprandial fullness, early satiety, upper abdominal bloating, postprandial nausea and excessive belching.
- ii. Epigastric Pain Syndrome (EPS) : These include symptoms such as epigastric pain which is intermittent, not generalized to other abdominal or chest regions, not relieved by defecation or passage of flatus and not fulfilling the criteria for gallbladder and sphincter of Oddi disorders. The pain is commonly induced or relieved by ingestion of a meal but may occur while fasting (Tack et al.,2006).

Various studies done in Europe, North America and Oceania have shown that the prevalence rate of dyspepsia in general population is between 3% to 40% and these variations of the prevalence rates are due the difference definition used⁷. Strid et al. investigated the relation between dyspeptic symptoms in patients in dialysis and pre-dialysis programs. They found increased dyspeptic symptoms among patients in hemodialysis⁸. The

prevalence of dyspepsia among hemodialysis patients varies between 48% and 70%^{9,10}.

In various studies age does not appear to have any effect on occurrence of dyspepsia. Although most of the studies have included patients above the age of 18 years or older the references regarding dyspepsia in children are limited, it appears that dyspepsia represents a common situation (60%-80%) under the broad spectrum of recurrent abdominal pain¹¹. However in a study from urban Mumbai found that dyspepsia was more prevalent in adults > 40 years¹².

Majority of population-based studies do not show any gender difference in dyspepsia prevalence¹³. While few studies from different populations, have noted a consistent female preponderance with dyspepsia^{7,14,15}.

A recent well done meta-analysis and Cochrane Database systematic reviews show that there is a small but significant benefit of eliminating H pylori in patients with dyspepsia¹⁶.

Study from Mumbai, India has shown that, type of diet vegetarians or non-vegetarian have no effect on dyspeptic symptoms. However spicy, fried or food prepared outside the home contributed insignificantly to worsening of symptoms¹².

In a survey from India of patients with UD have showed regular smoking as an identifiable risk factor¹²

Objectives :

1. To study prevalence of dyspepsia in CKD patients using ROME III questionnaire.
2. To correlate severity of kidney dysfunction assessed by e-GFR with presence of dyspepsia

Methodology :

This cross-sectional study was conducted at Lata Mangeshkar Hospital, Nagpur over a period of two months from May 2018 to July 2018.

Inclusion Criteria :

1. Patients of CKD irrespective of its stage
2. Age > 18 years
3. Patients willing to participate in study

Exclusion criteria :

1. Presence of disease or clinical situation that could prevent patients from answering the questionnaires
2. Patients not willing for upper GI endoscopy
3. Patients with known gastric disease

After getting approval from Institute's Ethics Committee, subjects fulfilling inclusion criteria were enrolled into the study. A written informed consent was obtained from all the participants and the study was conducted in accordance with the tenets of the Helsinki Declaration.

All the CKD patients admitted in Medicine wards / Dialysis Unit were included in the study. CKD was diagnosed on the basis of history, blood urea and serum creatinine level, USG findings- kidney size, cortico-medullary differentiation and cortical thickness. Demographic data was collected in all patients. Patients were screened for presence of anaemia and hypertension. Laboratory investigations in the form of complete blood count (CBC) and Kidney Function Tests were done in each patient. e-GFR was calculated as per the application of the simplified MDRD formula, taking the values

of serum creatinine into consideration and patients were categorized according to 5 stages of CKD.

All the patients were interviewed using the ROME III questionnaire. ROME III questionnaire consists of 18 questions related to various upper GI symptoms, their duration and pattern. (Annexure). The questionnaire was also translated in the vernacular language (Marathi/Hindi) for non-English speaking subjects. The eligible patients who had consented for participation in the study were interviewed in their vernacular language.

