Research Article

A Prospective study on symptomatic betterment of *Helicobacter pylori* positive patients taking standard triple therapy

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Abstract

Background: Different treatment strategies are being developed and adopted from day to day in the research fields and clinical setting for helicobacter pylori infection. **Aim:** This study shows the effectiveness and betterment achieved by H. pylori affected individuals who followed a 14 day therapy that included 40 mg of Proton pump inhibitor (before food), 1000 mg of Amoxicillin (after food) and 500 mg of Clarithromycin (after food), each twice daily. **Methods:** This treatment regimen is commonly called as the Standard Triple Therapy. For this study, 90 patients were recruited and their symptomatic betterment were assessed using the GSR scale that were administered twice to the patients- prior to the initiation of the treatment and after the completion of the treatment. **Results:** After the successful treatment of 88 patients, an overall symptom reduction by 93.2% was observed. For better understanding the symptoms scores were categorized into reflux score, abdominal pain score, indigestion score, diarrhoea sore and constipation score. And a reduction of these symptoms by 90.9%, 86.4%, 92%, 90.9% and 90.9% respectively were observed. **Conclusion:** This study contradicts many other studies that showed a better effectiveness of sequential therapy over standard triple therapy in H. pylori positive patients.

***Keywords*:** symptomatic betterment, standard triple therapy

Introduction

Helicobacter pylori infection is a common bacterial, gastric infectious disease with a prevalence of 10% in developed western countries to 80% among the indigent population.

Helicobacter pylori is a Gram-negative bacterium that selectively colonizes the gastric epithelium of humans. According to Barkun et al. (2015), Marshall and Warren first identified *H. pylori* in 1983 where it was juxtaposed to the gastric epithelium of patients with chronic gastritis. Unless treated, the H. pylori infection may persist for a lifetime and may contribute many other gastro-intestinal diseases such as chronic active gastritis, peptic ulceration, gastric adenocarcinoma and gastric mucosa assosciated lymphoid tissue lymphoma (Kusters et al., 2006). PUD is one of the most common complication of *Helicobacter pylori* infection.

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Approximately 10% of Americans develop chronic PUD during their lifetime. The incidence varies with ulcer type, age, gender, and geographic location. Race, occupation, genetic predisposition, and societal factors may play a minor role in ulcer pathogenesis, but are attenuated by the importance of HP infection and NSAID use. The prevalence of PUD in the United States has shifted from predominance in men to nearly comparable prevalence in men and women.

The decline in hospitalizations has resulted from a reduction in hospital admissions for uncomplicated duodenal ulcer. However, hospitalizations of older adults for ulcer-related complications (bleeding and perforation) have increased. Although the overall mortality from PUD has decreased, death rates have increased in patients older than 75 years of age, most likely a result of increased consumption of NSAIDs and an aging population. In the UK, the prevalence of *H. pylori* infection rises with age (reaching 50% in those aged >50) in the developing world, it affects up to 90%. Patients with gastric ulcer have a higher mortality rate than those with duodenal ulcer because gastric ulcer is more prevalent in older individuals.

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Despite these trends, PUD remains one of the most common GI diseases, resulting in impaired quality of life, work loss, and high-cost medical care. To date, H2-receptor antagonists (H2RAs), proton pump inhibitors (PPIs), and drugs that promote mucosal defense have not altered PUD complication rates.

Risk Factors

H. *pylori* infection and NSAID or ASA use are the major risk factors for PUD. Causes of non H- pylori non-NSAID ulcers are stress, *Helicobacter heilmanii*, cytomegalovirus infections, Behcet disease, Zollinger Ellison syndrome, Crohns disease, and cirrhosis with portal hypertension. Other risk factors include older age and ethnicity.

Pathophysiology

Infection with *H. pylori* is widespread and probably acquired during childhood mainly via the fecal-oral route. In addition to this low socioeconomic status appears to be inversely related to the prevalence of infection.

The *H. pylori* bacterium infects the layers of stomach by burrowing deep beneath mucous layers of the epithelial surface and secretes the BabA adhesion molecules that bind to the lewis b antigen. Here the surface pH is close to neutral and acidity is buffered by the production of enzyme urease that raises the pH due to formation of ammonia between its two cell membrane layers. The bacteria spread from person to person through contact with vomit, feces or gastric refluxate.

