

Review Article

Dyspepsia in primary care practice in Bangladesh

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Abstract

Dyspepsia generally refers to pain or discomfort in epigastric region. It is a common problem in the community and clinical practice. It affects quality of life, productivity and causes significant resources utilization. There are a number of different causes of dyspepsia which varies from country to country. But the commonest cause in all the countries is functional dyspepsia. Investigations needed to diagnose the cause of dyspepsia are many and treatment options also vary. Consequently different scientific bodies have issued guidelines regarding the management strategy of this common disorder. But the strategy should depend on local prevalence of Helicobactor pylori infection, available health care resources and underlying serious diseases. Most dyspeptic patients are managed by primary care physicians. In Bangladesh, investigation facilities are lacking in most parts of the country. Furthermore, eradication rate of H. pylori is low and recurrence rate is high. In this article, we have reviewed the current evidences and recommendations on evaluation and treatment of dyspepsia and discussed the preferred option in primary care settings in Bangladesh.

Key Words: Dyspepsia, functional dyspepsia, Helicobactor pylori, peptic ulcer disease, primary care practice

Introduction

Dyspepsia means a symptom or set of symptoms that is (are) considered to arise from the gastroduodenal region.¹ The dyspeptic symptoms are epigastric pain, epigastric burning, postprandial fullness or early satiety. Bloating, nausea and vomiting may co-exist and are supportive symptoms but not included in definitions.^{1,2} Typical symptoms of gastroesophageal reflux disease such as heartburn and acid eructation have been excluded from the dyspeptic symptoms as these primarily arise from the oesophagus.¹ Dyspepsia is a worldwide health and economic problem. It is associated with significant morbidity and impairment of quality of life.³ It imposes a huge burden on health care system due to its high prevalence and resource utilization from consultation, investigations, drug consumption and considerable time loss from the work.^{3,4,5}

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Dyspepsia is caused by different diseases. There are various investigations to determine the underlying cause of dyspepsia. Treatment options are also variable. It is often a challenge to primary care physicians to find the best approach. But it is important to have a cost effective management strategy for the patients and health care services. There are differences in predominant causes of dyspepsia in different countries. Investigation facilities and available health resources are also different in different countries. For these reasons, different international and regional guidelines have recommended that management strategy of dyspepsia should be tailored for each country.⁶⁻⁸ In Bangladesh; investigation facilities for evaluation of dyspepsia are limited. In fact, in many parts of the country there are no investigations facilities at all. Management of dyspepsia in such situation is really difficult for the general practitioners who deal with most of the patients. International and regional guidelines have not addressed the issue of management of dyspepsia in such resource constraint situation. In this article, we have reviewed the current literature on evaluation and treatment of dyspepsia and discussed the preferred strategy in primary care settings in Bangladesh.

Practice points

- Dyspepsia means a symptom or set of symptoms that is (are) considered to arise from the gastroduodenal region.
- There are many causes of dyspepsia which vary from country to country
- Guidelines for management should be based on local facts.

Epidemiology

The prevalence of dyspepsia varies from 7% to 41% and it is estimated that 25% of the general population suffer from dyspeptic symptoms worldwide.⁹⁻¹¹ The prevalence of dyspepsia in general population is 8 % to 41% in Bangladesh.¹²⁻¹³ This difference in prevalence may be due to different populations studied or differences in definition of dyspepsia used. Epidemiological factors that influence the prevalence of dyspepsia are race, culture, age, sex, alcohol consumption, cigarette smoking, use of non-steroidal anti-inflammatory drugs (NSAIDs), H. pylori infection and obesity.¹⁴ About 30% of the dyspeptic patients seek medical consultation -mostly from primary care physicians. More than 50% dyspeptic subjects take medications most of the days and 30% take leave from the work occasionally in the United Kingdom.¹⁵

Practice points

- Many patients suffer from dyspepsia in all the countries of the world including Bangladesh.
- Dyspepsia causes work loss, loss of resources due to consultations, investigations and medications taken

Causes of dyspepsia

Common differential diagnosis of dyspepsia is shown in Table-I.