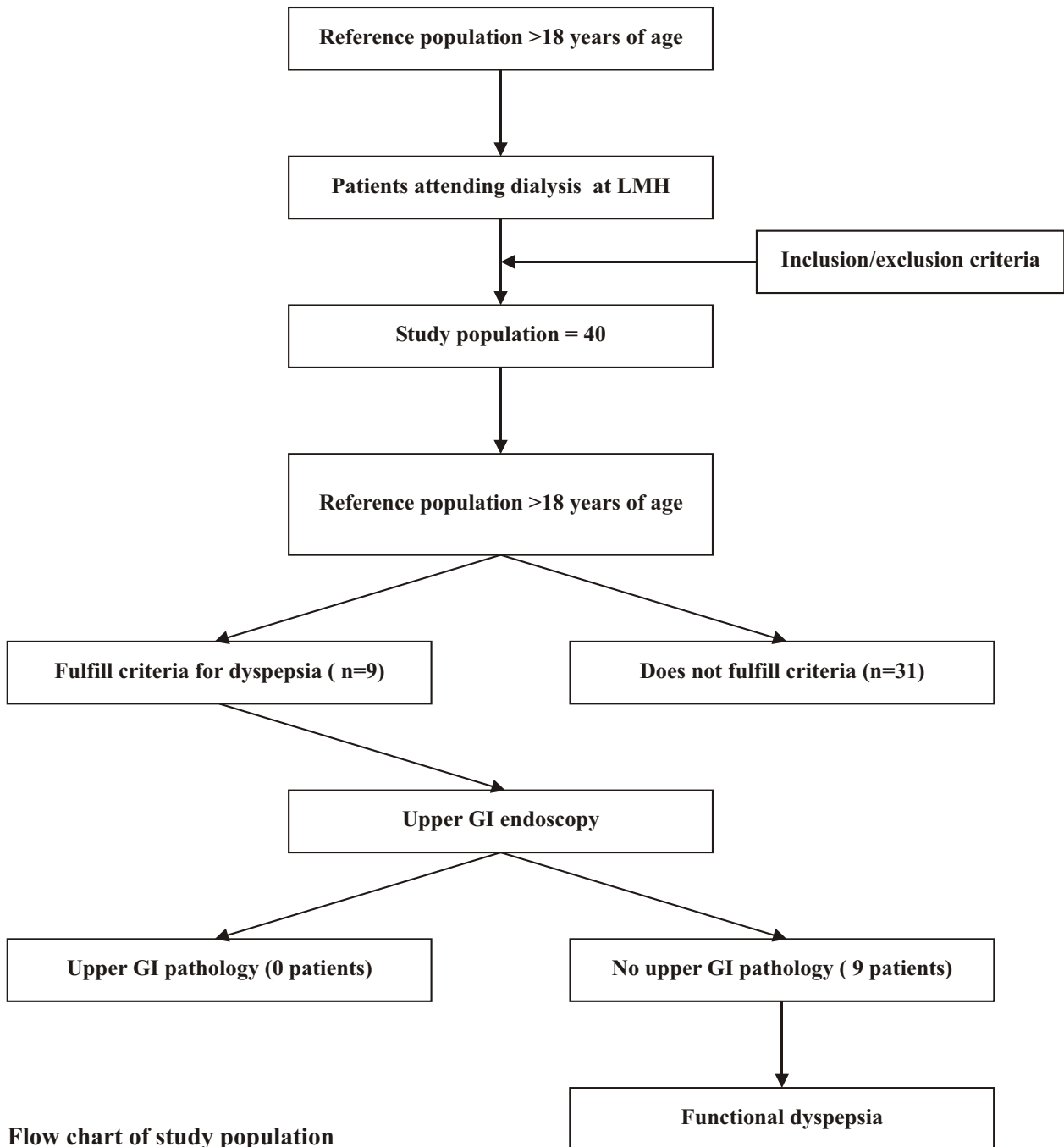
The patients having alarming symptoms in the form of hematemesis or significant weight loss were subjected to endoscopy.