H. pylori effectively colonizes gastric epithelium and is only found in the duodenum in association with patches of gastric metaplasia. The bacterium stimulates chronic gastritis by provoking a local inflammatory response in the underlying epithelium. This depends on numerous factors, notably expression of bacterial cagA and vacA genes. cagA gene product is injected into epithelial cells ultimately interacting with numerous cell signaling pathways involved in cell replication and apoptosis.

H. pylori strains expressing cagA are more often associated with the disease than cagA. Most strains also secrete a large pore forming protein cells vacA which causes large vacuoles to form in cells in-vitro. In-vivo vacA has many effects including increased cell permeability, efflux of micronutrients induction of apoptosis and suppression of local immune cell activity. Several forms of vacA exist and pathology is most strongly associated s1/ml form of the toxin (Elta et al., 2008; Hernandez et al., 2000; Kusters et al., 2006).

Table 1. Mechanisms of *Helicobacter pylori*-associated peptic ulceration

Effects on immune response	Release of cytokines (esp. IL-8) Recruitment of inflammatory cells and mediators
Effect on acid secretion	Hypochlorhydria to hyperchlorhydria
	Hypergastrinaemia
	Reduced somatostatin levels
	Reduced secretin levels
Local effects	Toxin release (vacA, cagA)
Effect on duodenal secretion	Reduced secretin Reduced bicarbonate

Complications

Upper GI bleeding, perforation is the most serious, life-threatening complications of chronic PUD (Elta et al., 2003; Hernandez et al., 2000). Bleeding is caused by the erosion of an ulcer into an artery. The bleeding may be occult (hidden) and insidious, or may present as melena (black-colored stools) or hematemesis (vomiting of blood).

Ulcer-related perforation into the peritoneal cavity is also common. The pain of perforation is usually sudden, sharp, and severe, beginning first in the epigastrium, but quickly spreading over the entire abdomen.

Gastric outlet obstruction occurs in about 2% of patients with peptic ulcers. Mechanical obstruction is caused by scarring or edema of the duodenal bulb or pyloric channel and can lead to gastric retention. Symptoms usually occur over several months and include early satiety, bloating, anorexia, nausea, vomiting, and weight loss. Perforation, penetration, and gastric outlet obstruction occur most often in patients with long-standing PUD.

Management

Treatment is mainly directed to eradication of infection. Eradication is usually achieved with a combination of acid-inhibiting therapy and antibiotics. Antibacterial therapy alone does result in healing, but the process is accelerated by addition of acid suppressants

Eradication rates depend on several factors: such as drug regimen, resistance rate to the antibiotic used, compliance with the drug, duration of therapy and genetic variations in drug-metabolizing enzymes.

Therapeutic Approaches Attempted for Eradication of *H. pylori*

Several regimens have been suggested by American Association of Gastroenterology (Chey et al., 2017). The most widely recommended treatment for the eradication of *Helicobacter pylori* is the Standard Triple Therapy. First-line therapy should be initiated with a PPI-based three-drug regimen for a minimum of 7 days, but preferably 10 to 14 days. If a second course of treatment is required, the PPI-based three-drug regimen should contain different antibiotics or a four-drug regimen with bismuth

Table 2. Therapy regimens suggested for *Helicobacter pylori* eradication in the current guidelines

Regimen	Therapy	Administration (daily)	Days
Standard triple therapy	Proton Pump Inhibitor + Clarithromycin 500 mg+ Amoxicillin 1000mg	b.i.d	14
	Proton Pump Inhibitor+ Clarithromycin 500mg+ Cinidazole 500 mg	b.i.d	14
Sequential therapy	Proton Pump Inhibitor +Amoxicillin 1000 mg (5 days) followed by Proton Pump Inhibitor+ Clarithromycin 500 mg+ Tinidazole 500 mg (5 days)	b.i.d.	10
Concomitant therapy	Proton Pump Inhibitor + Clarithromycin 500 mg + Amoxicillin 1000 mg + Tinidazole 500 mg	b.i.d.	10-14
Bismuth-based quadruple Therapy	Proton Pump Inhibitor + Bismuth subsalicylate 120 mg + Tetracycline 500 mg +Metronidazole 400 mg	b.i.d. q.i.d. t.i.d.	7-14 days
Levofloxacin-based triple therapy	Proton Pump Inhibitor +Amoxicillin 1000mg + Levofloxacin 500mg	b.i.d. q.i.d.	10-14
Levofloxacin sequential therapy	Proton Pump Inhibitor +Amoxicillin 1000mg, Proton Pump Inhibitor +Amoxicillin 1000mg + Levofloxacin 500 mg + Nitroimidazole 500 mg	b.i.d. b.i.d.	5-7 days

subsalicylate, metronidazole, tetracycline, and a PPI should be used (Hobbs et al., 1996; lee et al., 2017; Mansour et al., 2011).