Table-I: Common causes of dyspepsia

Peptic ulcer disease
Gastroesophageal reflux disease
Gastric cancer and other tumors
Cholelithiasis
Medications, e.g., NSAIDs
Functional dyspepsia

Patients with dyspepsia who have not been investigated by endoscopy of upper gastrointestinal (GI) tract are categorized as uninvestigated dyspepsia. Overall, 70-80% of patients with dyspepsia have no clinically significant findings at endoscopy. If no organic, systemic or metabolic cause is found to explain the dyspeptic symptoms then it is called functional dyspepsia (FD).¹ Rome III committee subdivided functional dyspepsia into two new diagnostic categories: meal induced postprandial distress syndrome (PDS) characterized by post-prandial fullness and early satiety; epigastric pain syndrome (EPS) characterized by epigastric pain and burning.¹ Functional dyspepsia is the commonest cause of dyspepsia. Pathogenesis of functional dyspepsia is multifactorial. Delayed gastric emptying, impaired gastric accommodation, hypersensitivity to gastric distension, psychological factors, excessive gastric acid secretion, Helicobacter pylori infection, genetic factors, diet, lifestyle and prior gastro intestinal infection have been implicated in the pathogenesis of functional dyspepsia.² Recent review of literature shows that peptic ulcer disease (PUD) is found in 11% of Asian patients with dyspepsia.¹⁶ The predominant cause of peptic ulcer diseases is Helicobacter pylori infection. Helicobacter pylori is found in up to 90% of patients with duodenal ulcer and 60%-80% patients with gastric ulcers.¹⁷ Second but less common cause of peptic ulcer diseases is NSAIDs. Effects of NSAIDs are mainly mediated through the interference with the production of protective prostaglandins in the gastric mucosa. Risk factors associated with development of peptic ulcer diseases in patients taking NSAIDs are shown in Table-II.

Table-II: Risk factors for development of peptic ulcer disease in patients taking NSAIDs

Prior history of peptic ulcer disease
Age more than 60 years
Presence of co-morbidity
High dose and prolonged use of NSAIDs
Presence of Dyspepsia
Co-therapy of NSAIDs with
Steroid
Anticoagulant
Other NSAIDs (Aspirin)
Selective serotonin reuptake inhibitor
Bisphosphonate
Types of NSAIDs
High risk- Indomethacin, Ketoprofen
Intermediate risk –Aspirin, diclofenac, naproxen
Low risk –meloxicam, ibuprofen

Practice points

- Functional dyspepsia is the commonest cause of dyspepsia.
- A small number of patients have peptic ulcer disease which is associated with H. pylori infection in the majority.

Investigations

The initial management of a patient with dyspepsia should begin with a thorough history and clinical examination. Clinical features do not reliably differentiate between organic and functional disease.^{18,19} Endoscopy of upper gastrointestinal tract is the most important investigation to establish the diagnosis of functional dyspepsia in which no organic lesion is found. However, it is not possible and cost-effective to perform endoscopy on every patient with dyspepsia. Moreover, it is an invasive procedure, costly and not widely available. The possibility of having organic disease is high in presence of certain symptoms and signs known as 'alarm features'. (Table-III)

Table-III: Alarm features

Unintended weight loss
Progressive dysphagia
Recurrent or persistent vomiting
Evidence of GI bleeding
Fever
Family history of gastric cancer
New onset dyspepsia in a patient over 50 years of age
Odynophagia
Unexplained iron deficiency anemia
Palpable mass or lymphadenopathy

So guidelines recommend that presence of alarm features is an indication for investigations.^{2,6-8} Alarm features are found in about 10% of patients presenting at primary care in the United Kingdom.²⁰

Chances of upper GI malignancy increase with age. In various guidelines, elderly age is considered as an 'alarm feature'. Age above a certain limit makes it necessary to have upper gastrointestinal endoscopy in dyspeptic patients. Threshold level for endoscopy depends on prevalence of upper GI malignancy in particular geographic area. Bangladesh is a low risk country for gastric cancer and age 50 years and above is indication for endoscopy even in the absence of other alarm features.²