Sample Size : The target sample size was approximately 40 as per the hospital based prevalence of CKD patients being admitted to the wards or in dialysis units for the said period of time.

Statistical Analysis : Statistical analysis was performed using SPSS software.

Table 1 : Demographic and socioeconomic parameters :

Characteristics	Levels	Dyspepsia		P-value
		Positive (n=9)	Negative (n=31)	
Age in years [Mean ± SD]		55.22 ± 8.73	47.90 ± 13.04	0.1232
Gender [No. (%)]	Male	6 (66.67%)	20 (64.51%)	0.9999
	Female	3 (33.33%)	11 (35.48%)	
Employment [No. (%)]	Employed	3 (33.33%)	12 (38.70%)	0.9999
	Unemployed	5 (55.56%)	18 (58.06%)	
Education [No. (%)]	≤ Middle school	5 (55.56%)	15 (48.38%)	0.9916
	High School	3 (33.33%)	10 (32.25%)	
	Graduation	1 (11.11%)	3 (9.68%)	
Region [No. (%)]	Rural	5 (55.56%)	10 (32.25%)	0.5395
	Urban	3 (33.33%)	14 (45.16%)	
	Diastolic			0.0764
Smoking [No. (%)]	Yes	1 (11.11%)	3 (9.68%)	
Alcohol [No. (%)]	Yes	2 (22.2%)	7 (22.58%)	
Kharra [No. (%)]	Yes	2 (22.2%)	4 (12.90%)	
Tobacco [No. (%)]	Yes	2 (22.2%)	4 (12.90%)	



Flow chart of study population

Observations and Results :

In this cross-sectional study conducted in a tertiary hospital, the following were the observations :-

Our sample consisted of 26 (65%) men and 14 (35%) women with mean age of 49.55 ± 12.34 years. Patients had mean BMI of 21.2 ± 2.95 . The laboratory results were haemoglobin of 7.71 ± 1.47 g/dl, total leukocyte count (TLC) of 7405 ± 2611

/ml, platelets 2.224 ± 0.72 lacs/ml, serum creatinine 9.9 ± 4.95 mg/dl, sodium level of 133.8 ± 6.3 mEq/L, potassium level of 4.6 ± 0.75 mEq/L and blood urea 106.15 ± 61.84 mg/dL. 9 (22.5 %) out of 40 patients were dyspeptic. There were no significant differences in the demographic and laboratory variables between patients with and without dyspepsia. Only two patients had alarming symptoms in the form of weight loss. They were

subjected to endoscopy. They had normal upper GI endoscopy.

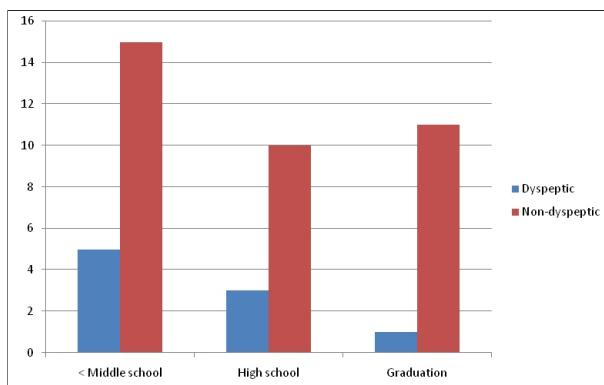
According to ROME III Questionnaire subjects were classified as having Functional dyspepsia, Post-prandial distress syndrome or Epigastric pain syndrome. Out of 40 patients, 9 subjects had functional dyspepsia, 6 subjects had post-prandial distress syndrome and 3 subject had epigastric pain syndrome.

