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ORIGINAL ARTICLE

Role of *Helicobacter pylori* eradication in patients with functional dyspepsia

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Abstract

Background *Helicobacter pylori* (*H. pylori*) is implicated in the pathogenesis of functional dyspepsia (FD). There is conflicting data regarding the benefit of *H. pylori* eradication for symptom relief in FD.

Aims To study the benefit of eradicating *H. pylori* in patients with FD as compared to standard medical treatment (SMT). Secondary aims were to find efficacy of *H. pylori* eradication therapy, recurrence of *H. pylori* after eradication, and predictors of efficacy.

Methods Consecutive adult patients of FD (ROME IV) with *H. pylori* infection presenting in the outpatient department of our hospital were enrolled. Patients with Global Overall Symptom (GOS) scale > 2 and *H. pylori* infection were included. Patients were randomized into two groups: group 1 received *H. pylori* eradication therapy and group 2 received SMT. Treatment success was defined as symptom relief (GOS score < 2 and reduction by at least 2 points at 6 months) and *H. pylori* eradication was defined as stool antigen negative at 4 weeks.

Results Of 329 participants with FD, 253 were *H. pylori* positive (rapid urease test and stool antigen test) (76.89%). After exclusions, 202 were randomized into two groups of 101 each. Thirty-two patients in group 1 and 31 in group 2 had treatment success (31.7% vs. 30.7%, p=1.000). The efficacy of *H. pylori* eradication therapy was 74.46% (70/94). *H. pylori* reinfection rate was 26.02% (19/73).

Conclusions *H. pylori* eradication therapy does not provide additional benefit in symptom relief in patients with FD as compared with SMT.

Trial registration NCT04697641 (retrospectively registered on www.clinicaltrials.gov in January 2021)

Keywords Epigastric pain syndrome · Functional dyspepsia · GOS scale · *H. pylori* eradication therapy · Stool antigen test · Likert scale · Non-ulcer dyspepsia · Postprandial distress syndrome · Rapid urease test · Rome IV criteria · Triple therapy

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Bullet points of the study highlights

What is already known?

- Some investigators have attempted *Helicobacter pylori (H pylori)* eradication for symptomatic relief in functional dyspepsia (FD).
- Results of such studies are conflicting due to heterogeneous inclusion criteria.

What is new in this study?

- In this randomized-controlled trial from India *H. pylori* eradication therapy was not found superior to standard medical treatment for symptom relief in patients with FD.
- Strict and validated definitions of response.

What are the future clinical and research implications of the study findings?

- Our data suggest that *H. pylori* eradication therapy may not be indicated in treatment of FD in India.
- Further research into mechanisms of pathogenesis of clinical symptoms in FD required.

Background

Functional dyspepsia (FD) is reported in as high as 30% adult population in India [1]. It is defined according to *Rome IV* criteria by one or more of the followings: postprandial fullness, early satiation, epigastric pain, and epigastric burning that are unexplained after a routine clinical evaluation and in the absence of an identifiable organic disease, during the last 3 months, with onset at least 6 months before [2].

The causal relationship between *Helicobacter pylori* (*H. pylori*) and superficial gastritis has been established. But whether *H. pylori* is responsible for symptoms of FD is a topic of debate [3]. Studies have reported various estimates of association between *H. pylori* eradication and improvement of dyspeptic symptoms [4–6]. There is scarcity of large randomized controlled studies and the available studies have great heterogeneity. Early meta-analyses concluded no benefit of *H. pylori* eradication on symptom relief in FD [7], while later meta-analyses showed some benefit [8]. This may be due to stringent criteria used in earlier studies to define response and lack of standard definition of FD used in these studies. The contradictory outcomes of various meta-analyses indicate that there is no compelling evidence of the benefit of eradication of *H. pylori* in patients of FD.

It has been suggested that a "test-and-treat" strategy for *H. pylori* is preferable in populations with infection rates higher than 10% in the community [9]. Kyoto Consensus proposes treatment of *H. pylori* in *H. pylori*–positive dyspepsia and makes a retrospective diagnosis of *H. pylori*-associated dyspepsia if there is sustained relief after 6–12 months [10].

However, a Cochrane Database Systematic Review did not find significant evidence to favor this approach [11]. Some studies have shown marginal cost-effectiveness in treating patients with non-ulcer dyspepsia (NUD) [9]. On the other hand, patients with FD with *H. pylori* infection have been found to have higher antibiotic resistance as compared to patients with peptic ulcer disease [12].

There is lack of enough data on *H. pylori* eradication for FD in India. We conducted a prospective randomized trial to study the benefit of eradicating *H. pylori* in patients with FD as compared to standard medical treatment only. We hypothesized that *H. pylori* eradication would provide additional benefit as compared to standard medical treatment for symptom relief in *H. pylori*–positive FD.

Methods

Study characteristics and participants

This was a single-center, open-label, prospective randomized controlled study. The study was done at Sir Ganga Ram Hospital, New Delhi, a tertiary center in northern India, between September 2017 and May 2019. Requisite ethical clearance from institutional ethical committee was obtained before

the initiation of the study. The trial was registered in Protocol Registration and Results System (NCT04697641).