Other tests that are useful in the evaluation of dyspepsia are complete blood count, blood biochemistry tests including tests for creatinine, electrolytes, glucose and liver function tests. Stool examination for parasites and occult blood tests are also useful. Ultrasonography or computed tomography (CT) may be employed if clinically indicated. Upper GI barium radiography has low sensitivity and specificity for detecting lesions compared to endoscopy and generally not recommended as part of the work -up for dyspepsia.^{7,21}

Practice points

- Vast majority of patients are treated after clinical evaluation without any investigation.
- Patients with 'alarm feature' should be investigated.

Management of un-investigated dyspepsia in the community by general practitioner

Test-and-treat and empiric acid suppressive therapy are two common strategies for the diagnosis and treatment of uninvestigated dyspepsia. Test-and treat strategy implies that presence of helicobacter pylori infection should be tested non-invasively and if found positive, should be treated by eradication therapy. It results in cure of helicobacter pylori infection and cure of peptic ulcer disease if it is present. In a number of functional dyspepsia patients, Helicobacter pylori eradication is followed by symptomatic improvement. Endoscopy is thus avoided in a good proportion of patients. Many Western guidelines have recommended that if prevalence of Helicobacter pylori infection is high (>10%-30%), patients should undergo test and treat strategy.^{6-8,22,23} Empiric acid suppressive therapy means treating patients with proton pump inhibitors (PPIs) empirically. It does not cure Helicobacter pylori infection particularly in those with underlying ulcer disease, resulting in frequent relapse of ulcer symptoms. The Asia-Pacific Working Party recommends antisecretory therapy (Proton pump inhibitors or H2 receptor blocker) or prokinetics at

standard dose with duration of 2–4 weeks and considers this approach to be a less expensive alternative and appropriate strategy in countries with limited health resources.²⁴ This recommendation is based on the fact that significant percentage of patients will improve with this treatment and subsequently have a long-term remission. A recent review of literature found no significant differences between test-and-treat and empiric acid suppressive therapy strategies in terms of symptom control and cost-effectiveness.²⁵ A current guideline recommends that either strategy can be used.²⁶

Bangladesh perspective

The prevalence of helicobacter pylori infection is high in Bangladesh. More than 90% apparently healthy adults have been found to have antibody to Helicobacter pylori in the blood.²⁷ Another study has demonstrated that 84% children become Helicobacter pylori infected by 6-9 years of age in Bangladesh.²⁸ In a community survey, the prevalence of peptic ulcer disease was also found to be high (15%).¹³ Test and treat approach can be useful in areas where helicobacter pylori infection can be diagnosed by non-invasive tests such as urea breath test (UBT), stool antigen test (SAT) and serological test. Adoption of test and treat strategy widely in Bangladesh has a number of limitations. Firstly, facilities for non-invasive helicobacter pylori test are not available in majority areas of Bangladesh. Urea breath test and Stool antigen test are preferred methods of diagnosing helicobacter pylori by non-invasive method. But these tests are commercially available in very limited centers. So, the only test available in Bangladesh to detect helicobacter pylori non-invasively is serological test which doesn't necessarily indicate active infection and is not useful as a test of eradication. This is because the test may remain positive for many years after successful helicobacter pylori eradication. Only validated IgG serology should be used due to variability in accuracy of different commercial tests and the favored method is ELISA.²³ The accurate serology test based on ELISA is not widely available in Bangladesh. Secondly, most studies have shown that helicobacter pylori eradication regimens in Bangladesh are not effective at internationally accepted rate of eradication (80%).²⁹⁻³⁴ Thirdly, a long-term follow up study from Bangladesh has shown that there is high recurrence of helicobacter pylori infection which is 39% at 5 years.³⁵ Considering the limited availability or unavailability of investigation facilities, poor eradication rate and high recurrence rate of helicobacter pylori therapy, the preferred method should be empirical therapy with proton pump inhibitors or H2 receptor blocker in primary care setting in Bangladesh (Figure-1).