Table 2 : Distribution of patients as per age

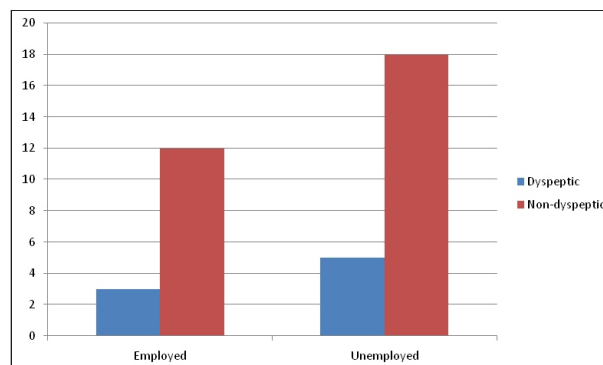
Age	Total	Dyspeptic (n=9)	Non-dyspeptic (n=31)
21-30	4	0 (0%)	4 (12.90%)
31-40	5	0 (0%)	5 (16.13%)
41-50	11	3 (33.34%)	8 (25.81%)
51-60	11	2 (22.22%)	9 (29.03%)
>60	9	4 (44.44%)	5 (16.13%)
	40	9	31

Maximum number of patients belong to 41-50 years and 51-60 years of age group .Maximum number of dyspeptics belong to >60 years of age group (4 patients). Maximum number of non-dyspeptics (29%) belong to 51-60 years of age group. There was no statistically significant difference found in two groups.

6 out of 20 (30%) men and 3 out of 11 (27.3%) women were dyspeptic. No statistically significant difference was found in gender distribution amongst 2 groups.

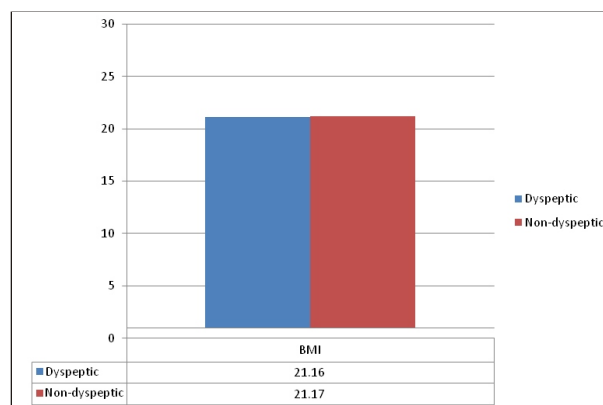


Graph 2 : showing distribution of patient as per educational level



Graph 3 : showing distribution of patients as per employment

Body Mass Index - The BMI of both dyspeptic and non-dyspeptic groups was almost identical.



Graph 4 : showing distribution of patient as per BMI

None of the laboratory parameters were shown to have statistically significant difference among 2 groups.

Mean Serum creatinine was 7.91 mg/dL in dyspeptic patients while it was 10.47 mg/dL in patients without dyspepsia. Surprisingly presence of dyspeptic symptoms was not associated with level of creatinine, which is one of the parameter revealing severity of kidney dysfunction. Similar trend was observed in Blood urea levels.

Table 4 : Distribution of patients as per duration of symptoms and frequency of dialysis

Characteristics	Levels	Dyspepsia		P-value
		Positive (n=9)	Negative (n=31)	
Duration of symptoms (in months) [Mean ± SD]		13.50 ± 15.33	12.84 ± 13.97	0.9085
Frequency of haemodialysis [No. (%)]	Once a week	0	2	0.6436
	2 times a week	8	22	
	3 times a week	1	1	
	4 times a week	0	1	

Table 5 : Distribution of patients as per Laboratory parameters :

Characteristics	Levels	Dyspepsia		P-value
		Positive (n=9)	Negative (n=31)	
Hb [Mean ± SD] (Please add units here and below)		7.41 ± 1.39	7.80 ± 1.52	0.4999
TLC [Mean ± SD]		6033.33 ± 1980.53	7803.23 ± 2704.75	0.0767
Platelet [Mean ± SD]		1.97 ± 0.79	2.30 ± 0.71	0.2488
Serum creatinine [Mean ± SD]		7.91 ± 3.95	10.47 ± 5.21	0.1813
Sodium [Mean ± SD]		133.00 ± 4.00	134.07 ± 6.96	0.6646
Potassium [Mean ± SD]		4.23 ± 0.55	4.67 ± 0.79	0.1331
Blood urea [Mean ± SD]		74.00 ± 43.37	115.48 ± 64.79	0.0800