Consecutive adult (>18 years age) patients with FD (ROME IV criteria) who were *H. pylori* positive were included in the study. Pregnant and lactating females; children and adolescents; those with predominant symptoms of heartburn, irritable bowel syndrome, history of peptic ulcer, upper gastrointestinal (GI) tract surgery, biliary colic, and allergies to study medication; those who received previous eradication therapy for *H. pylori*; patients who received antibiotics or bismuth during 4 weeks before enrolment, proton pump inhibitors (PPI) 2 weeks before enrolment, and histamine-2 receptor blockers in the week before enrolment; patients on drugs which have interactions with anti-*H. pylori* drugs (Annexure 1); or those unable to answer the study questionnaires were excluded from the study. Those with uncontrolled diabetes mellitus (hemoglobin A1c [HbA1c] > 9 mmol/mol) and uncontrolled thyroid status (thyroid-stimulating hormone [TSH] > 10 mIU/L or < 0.5 mIU/L) were further excluded after investigations.

Evaluation

All patients underwent routine investigations including complete hemogram, liver function tests, renal function tests, TSH, urine analysis, fasting and postprandial blood sugar levels, HbA1c, and ultrasound abdomen. All patients underwent upper GI endoscopy. Those with esophagitis, peptic ulcer, polyp, or mass lesion were excluded. *H. pylori* infection was diagnosed when both rapid urease test (RUT) (Halifax Research Laboratory, Kolkata, India) and *H. pylori* stool antigen test (SAT) by immunochromatography were positive [13, 14].

Symptom assessment

The Global Overall Symptom (GOS) scale was used for symptom assessment in the study population [15]. The symptoms were self-reported on a 7-point Likert scale ranging from 1 = no problem to 7 = a very severe problem (Annexure 2). Those with moderate to high intensity (>2 on GOS) symptoms were included in the study. Patients were also asked to rate the severity of 10 specific upper GI symptoms (specific symptom subtypes [SSS] using the same 7-point Likert scale as for the GOS scale: epigastric pain, epigastric discomfort, heartburn, acid regurgitation, upper abdominal bloating, excessive belching, nausea, early satiety, postprandial fullness, and other epigastric symptoms) (Annexure 3). SSS was used for dividing participants into two symptom subgroups: predominantly epigastric pain syndrome (EPS)—if first four symptom score was higher; and predominantly postprandial distress syndrome (PDS)—if last six symptom score was higher. Although there is significant overlap in patients with EPS and PDS as is shown in a previous study [16], this was an arbitrary division based on predominant symptoms.

Randomization and intervention

Subjects were randomized into two groups based on computer-generated randomization.

The group allocation was concealed in a sealed opaque envelope and opened at randomization. Participants allotted to group 1 received *H. pylori* eradication therapy in the form of 14 days of clarithromycin 500 mg twice a day, amoxicillin 1000 mg twice a day, and pantoprazole 40 mg twice a day followed by 6 more weeks of pantoprazole 40 mg once daily. Prokinetics before meals (levosulpiride 25 mg, acotiamide 100 mg, itopride 50 mg) were given as and when required for PDS. Participants allotted to group 2 received the standard of care treatment for FD. They received PPI (pantoprazole 40 mg or equivalent) for 8 weeks and/or prokinetics before meals (levosulpiride 25 mg, acotiamide 100 mg, itopride 50 mg) when required in patients with PDS. Both the recipients and investigators were aware of the therapy given.

Follow-up

The first follow-up was at 12 weeks, 4 weeks after completion of the 8-week treatment. At this follow-up, participants were asked to rate their symptoms over the preceding week and GOS reduction by at least 2 and GOS < 2 was considered symptom relief and taken as treatment success. Patients who were lost to follow-up were included in the intention-to-treat analysis with negative outcome. *H. pylori* SAT was done at this follow-up. A positive *H. pylori* SAT was taken as failure of *H. pylori* eradication. In the case of patients who did not undergo these tests, the status was defined as unknown.

The second follow-up was 6 months after completion of the 8-week treatment. GOS was administered and *H. pylori* SAT was repeated. All participants were allowed medications for symptom relief over these 6 months and adverse events were noted.

Outcome measures

Primary outcome

Treatment success was defined as absence of symptoms or minimal symptoms (GOS score < 2 and reduction by at least 2 points), 6 months after treatment.

Secondary outcomes

- Efficacy of *H. pylori* eradication therapy defined as stool *H. pylori* antigen negative at 4 weeks after treatment.
- Rate of *H. pylori* reinfection defined as stool *H. pylori* antigen positivity at 6 months in those who were negative at 4 weeks.

