

## Research Article

# Role of Probiotic as an Add-on Therapy in Eradicating Helicobacter Pylori Infection

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### Abstract:

**Background:** To compare the Helicobacter pylori eradication rate with and without use of Probiotic in conjunction with standard triple regimen.

**Methods:** The patients with symptomatology of Gastritis and Dyspepsia were enrolled for the study. The presence of Helicobacter pylori was confirmed with Urea breath test. The experimental group received probiotic along with triple regimen therapy, while the control group received only triple regimen therapy. After four weeks of completion of treatment, urea breath test was repeated for confirmation of Helicobacter pylori eradication. Patients with negative urea breath test were considered as treatment success.

**Results:** Total 160 patients with Helicobacter pylori infection were enrolled in this study. Patients were divided in two groups i.e. Group-A (Probiotic + triple regimen therapy) and Group-B (Only triple regimen therapy). The mean age of patients in group-A was 35.1±11.2 years and in group-B 37.5±12.9 years. In group-A, H. pylori eradication was seen in 71(88.8%) and 59(73.8%) in group-B with a p-value of 0.015 which is statistically significant.

**Conclusion:** In Helicobacter pylori confirmed Gastritis or Dyspepsia patients, addition of probiotic to standard triple regimen therapy improve eradication rate of H. pylori infection.

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**Key Words:** Helicobacter Pylori, Probiotic, Standard Triple Regimen.

### Introduction:

Peptic ulcer is at least 0.5cm breach in continuity of gastric mucosa or upper small intestine reaching up-to muscularis mucosa. Helicobacter pylori, a gram negative bacillus first identified in 1982 by Barry Marshal and Robin Warren, has been known to be a causative agent for gastroduodenal ulcers<sup>1</sup> and is said to be a grade 1 carcinogen,<sup>2,4</sup> responsible for gastric carcinoma, MALT lymphoma.<sup>4,5</sup> Early eradication of H. pylori may reduce its progression to gastric carcinoma.<sup>6</sup>

Although only a small proportion (<1%) of gastric ulcers have been reported to progress to gastric adeno-

carcinoma,<sup>7</sup> but it is the third leading cause of cancer mortality in the world.<sup>3,4,9</sup> Although Helicobacter pylori is prevalent worldwide, but in developing countries its prevalence has been reported up-to 80%.<sup>5</sup> The excessive use of antibiotics has led to increase in resistance and failure of eradication therapy.<sup>5</sup>

Owing to increase in antibiotic resistance, H pylori eradication rate has reduced from 90% in 1990s to <70%. Probiotics are live microorganisms that are beneficial for the host. Probiotics harmonize intestinal ecosystem immune and non immune system. Immune system activated by innate and acquired immunity. Non immune

system helps with antimicrobial metabolite productions, competitors for adhesion receptors and nutrients and reinforcement of epithelial barrier function. Probiotics have been found to increase mucosal protection and angiogenesis.<sup>9</sup> They have dual action i.e. increasing eradication efficacy on one hand and decreasing side effects of antibiotics on the other hand.<sup>10-11</sup> Eradication rate in patients taking probiotics along with their standard regimen is 86.8% as compared to patients taking only standard regime with eradication rate of 70.8%.<sup>10</sup>

The rationale of this study was to find evidence about role of probiotics in eradication of *Helicobacter pylori* in our population. Furthermore the current study will help health care providers about the response rate of standard triple regimen therapy and the improvement in outcome by addition of probiotics in our population.

### Methods:

Sample Selection: Sample size was calculated as WHO calculator.

Taking confidence level: 95%

Power of study: 80%

For one sided hypothesis testing sample size calculated as 80 subjects per group. Total sample size of 160 subjects.

### Inclusion Criteria:

- Confirmed cases of *H. pylori* infection as per operational definition, who were of both genders age, 18-70 years giving consent for the study.
- Exclusion Criteria
- Patients with history of eradication therapy within previous 6 weeks.
- Use of probiotic products within previous month
- History of Gastric surgery
- History of allergy to drugs used in the study
- Taking any antibiotics, any H<sub>2</sub>-receptor antagonists, bismuth or PPI during last 2 weeks

### Data Collection Procedure:

The study was carried out in the Department of Gastroenterology, HFH, Rawalpindi (OPD) after approval from ethical committee. The written informed consent was taken from the subjects after explaining them the details of study. The patients with symptomatology of Gastritis and Dyspepsia (diagnosed using Rome IV criteria) were enrolled for the study.