EGFR and staging of CKD : Dyspepsia

EGFR (60 mL/ min/1.73 m ²)	Positive (n=9)	Negative (n=31)	P-value
Mean	8.78	8.42	0.9249
SD	4.15	11.07	
Median	9	7	
Min	4	1	
Max	15	66	

The mean eGFR of dyspeptic subjects is 8.78 ± 4.15 60 mL/min/1.73m². Mean eGFR of Non-dyspeptic subjects is 8.42 ± 11.07 60mL/min/1.73m².

Discussion :

Dyspeptic symptoms are commonly experienced by CKD patients. In our study there was no positive correlation between worsening of renal function and dyspepsia. This result is in agreement with previous study that also found no relation between the two¹. Two patients had alarming symptoms and were subjected to endoscopy.

Stage (eGFR)	No. of patients	Dyspeptic	Non dyspeptic
1 (90+)	0	0	0
2 (60-89)	1	0	1
3 (30-59)	0	0	0
4 (15-29)	0	0	0
5 (<15 or dialysis)	39	9	30

There was no statistically significant relation found in stage of CKD and presence of dyspepsia.

In our study functional dyspepsia was more common in > 60 years of age group. This is not in agreement with the results from previous study that found that age was not predictive of FD^{17,18}. However, Li et al found that the prevalence of FD was peak at the age of 41 to 50 years old¹⁹.

No relation was found with educational level or employment. Similar findings regarding education was demonstrated by Aro et al in there study¹⁷. However Zagari et al found association of functional dyspepsia and unemployment¹⁸.

In a study, functional dyspepsia had no relation to BMI in chronic kidney disease patients²⁰. Similar findings were reported in our study.

Serum creatinine levels was found not be a risk factor for dyspepsia. Similar findings were reported in the previous study which found creatinine not to be a risk factor for dyspepsia¹.

There was no relation between haemoglobin levels and prevalence of dyspepsia. Similar findings were reported by Salles et al²⁰ who found no relation of dyspepsia with haemoglobin.

There was no relation between blood urea levels and prevalence of dyspepsia. Bacci and Chehter also found no relation between the two¹.

No significant relation was found between eGFR and dyspepsia. This is in contrast to the study conducted by Bacci and Chehter who found that patients with a high eGFR are at higher chances of developing dyspepsia¹.

Also, no relation was found between total leukocyte count and platelet count with prevalence of dyspepsia.

Definitions and diagnostic criteria influence the prevalence rates of FD. In Kalixanda study in which Rome III criteria was used, the prevalence of FD was 15.7%¹⁷. An Italian study found that the prevalence of FD was 11% when a modified Rome II criteria was used (Zagari et al., 2010)¹⁸.

Conclusion :

Prevalence of dyspepsia among CKD patients obtained in this study was 22.5%. There was no significant relationship found between Functional Dyspepsia and sociodemographic factors like Body mass index, employment and education. Slight relation was found with age. Higher incidence was found in age group of > 60 years. None of the lab parameters were found to have association with dyspepsia amongst CKD patients. CKD patients should be screened for dyspepsia and appropriate treatment and counseling should be done. There was no statistically significant relation found in stage of CKD and presence of dyspepsia.

Limitations :

The prevalence of functional dyspepsia among CKD patients in this study could not be generalized to the different ethnic background in India due to the difference distribution of population in this region with the majority of them were Maharastrian. As this study employed questionnaires method for data collection, it might lead to recall bias and language bias. Some of the subjects in this study had actually being treated for their dyspeptic symptoms and this would change the course of the symptoms and could affect the true prevalence of FD.

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