Statistical analysis

Sample size was calculated assuming the rate of treatment success to be 40% in the group assigned to receive *H. pylori* eradication therapy and 20% in the group assigned to receive standard of care alone [17]. Considering this study to be binary outcome superiority trial, 158 *H. pylori*–positive patients were required to have 80% chance of detecting an increase in the primary outcome measure from 20% in the standard medical treatment group to 40% in the eradication group. Analysis of data was done using Statistical Package for the Social Sciences (SPSS) version 22 (IBM, New York, USA). Continuous variables were presented as mean and SD. Categorical variables were presented as proportions.

Two-sample *t* tests were used to compare the mean values of variables considered continuous in the treatment and placebo groups. Chi-square tests were used to analyze categorical variables. Multivariate analysis was done in variables found significant on univariate analysis to asses predictors of response. Intention-to-treat analyses included all patients who received at least one dose of medication and who were *H. pylori* positive at entry.

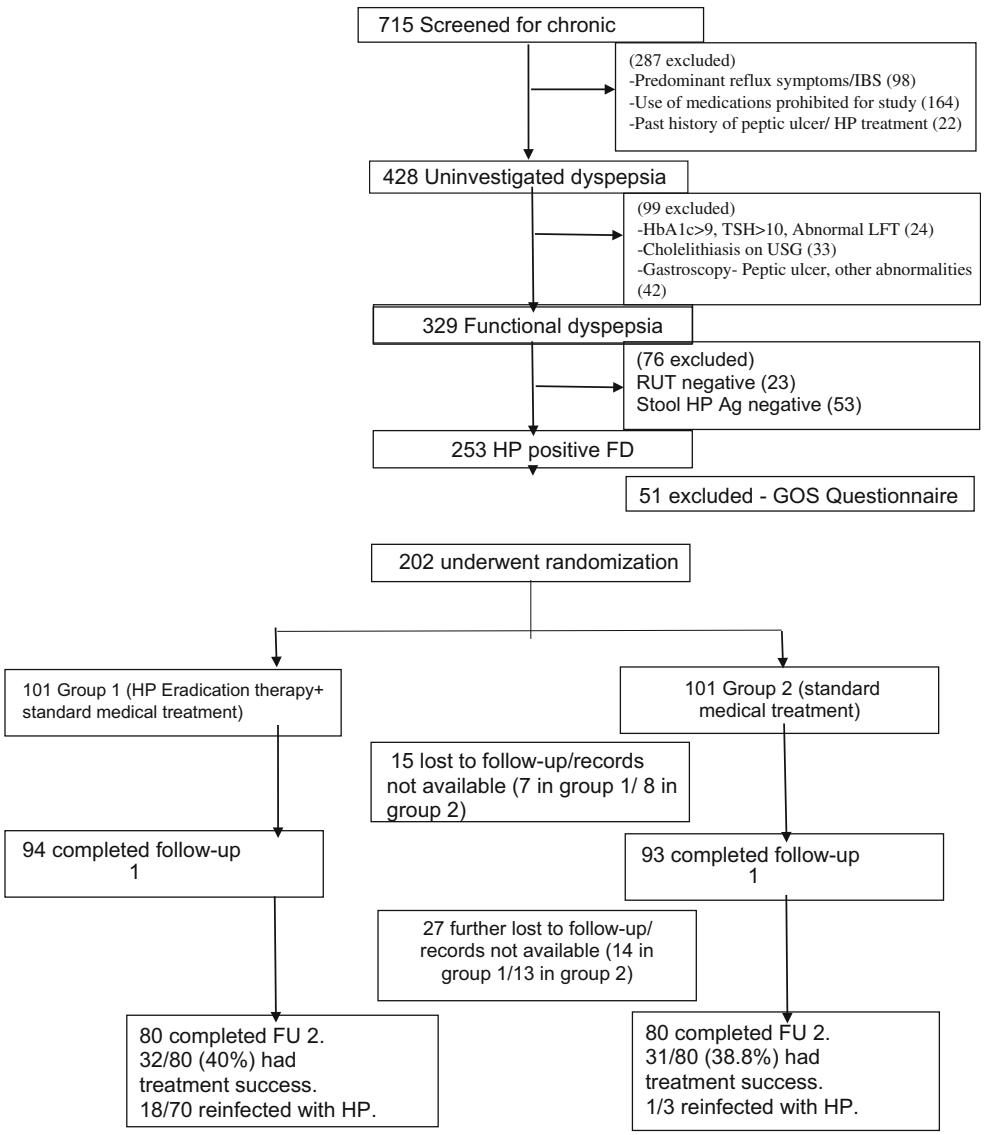

Fig. 1 Flow chart showing various exclusion criteria applied, randomization, and follow-up of patients enrolled in the study

IBS irritable bowel syndrome, *HP Helicobacter pylori*, *LFT* liver function test, *USG* ultrasonography, *RUT* rapid urease test, *GOS* Global overall scale, *FU* follow-up, *TSH* thyroid-stimulating hormone. *FD* functional dyspepsia

Table 1 Comparison of baseline characteristics in those who received *Helicobacter pylori* eradication (group 1) and those who received standard medical treatment (group 2). *BMI* body mass index, *CAD* coronary artery disease, *EPS* epigastric pain syndrome, *PDS* post-prandial distress syndrome, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *ALP* alkaline phosphatase, *GGT* gamma-glutamyl transferase