Concomitant therapy is not recommended because it adds to drug costs without enhancing efficacy.

Maintenance therapy with a Proton Pump Inhibitor or H2 receptor antagonist is recommended for high-risk patients with ulcer complications.

Chet et al., (2017) indicates that many therapeutic strategies and courses have been developed and suggested for the treatment of *Helicobacer pylori* infection by the American Association of Gastroenterology in the recent years.

Experimental methods

The study was conducted in a tertiary care hospital for a period of 6 months. 90 patients who were diagnosed with positive rapid urease test between the ages of 18 to 80 were recruited for the study. Patients with any previous history of H. pylori infection, hepatic or renal impairment, allergy to antibiotics or those who were on prolonged treatment with proton pump inhibitors, antibiotics, anticoagulants or NSAIDs were excluded from the study. Pregnant and lactating women were also avoided from the study. Prior to the initiation of study, written informed consents were obtained from the patients who satisfied the inclusion and exclusion criteria and were willing to participate in the study. All information of the patient relevant to the study were either collected by directly interviewing the patients or from the case records. The symptoms of these patients were recorded and scored using the gastro-intestinal symptom rating scale as the same used by Suzuki et al. (2005). This was done twice during the study, firstly before the initiation of therapy and finally after the completion of the therapy. Standard triple therapy was followed by the patients. The scores were calculated and statistically analysed using the software SPSS v.22 Version for WINDOWS. The improvements of symptoms were statistically assessed using paired t-test.

Results and discussion

Among 90 patients who enrolled for the study only 88 patients completed the medication course. An overall symptomatic betterment by 93.2% was observed in these 88 patients. Only 6 patients presented with minor discomfort even though it can be easily ignored without effort. It is diagrammatically shown in figure 1. Most of the patients were observed to have complete reduction of symptoms.

For wider understanding of symptomatic betterment the symptoms scores were categorized into 5- reflux score, indigestion score, abdominal pain score, diarrhoea score and constipation score.

In the eradication regimen of *H. pylori,* reflux score before treatment is very severe in 30 (34.1%) patients and severe reflux discomfort in 20 (22.7%). Reflux score was moderately severe in 12 (13.6%), moderately in 4 (4.5%),

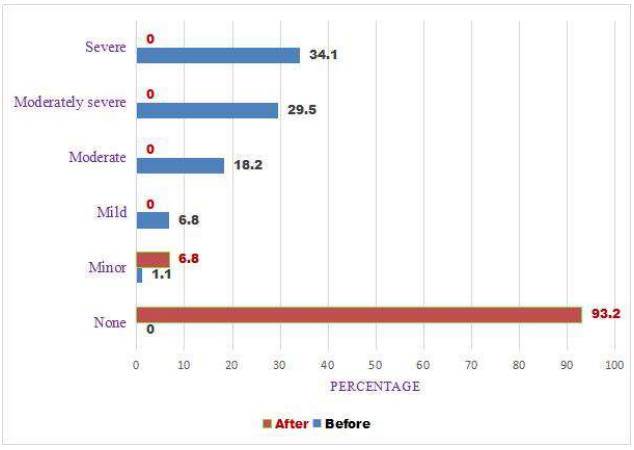

Figure 1. Diagrammatic representation of distribution of overall symptoms using GSRS score