The presence of *Helicobacter pylori* was confirmed with Urea breath test. The carbon 13 UBT is based on the detection of products created when urea is split by the organism. The UBT was performed using 75mg <sup>13</sup>C urea, which comprises of urea with 99.9% <sup>13</sup>C (stable and non-radioactive isotope) with test meal to delay gastric emptying. After 6 hours fasting, baseline breath sample in 10ml glass tube was collected. After this, patient was allowed to drink substrate solution containing 75mg <sup>13</sup>C enriched urea and after every 10 min, breath samples up to 60 min were collected. The patients were recruited with consecutive sampling followed by random allocation in two groups. The experimental group received probiotic (ECOTEC sachet, once daily, LA-5, BB-12, STY-31, LBY-27) along with triple regimen therapy (Amoxicillin 1gm twice daily, Clarithromycin 500 mg twice daily for 14 days and PPI for four weeks while the control group received only triple regimen therapy only.

The patients were thoroughly instructed about the medications used in the study, how to take these medications, their possible side effects and how to report to the researchers if they feel any side effects or discontinue medication due to any reason.

After four weeks of completion of treatment, patients repeated urea breath test for confirmation of *H. pylori* eradication. Patients with negative urea breath test were designated as with treatment success. The relevant information for the study was recorded on proforma that contained patients personal, demographic and clinical information required for the study.

### Data Analysis Plan:

All the collected data were compiled and analyzed by SPSS v25.0. Mean and standard deviation was calculated for quantitative data like age. Frequency and percentage were calculated for qualitative data like gender and eradication rate. The primary outcome, eradication rates of *H. pylori* in both groups was compared by using Chi-Square test. Data were stratified according to age, gender and socio-economic status to document the modifiers effect. A p-value  $\leq 0.05$  was taken as significant.

### Results:

Total 160 patients with *Helicobacter pylori* infection

were enrolled in this study. Patients were divided in two groups i.e. Group-A (Probiotic + eradication therapy) and Group-B (eradication therapy only). In group-A, 45(56.3%) were males and 35(43.8%) females, while in group-B, 33(41.3%) were males and 47(58.8%) females.

Age range was from 18 to 70 years with mean age of  $36.3 \pm 6.4$  years. The mean age of patients in group-A

**Table-1:** Comparison of *H. pylori* eradication between study groups

| H. pylori eradication | Groups       |              | Total         | p-value |
|-----------------------|--------------|--------------|---------------|---------|
|                       | A            | B            |               |         |
| Yes                   | 71<br>88.75% | 59<br>73.75% | 130<br>81.25% | 0.015   |
| No                    | 9<br>11.25%  | 21<br>26.25% | 30<br>18.75%  |         |
| <b>Total</b>          | 80<br>100.0% | 80<br>100.0% | 160<br>100.0% |         |

was  $35.1 \pm 11.2$  years and in group-B  $37.5 \pm 12.9$  years.

In group-A, majority of the patients 34(42.5%) were in

31-45 years age group, while 33(41.3%) and 13(16.3%) in 18-30 years and >45 years age groups respectively. In group-B, majority of the patients 29(36.3%) were in 18-30 years age group, while 27(33.8%) and 24(30.0%) in 31-45 years and >45 years age groups respectively.

In group-A, 29(36.3%) had Low socio-economic status (SES), while 28(35.0%) and 23(28.7%) belonged to Middle and High SES. In group-B, 23(28.7%) had Low socio-economic status (SES), while 37(46.3%) and 20(25.0%) had Middle and High SES.

In group-A, *Helicobacter pylori* eradication was seen in 71(88.8%) and 59(73.8%) in group-B with statistically significant p-value of 0.015.

### Discussion:

Our findings in this local study observed significantly better *Helicobacter pylori* eradication rate (88.8% vs. 73.8%) and fewer treatment-associated adverse effects with probiotic (cap Ecotec, *Lactobacillus Delbrueckii* ssp) as an adjuvant to standard triple regimen treatment

**Table-2:** Stratification of *H. pylori* eradication between groups with respect to socio-economic status

| Socio-economic status          | H. pylori eradication | Groups                  |                  | Total        | p-value |
|--------------------------------|-----------------------|-------------------------|------------------|--------------|---------|
|                                |                       | Probiotic + ERA Therapy | Only ERA Therapy |              |         |
| Low<br>(Rs.<20,000/Month)      | Yes                   | 21<br>72.4%             | 9<br>39.1%       | 30<br>57.7%  | 0.016   |
|                                | No                    | 8<br>27.6%              | 14<br>60.9%      | 22<br>42.3%  |         |
|                                | <b>Total</b>          | 29<br>100.0%            | 23<br>100.0%     | 52<br>100.0% |         |
| Middle<br>(Rs.20-50,000/Month) | Yes                   | 27<br>96.4%             | 32<br>86.5%      | 59<br>90.8%  | 0.170   |
|                                | No                    | 1<br>3.6%               | 5<br>13.5%       | 6<br>9.2%    |         |
|                                | <b>Total</b>          | 28<br>100.0%            | 37<br>100.0%     | 65<br>100.0% |         |
| High<br>(Rs.>50,000/Month)     | Yes                   | 23<br>100.0%            | 18<br>90.0%      | 41<br>95.3%  | 0.120   |
|                                | No                    | 0<br>0.0%               | 2<br>10.0%       | 2<br>4.7%    |         |
|                                | <b>Total</b>          | 23<br>100.0%            | 20<br>100.0%     | 43<br>100.0% |         |

than with the use of triple regimen without probiotic.