	Group 1 (*n*=101)	Group 2 (*n*=101)	*p*-value
Age	42.78 years (9.64)	40.84 years (8.49)	0.131
Weight	65.04 kg (7.49)	64.67 kg (6.76)	0.716
Height	1.622 m (.075)	1.626 m (.07)	0.709
BMI	24.79 kg/m^2 (3.17)	24.58 kg/m^2 (3.27)	0.636
Gender*			
Male	49 (48.5%)	56 (55.4%)	0.324
Female	52 (51.5%)	45 (44.6%)	
Diabetes mellitus*	33 (32.7%)	29 (28.7%)	0.542
Hypertension*	37 (36.6%)	36 (35.6%)	0.884
CAD*	14 (13.9%)	10 (9.9%)	0.384
Thyroid disorders*	10 (9.9%)	11 (10.9%)	0.818
Alcohol consumption*	15 (14.9%)	8 (7.9%)	0.121
Tobacco*	20 (19.8%)	14 (13.9%)	0.259
Smoking*	15 (14.9%)	14 (13.9%)	0.841
Symptom type*			
EPS	47 (46.5%)	52 (51.5%)	0.482
PDS	54 (53.5%)	49 (48.5%)	
Hemoglobin	11.99 g%(1.56)	12.11 g% (1.48)	0.575
Hba1c	5.636% (0.71)	5.638% (0.67)	0.989
AST	30.18 IU/L (5.92)	30.37 IU/L (5.61)	0.817
ALT	32.06 IU/L (7.39)	32.38 IU/L (6.72)	0.75
ALP	76.76 IU/L (13.29)	79.33 IU/L (12.90)	0.164
GGT	61.3 IU/L (19.88)	60.81 IU/L (20.14)	0.861

Data expressed as mean (SD), unless specified

**n* (%)

Results

1. Patient recruitment and characteristics

A total of 715 patients with dyspepsia for more than 3 months were screened. Of them, 287 were excluded because they had predominantly reflux symptoms, consumed medications prohibited in the study, or had received *H. pylori* eradication treatment. Twenty-four were excluded due to

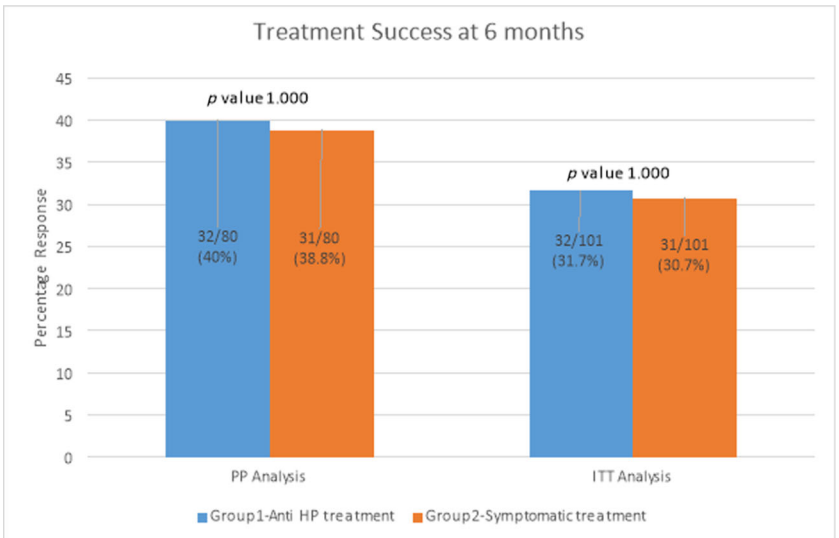

Fig. 2 Comparison of treatment success in those who received *H. pylori* eradication (group 1) versus those who received standard medical treatment (group 2)

PP per protocol, *ITT* intention to treat, *HP Helicobacter pylori*

biochemical abnormalities (HbA1c >9%, TSH >10, abnormal liver function test [LFT]), 33 due to cholelithiasis on ultrasonography (USG), and 42 for endoscopic abnormalities. The remaining 329 participants were diagnosed as FD, of whom 76 were *H. pylori* negative. Fifty-one patients were further excluded as they had GOS ≤ 2.

The remaining 202 patients were diagnosed as *H. pylori*–positive FD and were randomized into two study groups of 101 each. Fifteen (7 in group 1; 8 in group 2) patients were lost to follow-up at the first follow-up, while at the second follow-up visit 27 more participants (14 in group 1; 13 in group 2) were lost to follow-up. A total of 160 participants (80 in each group) completed the study (Fig. 1). Of the 202 patients who were randomized, 105 (52%) were males. The mean age of the participants was 41.8 years (SD 9.1 years). Ninety-nine patients had EPS and 103 had PDS. The mean GOS score was 4.168 (SD 0.84, range 3–6). Each group had 101 participants; baseline demographic, biochemical parameters, and GOS scores were comparable in both the groups (p >0.05; Table 1).