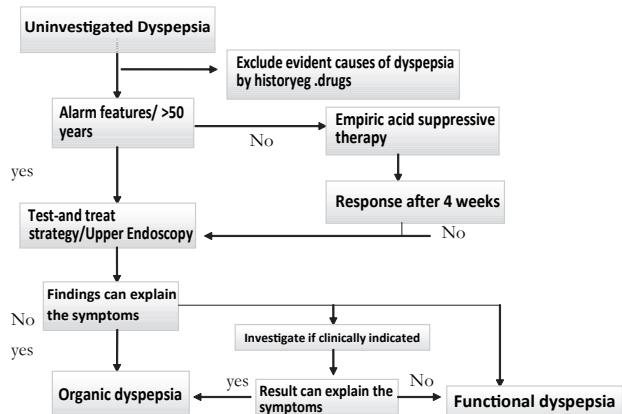


Figure-1: Diagnostic algorithm for uninvestigated dyspepsia

The available options for patients who do not respond to initial empiric PPI therapy for 2-4 weeks are: step up therapy (changing dose or drug class) test-and-treat for H pylori or endoscopy. Same treatment is justified in patients who responded to initial PPI therapy and in whom symptoms recur.⁶⁻⁸

Practice points

- Test and treat therapy-non-invasive test for H. pylori and eradication therapy for patients who test positive. A proportion of patients improve. But non invasive tests are not available in most parts of Bangladesh.
- Empirical acid suppressive therapy- results are similar to the test and treat method.
- Prevalence of H. pylori infection is high in Bangladesh. Eradication therapy has a lower success rate compared to western countries. Recurrence rate is high.

Management of functional dyspepsia

As functional dyspepsia is a heterogeneous disorder the treatment is also variable. PPIs, prokinetics and H. pylori eradication therapy are the main options for treatment of functional dyspepsia. PPI in standard dose is effective in controlling symptoms in a proportion of patients with functional dyspepsia. The standard dose for omeprazole, esomeprazole and rabeprazole is 20 mg daily. Equivalent dose for lansoprazole and pantoprazole is 30 mg and 40 mg daily respectively. Higher dose PPI is no more effective than standard dose.² PPIs are more effective in management of epigastric pain syndrome than postprandial distress syndrome. Prokinetic agents such as domperidone and metoclopramide may provide symptom relief in some functional dyspepsia patients particularly in postprandial distress syndrome. The benefit of H. pylori eradication in functional dyspepsia is less distinct compared to peptic ulcer disease. A recent review of literature showed that the number needed to treat (NNT) for improvement of symptoms after eradication therapy was 14 for functional dyspepsia. Asian functional dyspepsia consensus report

stated that H. pylori testing and eradication should be part of the management strategy for all patients in Asia who present with dyspepsia where socio-economic conditions allow. Considering the widespread lack of investigation facilities, higher cost, low eradication rate, high recurrence rate and symptoms improvement in a small number of patients, H. pylori eradication should not be routine part of management strategy for functional dyspepsia in Bangladesh.

Antidepressants and anxiolytics such as amitriptyline, imipramine, fluoxetine etc. have a role in the management of functional dyspepsia. These drugs are useful in refractory to treat patients and their action is mediated through central mechanism. Psychological disturbances and sleep disturbances may be important determinants of response to anti-depressant treatment in functional dyspepsia patients. Specific food ingredients such as chilli, spice and fats may provoke dyspeptic symptoms and dietary modification can be considered in patients with functional dyspepsia.

Practice points

- PPI in standard dose is effective in a number of patients. Higher dose confer no additional benefit.
- Prokinetics may be effective in a small number of patients.
- Very few patients get benefit from H. pylori eradication therapy.
- Antidepressants and anxiolytics may help some patients.
- No specific dietary recommendation is given.