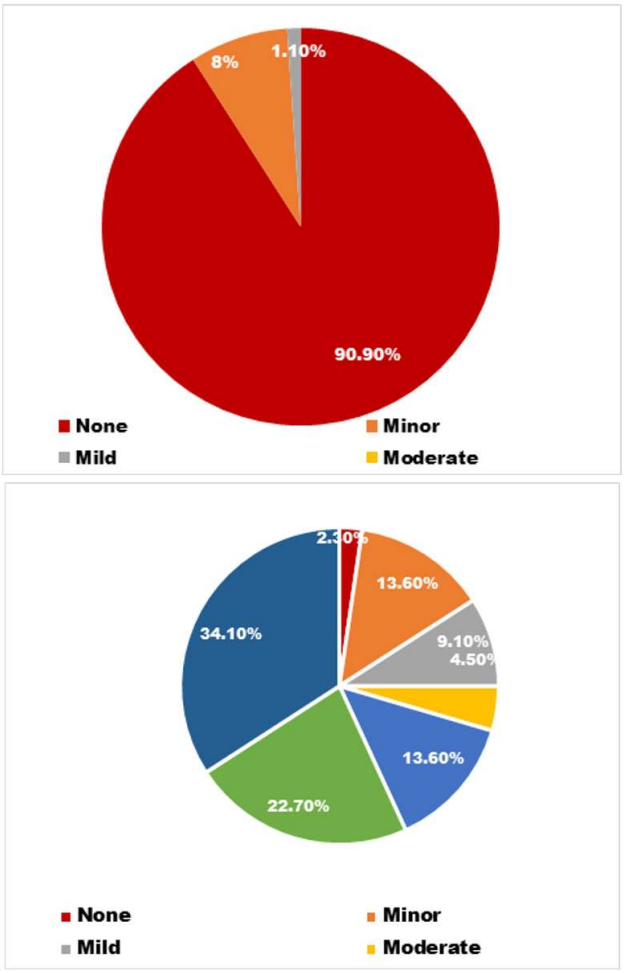

Figure 2. Diagrammatic representation of distribution of reflux score before and after treatment

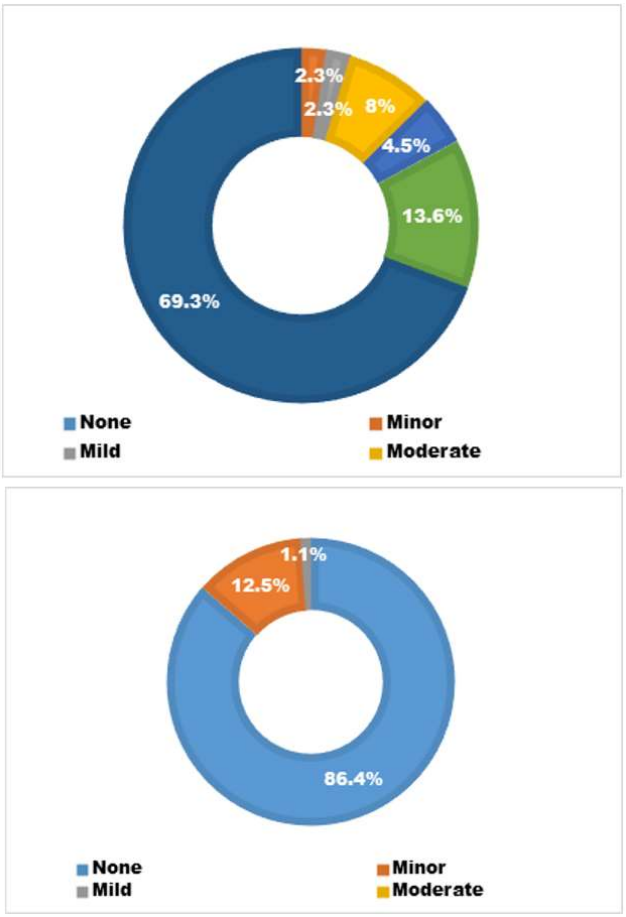

Figure 3. Diagrammatic representation of distribution of abdominal pain before and after treatment

mild problems with 8 (9.1%) and 12 (13.6%) patients had only minor discomfort of reflux. Complete resolution of dyspeptic symptom is a powerful predictor of eradication of *H. pylori* in ulcer patients. There were two (2.3%) patients who don't have any complaints of reflux during the study period. After the regimen reflux score reduced to low score. 80 (90.0%) patients out of the total observed had no discomfort upon the completion of therapy. Minor discomfort of reflux presented with 7 (8.0%) and one (1.1%) patient persists symptoms mildly (Figure 2).