2. Primary outcome

At 6 months follow-up, 63 patients achieved treatment success, 32 from group 1 and 31 from group 2. This difference was insignificant on both per protocol and intention-to-treat analysis (p=1.000; Fig. 2). The mean GOS score at 6 months was 2.51 in group 1 and 2.52 at 6 months follow-up; 63 patients achieved treatment success, 32 from group 1 and in group 2 (p = 0.937) (Fig. 2).

3. Predictors of response

Patients achieving and not achieving treatment success did not have significant difference in *H. pylori* eradication therapy and *H. pylori* positive status (p-value 0.871 and 0.870, respectively). On univariate analysis, type of symptom presentation (EPS or PDS) was the only factor significantly different in those who had treatment success or not. 38/80 (47.5%) patients with EPS and 25/80 (31.3%) PDS patients had treatment success (p=0.035). Age, gender, body mass index (BMI), *H. pylori* eradication therapy, or *H. pylori* status were not significantly different on univariate analysis (Tables 1 and 2). Patients with EPS and PDS had similar proportion of those treated for *H. pylori* (47.5% and 52.4% respectively, p = 0.574) and those who achieved eradication (63% and 59% respectively, p = 0.653).

Secondary outcomes

Prevalence of *H. pylori* in FD in our study was 76.89% (253 of 329 patients with FD).

Efficacy of *H. pylori* eradication therapy was 74.5% (94 patients in group 1 who completed first follow-up, 70 were *H. pylori* stool antigen negative). During the first follow-up, a total of 73 (70 in group 1, 3 in group 2) patients had cleared *H. pylori* infection. Of them, 19 had stool *H. pylori* antigen

Table 2 Comparison of parameters in those who achieved treatment success and those who did not

	Treatment success, n= 63	Treatment failure, n=97	p-value
Age*	39.96 years	41.24 years	0.370
Gender			
Males	32 (50.8%)	48 (49.5%)	0.871
Females	31 (49.2%)	49 (50.5%)	
BMI*	25.16 kg/m^2	24.80 kg/m^2	0.500
Symptom type			
EPS	38 (60.3%)	42 (43.3%)	0.035
PDS	25 (39.7%)	55 (56.7%)	
Treatment groups			
Group 1	32 (50.8%)	48 (49.5%)	0.871
Group 2	31 (49.2%)	49 (50.5%)	
Stool *H. pylori* positive	43 (68.3%)	65 (67%)	0.870
Diabetes mellitus	22 (34.9%)	28 (28.9%)	0.420
Hypertension	23 (36.5%)	3544 (36.1%)	0.956
CAD	3 (4.8%)	7 (7.2%)	0.531
Thyroid disease	4 (6.3%)	8 (8.2%)	0.656
Alcohol addiction	6 (9.5%)	10 (10.3%)	0.871
Tobacco chewing	10 (15.9%)	13 (13.4%)	0.663
Smoking	12 (19%)	10 (10.3%)	0.117

*Mean values

BMI body mass index, *EPS* epigastric pain syndrome, *PDS* postprandial distress syndrome, *H. pylori Helicobacter pylori*, *CAD* coronary artery disease

Table 3 Studies evaluating outcomes of *Helicobacter pylori* eradication in functional dyspepsia. *NA* not available

Author/year/region	Functional dyspepsia (FD) definition	% of *Helicobacter pylori* in FD	Placebo arm	Efficacy of *Helicobacter* eradication	Improvement with *H. pylori* eradication	Predictors of relief
Blum et al. [17], 1998, Europe and USA	Dyspepsia for 6 months	N.A.	Yes	79%	No	N.A.
Koskenpato et al. [21], 2001, Europe	Dyspepsia for 3 months	30%	Yes	82%	No	N.A.
Sodhi et al. [22], 2013, India	Rome II	58%	Yes	69.8%	No	N.A.
Tsuda et al. [30], 2020, Asia	Rome IV	46.7%	No	84.6%	N.A.	*H. pylori* eradication, epigastric pain, postprandial fullness
Suzuki et al. [33], 2005, Asia	Rome II	N.A.	No		N.A.	*H. pylori* eradication, ulcer-like and dysmotility-like symptoms
Mccoll et al. [23], 1998, UK	Dyspepsia for 4 months	67%	Yes	88%	Yes	Shorter Duration of symptoms
Mazolleni et al. [24], 2011, Brazil	Rome III	66%	Yes	88.6%	Yes	*H. pylori* eradication, shorter duration of symptoms
Gwee et al. [27], 2009, Asia	Rome II	72.5%	Yes	68.3%	Yes	*H. pylori* eradication
Kim et al. [26], 2013, Asia	Rome III	56.3%	Yes	88.1%	Yes	*H. pylori* eradication, male, higher BMI, psychiatric medication
Dhali et al. [28], 1999, India	Dyspepsia for 4 weeks	N.A.	Yes	88%	Yes	Antral gastritis
Yamada et al. [25], 2018, Asia	N.A.	N.A.	Yes	N.A.	Yes	Young, higher symptom score

H. pylori Helicobacter pylori, *BMI* body mass index

positivity at second follow-up. Thus, *H. pylori* reinfection rate in our study was 26.02% (Figs. 1 and 2).