The rescue regimens of *Helicobacter pylori* eradication rate have been observed to vary from 70% to 90% on a global basis.<sup>14</sup> while the sequential therapy success ratio has been documented from 90% to 94%,<sup>12</sup> a study result has disclosed that with standard triple therapy, the eradication rate was to be 53% and 78% with sequential therapy.<sup>24</sup> Accordingly, a favorable eradication rate resulted in our study (88.8%) with the use of probiotic as an add-on to standard triple therapy, emphasizes the importance of add-on probiotics use to get greater efficacy of sequential regimen in areas, where clarithromycin resistance is high.<sup>13,24</sup>

Wang et al. meta-analysis of 10 clinical trials (n=1,469) has documented the favorable results of *Lactobacillus* and *Bifidobacterium* containing probiotics regarding eradication and total side effects incidence during *H. Pylori* treatment therapy.<sup>21</sup>

Dang et al. meta-analysis of 33 RCTs (n = 4,459),<sup>14</sup> notably higher rates of eradication have been described in probiotics addition groups versus control groups, however it has been confirmed only in four individual *Lactobacillus* and *Bifidobacterium* strains and comparatively for ineffective antibiotic treatment regimens.<sup>15</sup>

Gong et al. meta-analysis of 23 trials (n=3,900),<sup>17</sup> it is observed that only 72.26% eradication rate of *Helicobacter pylori* have been achieved with triple treatment regimen alone and 80.74% when triple regimen combined with probiotics. Especially, it has been observed that eradication rate increases from 78.3% to 91.3% when *Lactobacillus* and *Bifidobacterium* combination was used as an add-on to PPI-based 1-week triple therapy.<sup>24</sup>

Our study findings are compatible with the results from many other meta-analysis who concluded that probiotics has significant effects on decreasing *H. Pylori* treatment-related side effects,<sup>16,19</sup> therefore increasing the probability of better eradication rates when used as an add-on therapy to *H. pylori* eradication regimens<sup>15-16,21,23</sup>.

Where antibiotic therapy for getting high eradication rate of *H. Pylori* infection considered to be ineffective, addition of probiotics has been strongly advocated.<sup>14</sup> Our finding regarding fewer treatment resistance in probiotic group patients, which probably indicates the

role of probiotic addition in abolishing resistant strains and hence improving the *H. pylori* elimination, most likely when antibiotic treatment regimen are comparatively ineffective.<sup>14</sup>

The supplementation effect of probiotic in improving eradication of *Helicobacter* has been documented in many meta-analysis and clinical studies,<sup>14,17-22</sup> there is lack of consistency regarding side effects benefit demonstration of overall side effects in probiotics groups<sup>19-20,22</sup>, but no significant changes observed in many others studies<sup>17-21</sup>.

Like our study, S. Alvi et al concluded in their review article that probiotics not only increase *Helicobacter pylori* eradication rate but also decreases antibiotics related side effects.<sup>25</sup>

It is also observed in our study that socioeconomic status of study population has significant impact on eradication rate of *Helicobacter Pylori* infection. when probiotic was added to standard triple therapy in low socioeconomic group, it remarkably increased eradication rate (table.2)

### Conclusion:

In *Helicobacter pylori* infection confirmed cases of Gastritis or Dyspepsia, addition of probiotic to standard triple regimen therapy improves eradication rate of *Helicobacter pylori* infection.

### Main Points :

- 1) As there is universal trend of increase in incidence of resistance against commonly used antibiotics for *Helicobacter pylori* and it leads to gradual decrease of eradication rate all over the world.
- 2) Probiotics are commonly being used for many gastrointestinal conditions without any significant adverse events.
- 3) Probiotics when used with antibiotics, they decrease the adverse events of antibiotics.
- 4) When probiotics used with PPI and antibiotics for eradication of *Helicobacter pylori* infection, they not only increase eradication rate but also decrease adverse events of these antibiotics.

**Ethical Approval:** Given

**Conflict of Interest:** The authors declare no conflict

of interest.

**Funding Source:** None

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