Before the therapy very severe abdominal pain was present in about 61 patients (69.3%) and severe discomfort among 12 (13.6%) patients. Moderately severe discomfort seen in 4 (4.5%) and moderate abdominal pain reported in 7 (8.0%) and two patients had mild (2.3%) problems and two had minor (2.3%) discomfort.

Aabdominal pain reduced to no symptoms in 76 (86.4%), minor symptoms in 11 (12.5%) and only one (1.1%) patient had reported mild abdominal pain (Figure 3).

Considering the indigestion score 32 (36.4%) patients out of 88 were observed to have very severe indigestion problems. Severe discomfort of indigestion found in 24 (27.3%), moderately severe problems in 16 (18.2%), six (6.8%) were reported of moderate symptoms, mild discomfort and minor discomfort seen in 7 (8.0%) and no discomfort was seen in 2 (2.3%) patients respectively. In case of indigestion score after treatment out of 88 patient 81 (92.0%) completely resolved of indigestion problems. Minor indigestion discomfort observed in 7 (8.0%) patients was shown in figure 4.

Very severe diarrhoea presented in 24 (27.3%), severely in 23 (26.1%) moderately severe in 11 (12.5%), and in 7 patient s moderately presented. Mild cases of diarrhoea presented in 5 and 13 had minor. There were 5 patients who had no symptoms of diarrhoea. Out of the total 80 (90.9%) *H. pylori* patients completely resolve their diarrhoea symptoms after the treatment period. The remaining 8 (9.1%) patients had symptoms in minor (Figure 5) 15 (17.0%) patients from the study population presented with very severe discomfort of constipation, as in table 12. It is observed that severe constipation score found in 7 (8.0%), symptoms of moderately severe in 11 (12.5%), mild and minor symptoms found in 21 and 14 respectively. About 4 patients does not show any symptoms of constipation in the study period. patients of study population 80 (90.9%) *H. pylori* patients completely resolve their constipation

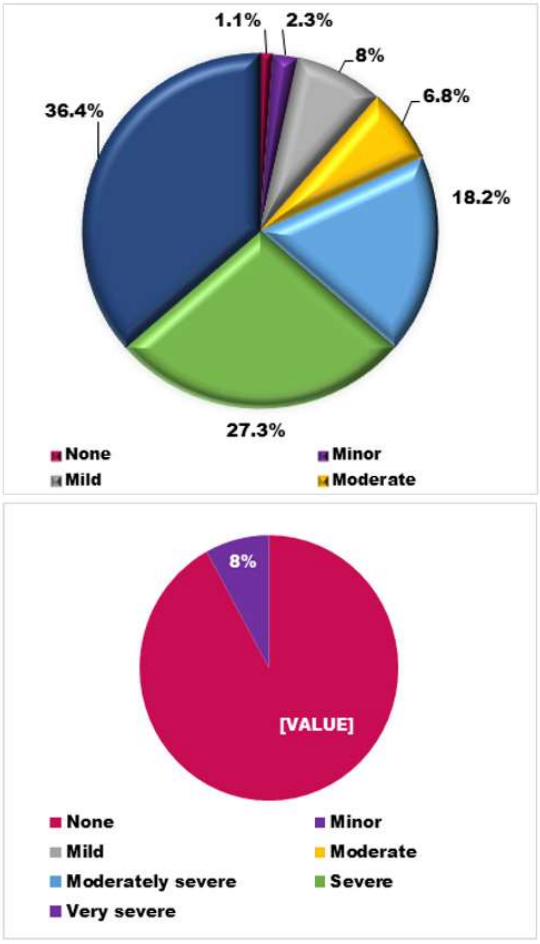

Figure 4. Diagrammatic representation of distribution of Indigestion score before and after treatment