Discussion

This is a single-center, open-label randomized trial comparing the efficacy of *H. pylori* eradication in symptom relief in patients with FD as compared to standard of care. There was no difference in symptom relief (treatment success) at 6 months in patients who received *H. pylori* treatment as compared to those who received standard therapy.

We used a standard inclusion criteria (ROME IV criteria) to reduce heterogeneity [18, 19]. Patients with significant symptom scores on validated scales were included in the study to maintain homogeneity and reduce bias. A follow-up of 6 months ensured adequate time for the effect of *H. pylori* eradication to become evident, as was observed in a previous study by Verdu et al. [20]. Three large RCTs from other countries by Talley et al., Blum et al., and Koskenpato et al. and an Indian study by Sodhi et al. also concluded that eradication of *H. pylori* does not lead to resolution of symptoms of FD [4, 17, 21, 22]. While Sodhi et al. used Rome II definition of FD, we used Rome IV definition. Repeat endoscopy and biopsy were done by Sodhi et al., while we used non-invasive *H. pylori* SAT on follow-up.

On the contrary, western studies by Mccoll et al. and Mazzoleni et al.; Asian studies by Gwee et al., Kim et al., and Yamada et al.; and an Indian study by Dhali et al. found significant improvement of symptoms after *H. pylori* eradication [23–28]. The criteria used to define response in these studies varied and included 50% reduction or partial response as a type of response [24]. This difference in western and Asian studies might be due to higher prevalence of *H. pylori* in Asian populations. The prevalence of *H. pylori* infection in FD patients in our study was 76.89%. This is higher than in other studies, which have shown prevalence of *H. pylori* in FD ranging from 30% to 70% [17, 22, 26, 28–32]. Important studies on the effect of *H. pylori* eradication in patients with FD are summarized in Table 3.

Inclusion of patients with significant reflux symptoms may also confound the results. In our study, we included patients with FD as defined by ROME IV criteria and we defined treatment success by stringent criteria. Our study had similar number of patients with EPS and PDS (49% EPS; 51% PDS) as compared to a study by Gwee et al. who had predominantly EPS patients [27].

We could not comment on status of gastritis as histopathological evaluation was not a part of our study; however, it has been shown earlier that there is a strong relationship between *H. pylori* eradication and resolution of gastritis [29]. But whether this resolution of gastritis results in symptom improvement is still controversial.

The efficacy of *H. pylori* eradication treatment in our study was 77.6%. This rate was lower as compared to an Indian study by Dhali et al. [28] and the other studies by Blum et al. Koskenpato et al., and Talley et al. [17, 21, 29].. A recent study from India has shown similar rates of *H. pylori* eradication as in our study [22]. We used triple therapy for 14 days, which has been proven to be efficacious and equivalent to sequential therapy for *H. pylori* eradication. A suboptimal efficacy of this regimen could be due to the resistance patterns of *H. pylori* in our country [34, 35]. There were 3 participants in group 2 who cleared *H. pylori* infection despite not receiving eradication therapy. Prolonged use of PPI in them might have caused decreased levels of infection, which might not have been detected by laboratory tests.

Analysis revealed that patients with EPS were more likely to achieve treatment success than PDS (47.5% vs. 31.3%; *p*-value 0.035). Other factors like *H. pylori* eradication treatment, gender, age of patient, comorbidities like diabetes mellitus and hypertension, smoking status, or tobacco chewing did not affect the likelihood of getting symptom resolution. Our results are in concordance with studies by Tsuda et al. and Suzuki et al. which showed that the response of patients with EPS symptoms was better [30, 33]. Of the 73 patients who had *H. pylori* clearance at the first follow-up, 19 (26.02%) were *H. pylori* positive at 6 months follow-up. This could be due to reinfection or recrudescence of *H. pylori* infection. Data from western and South East Asian countries show a very low rate of reinfection [36–38]. Whereas, reports from the Indian subcontinent and other developing countries show reinfection rates after successful *H. pylori* eradication in the range of 5% to 15% [39, 40].

The limitations of our study are as follows: this was a single-center study, which may limit external validation of the results. Although, published literature does not show variation in FD prevalence across geographical areas in India. We excluded patients who had previous *H. pylori* eradication treatment and those who had recent PPI use in order to homogenize entry criteria and reduce the effect of referral bias.

This was a non-blinded study as standard medications were used in both groups and this may affect results of the study. However, responses were recorded using an elaborate tool, thus minimizing such bias. Another potential limitation is that in patients who were given *H. pylori* eradication therapy, no prokinetic was used in them. This was done to maintain homogeneity and assess the effect of *H. pylori* eradication. Patients with FD have psychiatric comorbidities and we did not do separate psychological assessment of patients. However, these patients would have been evenly distributed in both the groups.