Management of patients with peptic ulcer disease

There are various acid neutralizing drugs, mucosa protective agents and anti-secretory drugs for the treatment of peptic ulcer disease. All the patients with peptic ulcer disease should be tested for H pylori and if positive should be offered anti H pylori therapy. Treatment with PPIs for four weeks in duodenal ulcer and 6-8 weeks in gastric ulcer lead to ulcer healing rate of more than 90%.³⁶ The main benefit of H.pylori eradication therapy is low recurrence of ulcers. The one year recurrence of ulcer with antisecretory therapy is 50% to 80%³⁷ whereas H. Pylori eradication therapy associated with < 2% recurrence rate.³⁵ In uncomplicated duodenal ulcer, prolonging acid inhibition with PPI is not necessary after H. Pylori therapy. In complicated duodenal ulcers and gastric ulcers prolonging PPI is recommended.²³ H pylori eradication and endoscopic healing should be confirmed in gastric ulcers after 4 weeks of treatment.²³ No dietary restriction is needed in patients with peptic ulcer disease. Patients should avoid those foods that precipitate symptoms.³⁶

Common treatment regimens for H. pylori eradication available in Bangladesh are shown in Table-IV.

Table-IV: H. Pylori eradication regimens available in Bangladesh

Regimen	Drug 1	Drug 2	Drug 3
Clarithromycin-based triple therapy (10–14 days)	Standard dose of PPI twice daily	Clarithromycin 500 mg twice daily	Metronidazole 500 mg twice daily or Amoxicillin 1 g twice daily
PPI-metronidazole - amoxicillin/tetracycline (10–14 days)	Standard dose of PPI twice daily	Metronidazole 500 mg twice daily	Amoxicillin 1g twice daily or Tetracycline 500 mg twice daily
Levofloxacin-based triple therapy (10-14 days)	Standard dose of PPI twice daily	Levofloxacin 500 mg once daily or 250mg twice daily	Amoxicillin 1 g twice Daily
Sequential therapy (10 days)	Standard dose of PPI twice daily and amoxicillin 1g twice daily for the first 5 days	Standard dose of PPI twice daily, clarithromycin 500mg twice daily, and tinidazole 500mg twice daily for the remaining 5 days	

Extending the duration of PPI- clarithromycin containing triple regimen treatment from 7 days to 10-14 days improves the eradication success by approximately 5%-7% and may be considered.²³ After failure of PPI-clarithromycin containing therapy levofloxacin based therapy is an option in Bangladesh.

Practice points

- All patients with peptic ulcer disease should be treated for presence of H. pylori infection and eradication therapy should be given to those who are positive.

Management of NSAIDs associated dyspepsia

NSAIDs are one of the most commonly used drugs all over the world. The most common side effects of NSAIDs are gastrointestinal complications which range from mild dyspepsia to life threatening ulcer complications such as perforation and hemorrhage. For the management of NSAIDs associated active ulcers, NSAIDs should be stopped if possible. H. Pylori should be tested and if positive should be eradicated. Anti-secretory drugs can be discontinued after 8 weeks. Antacids, sucralfate and misoprostol have no advantage over PPI and are not recommended for this purpose.³⁷ If continuous NSAIDs treatment is necessary, PPI are the most effective agents.

Practice points

- If possible NSAIDs therapy should be stopped.
- If continuous NSAIDs therapy is necessary, concomitant PPI therapy may lower the incidence of peptic ulcer and its complications.

Dyspepsia is a common problem. Primary care physicians deal with most of the patients with dyspepsia. After investigations majority of the patients are found to have functional dyspepsia. Two most common strategies for the management of uninvestigated dyspepsia are: test-and-treat and empiric acid suppressive therapy. Recent evidence suggests no significant differences between test-and-treat and empiric acid suppressive therapy strategies in terms of symptom control and cost-effectiveness. In most areas of Bangladesh the diagnostic facilities are lacking. Anti H. pylori therapy is associated with low eradication rate and high recurrences in this country. If we consider these factors, the preferred strategy for uninvestigated dyspepsia without alarm features and age less than 50 years should be empiric acid suppressive therapy in primary care practice in Bangladesh. In patients who do not respond to initial empiric therapy, investigations including upper GI endoscopy should be undertaken. Investigations are also warranted in all patients who present with 'alarm feature' and who are more than 50 years of age.

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