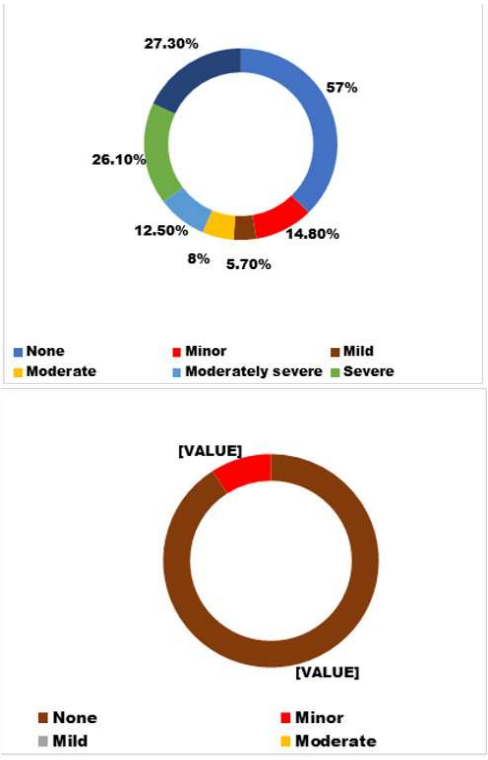

Figure 5. Diagrammatic representation of distribution of Diarrhoea score before and after treatment

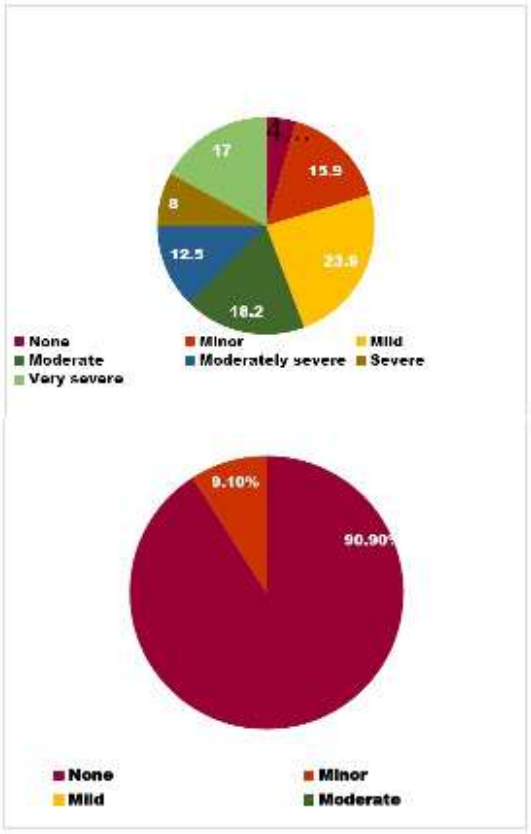

Figure 6. Diagrammatic representation of distribution of constipation score before and after treatment

symptoms after the treatment period. The remaining 8 (9.1%) patients had symptoms in minor. The minor discomfort of constipation can be easily ignored without effort. The stages of discomfort as mild, moderate, moderately severe, severe and very severe problems were absent in the after-eradication regimen of *H. pylori.*

This study obtained better results than some previous similar studies such as Chang et al. (2017) and Mohi-Ud-Din et al. (2018).

Conclusion

The present study was conducted to assess the benefits of Standard Triple Therapy. Standard triple therapy proves to provide high resolution of *Helicobacter pylori* infection by symptomatic improvement.The study evaluates the symptomatic betterment of *H. pylori* positive patients taking triple therapy. The study was conducted in 90 *H. pylori* positive patients in the Gastroenterology department. Patients between the age group 18-80 were enrolled in our study.

Upper GI endoscopy and Rapid Urease test were carried out in these patients for *H. pylori* detection. The recruited patients were treated with Standard triple therapy for 14 days. Standard triple therapy includes proton pump inhibitor (40 mg) bid, amoxicillin (1000 mg) bid and clarithromycin (500 mg) bid. Symptomatic betterment was assessed using GSRS

questionnaire that was administered after the diagnosis of the disease and then after the completion treatment course. The data analysis revealed an Overall symptom betterment of 93.2 % after the completion of the treatment regimen. Individual symptom betterment was also calculated for better understanding. 92% betterment in indigestion symptoms were obtained whereas 90.3% betterment was obtained in diarrhea, constipation and reflux symptoms each. Abdominal pain resolution of 86% was achieved in this study.

From the study we can assess that male patients (57%) have higher risk of getting infected with *H. Pylori* compared to females. The study also reveals that the patients of age group 40-59 were more susceptible to this infection. Patient counselling was done at the time of diagnosis and during the follow ups as required.

This study shows an enormous success rate of standard triple therapy which contradicts many studies that claims superiority of other treatment regimens such as sequential therapy (Chang et al., 2017; Mohi-Ud-Din et al., 2018). This shows the superiority of this regimen over other regimens.

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Conflict of interest

Conflict of interest declared none.

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