Similarly patients with other potential confounders like smoking were included but they were equally distributed in both the groups and did not affect response. Another limitation of our study is that we used triple therapy for *H. pylori* eradication; however, we did not have local antibiotic resistance profiles as we did not culture *H. pylori*. But this is a commonly used regimen in our country and results of this study can be applied widely. Biopsy was not done to assess gastritis; however, correlation of biopsy and symptom relief was not part of our study. Both groups had similar rate of attrition and number of participants who completed the study was more than the number needed for adequately powered study.

In conclusion, this prospective study, the prevalence of *H. pylori* in FD was76.89% and efficacy of *H. pylori* eradication therapy was 74.5%. *H. pylori* eradication therapy was not found superior to standard medical treatment for symptom relief in FD.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s12664-021-01195-3.

Declarations

The study design and conduct is in accordance with the Consort statement 2010 [39].

Conflict of interest PP, PR, MS, and MK declare that they have no conflict of interest.

Ethics statement The study was performed conforming to the Helsinki declaration of 1975, as revised in 2000 and 2008 concerning human and animal rights, and the authors followed the policy concerning informed consent as shown on Springer.com.

Consent to participate Informed consent was obtained from all individual participants included in the study.

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References

1. Ghoshal UC, Singh R, Chang FY, et al. Epidemiology 4 4 5 5 of uninvestigated and functional dyspepsia in Asia: facts and fiction. J Neurogastroenterol Motil. 2011;17:235–44.
2. Drossman DA, Hasler WL. Rome IV—functional GI disorders: disorders of gut-brain interaction. Gastroenterology. 2016;150:1257–61.
3. Veldhuyzen Van Zanten SJO. The role of Helicobacter pylori infection in non-ulcer dyspepsia. Aliment Pharmacol Ther. 1997;11:63–9.
4. Talley NJ, Vakil N, Ballard ED, Fennerty MB. Absence of benefit of eradicating Helicobacter pylori in patients with nonulcer dyspepsia. N Engl J Med. 1999;341:1106–11.
5. McColl K, Murray L, El-Omar E, et al. Symptomatic benefit from eradicating Helicobacter pylori infection in patients with nonulcer dyspepsia. N Engl J Med. 1998;339:1869–74.
6. Zhao B, Zhao J, Cheng W-F, et al. Efficacy of Helicobacter pylori eradication therapy on functional dyspepsia. J Clin Gastroenterol. 2014;48:241–7.
7. Veldhuyzen Van Zanten SJO. A systematic overview (meta-analysis) of outcome measures in Helicobacter pylori gastritis trials and functional dyspepsia. Scand J Gastroenterol. 1993;28:40–3.
8. Moayyedi P, Soo S, Deeks J, et al. Eradication of Helicobacter pylori for non-ulcer dyspepsia. Cochrane Database Syst Rev. 2005;CD002096.
9. Talley NJ, Vakil N. Guidelines for the management of dyspepsia. Am J Gastroenterol. 2005;100:2324–37.
10. Sugano K, Tack J, Kuipers EJ, et al. Kyoto global consensus report on Helicobacter pylori gastritis. Gut. 2015;64:1353–67.
11. Delaney B, Ford AC, Forman D, Moayyedi P, Qume M. Initial management strategies for dyspepsia. Cochrane Database of Systematic Reviews. 2005: CD001961.
12. Broutet N, Tchamgoué S, Pereira E, Lamouliatte H, Salamon R, Mégraud F. Risk factors for failure of Helicobacter pylori therapy–results of an individual data analysis of 2751 patients. Aliment Pharmacol Ther. 2003;17:99–109.
13. Vaira D, Malfertheiner P, Megraud F, Axon AT. Diagnosis of Helicobacter pylori infection by HpSA test. European Helicobacter pylori HpSA Study Group. Lancet. 1999;354:1732.
14. Dewan R, Sachdev GK. Diagnosis of Helicobacter pylori infection in primary and tertiary care centers. Indian J Gastroenterol. 2000;19 Suppl 1:S11–4; discussion S15.
15. Veldhuyzen Van Zanten SJO, Chiba N, Armstrong D, et al. Validation of a 7-point Global Overall Symptom scale to measure the severity of dyspepsia symptoms in clinical trials. Aliment Pharmacol Ther. 2006;23:521–9.
16. Ghoshal UC, Singh R. Frequency and risk factors of functional gastro- intestinal disorders in a rural Indian population. J Gastroenterol Hepatol. 2017;32:378–87.
17. Blum AL, Talley NJ, O'Moráin C, et al. lack of effect of treating Helicobacter pylori infection in patients with nonulcer dyspepsia. N Engl J Med. 1998;339:1875–81.
18. Talley NJ. A critique of therapeutic trials in Helicobacter pylori-positive functional dyspepsia. Gastroenterology. 1994;106:1174–83.
19. Veldhuyzen Van Zanten SJO, Cleary C, Talley NJ, et al. Drug treatment of functional dyspepsia: a systematic analysis of trial methodology with recommendations for design of future trials. Am J Gastroenterol. 1996;91:660–73.
20. Verdú EF, Armstrong D, Idström JP, et al. Intragastric pH during treatment with omeprazole: role of Helicobacter pylori and H. pylori-associated gastritis. Scand J Gastroenterol. 1996;31:1151–6.
21. Koskenpato J, Färkkilä M, Sipponen P. Helicobacter pylori eradication and standardized 3-month omeprazole therapy in functional dyspepsia. Am J Gastroenterol. 2001;96:2866–72.
22. Sodhi JS, Javid G, Zargar SA, et al. Prevalence of Helicobacter pylori infection and the effect of its eradication on symptoms of functional dyspepsia in Kashmir, India. J Gastroenterol Hepatol. 2013;28:808–13.
23. McColl K, Murray L, El-Omar E, et al. Symptomatic benefit from eradicating *Helicobacter pylori* infection in patients with nonulcer dyspepsia. N Engl J Med. 1998;339:1869–74.
24. Mazzoleni LE, Sander GB, de Francesconi CFM, et al. Helicobacter pylori eradication in functional dyspepsia. Arch Intern Med. 2011;171:1929.

25. Yamada S, Tomatsuri N, Kawakami T, et al. Helicobacter pylori eradication therapy ameliorates latent digestive symptoms in chronic atrophic gastritis. Digestion. 2018;97:333–9.
26. Kim SE, Park YS, Kim N, et al. Effect of Helicobacter pylori eradication on functional dyspepsia. J Neurogastroenterol Motil. 2013;19:233–43.
27. Gwee KA, Teng L, Wong RK, Ho KY, Sutedja DS, Yeoh KG. The response of Asian patients with functional dyspepsia to eradication of Helicobacter pylori infection. Eur J Gastroenterol Hepatol. 2009;21:417–24.
28. Dhali GK, Garg PK, Sharma MP. Role of anti-Helicobacter pylori treatment in H. pylori-positive and cytoprotective drugs in H. pylori-negative, non-ulcer dyspepsia: results of a randomized, double-blind, controlled trial in Asian Indians. J Gastroenterol Hepatol. 1999;14:523–8.
29. Talley NJ, Janssens J, Lauritsen K, Rácz I, Bolling-Sternevald E. Eradication of Helicobacter pylori in functional dyspepsia: randomised double blind placebo controlled trial with 12 months' follow up. The Optimal Regimen Cures Helicobacter Induced Dyspepsia (ORCHID) Study Group. BMJ. 1999;318:833–7.
30. Tsuda M, Kato M, Ono S, et al. Changes of dyspeptic symptom after successful eradication in Helicobacter pylori-associated dyspepsia. Digestion. 2020;101:165–73.
31. Bektas M, Soykan I, Altan M, Alkan M, Ozden A. The effect of Helicobacter pylori eradication on dyspeptic symptoms, acid reflux and quality of life in patients with functional dyspepsia. Eur J Intern Med. 2009;20:419–23.
32. Bazzoli F, Palli D, Zagari RM, et al. The Loiano-Monghidoro population-based study of Helicobacter pylori infection: prevalence by 13C- urea breath test and associated factors. Aliment Pharmacol Ther. 2001;15:1001–7.
33. Suzuki H, Masaoka T, Sakai G, Ishii H, Hibi T. Improvement of gastrointestinal quality of life scores in cases of Helicobacter pylori-positive functional dyspepsia after successful eradication therapy. J Gastroenterol Hepatol. 2005;20:1652–60.
34. Wani FA, Bashir G, Khan MA, Zargar SA, Rasool Z, Qadri Q. Antibiotic resistance in Helicobacter pylori: A mutational analysis from a tertiary care hospital in Kashmir, India. Indian J Med Microbiol. 2018;36:265–72.
35. Savoldi A, Carrara E, Graham DY, Conti M, Tacconelli E. Prevalence of Antibiotic Resistance in Helicobacter pylori: A Systematic Review and Meta-analysis in World Health Organization Regions. Gastroenterology. 2018;155:1372–82.
36. Kim MS, Kim N, Kim SE, et al. Long-term follow up Helicobacter Pylori reinfection rate after second-line treatment: bismuth-containing quadruple therapy versus moxifloxacin-based triple therapy. BMC Gastroenterol. 2013;13:138.
37. Thong-Ngam D, Mahachai V, Kullavanijaya P. Incidence of Helicobacter pylori recurrent infection and associated factors in Thailand. J Med Assoc Thail. 2007;90:1406.
38. Goh KL, Navaratnam P, Peh SC. Reinfection and duodenal ulcer relapse in south-east Asian patients following successful Helicobacter pylori eradication: results of a 2-year follow-up. Eur J Gastroenterol Hepatol. 1996;8:1157–60.
39. Najafi M, Sobhani M, Khodadad A, Farahmand F, Motamed F. Reinfection rate after successful Helicobacter pylori eradication in children. Iran J Pediatr. 2010;20:58–62.
40. Ahmad MM, Ahmed DS, Rowshon AH, et al. Long-term re-infection rate after helicobacter pylori eradication in Bangladeshi adults. Digestion. 2007;75:173–6.