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# Study of efficacy of spray dried lactobacillus reuteri for helicobacter pylori infection treatment

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**Abstract**--The present study was conducted to study the effectiveness of spray dried Lactobacillus reuteri in treatment of Helicobacter pylori infection at a tertiary healthcare institute. We evaluated the compliance and outcome of spray dried Lactobacillus reuteri in the treatment of patients with Helicobacter pylori. In our study, we included patients who were positive for Helicobacter pylori on Rapid Urease test. We assessed Rapid urease test findings on follow up visit among the study subjects and observed that 63.64% study subjects reported Helicobacter pylori negative after treatment with spray dried Lactobacillus reuteri. The study showed that majority of the study subjects were females (54.55%), whereas 45.45% subjects were males, M:F ratio in the current study was 1:1.2. and the mean age of the study subjects was  $41.61 \pm 10.84$  years. 54.55% study subjects belonged to rural area, whereas 45.45% subjects belonged to urban area. Our study's results are comparable and similar to the other studies which show that Lactobacillus reuteri (Probiotics) are useful in the Helicobacter pylori infection treatment. The observations in the current study are found to be statistically significant, and probiotics, in our study spray dried Lactobacillus reuteri DSM 17648 capsules are proved to be significantly effective in eradication of Helicobacter pylori among the study subjects. (T-value: 7.5, p-value:  $<0.0001$ ).

**Keywords**---efficacy, spray dried lactobacillus reuteri, helicobacter pylori infection.

## Introduction

*Helicobacter pylori*, previously known as *Campylobacter pylori*, is a Gram-negative, microaerophilic bacterium usually found in the stomach. It was identified in 1982 by Australian doctors Barry Marshall and Robin Warren, who found that it was present in a person with chronic gastritis and gastric ulcers, conditions not previously believed to have a microbial cause.<sup>[1-3]</sup> Since then, *Helicobacter pylori* infection has been thought intensely related to peptic ulcer disease, with incidences range from 0.03% to 0.19% every year.<sup>[4-5]</sup> Once *Helicobacter pylori* infect the stomach, they can persistently exist for decades in the acidic gastric environment, where they disrupt gastric mucosa, alter the patterns of hormone secretion, and ultimately lead to chronic gastritis and peptic ulcer disease.<sup>[6]</sup>

*Helicobacter pylori* infects at least 50% of the global population causing gastric symptoms and leading to further disease in 20% of those infected. The prevalence of *Helicobacter pylori* infection differs between regions of the developing world (e.g. Southeast Asia; the Indian subcontinent; Latin America) where prevalence rate in adults is up to 80%, and industrialized nations, where the incidence is significantly less (20 to 50%)<sup>[7-8]</sup>.

*Helicobacter pylori* infection has been classified as a grade I carcinogen.<sup>[9-11]</sup> *Helicobacter pylori* infection can induce chronic gastritis, which progresses through the premalignant stages of atrophic gastritis, intestinal metaplasia, and dysplasia, before finally leading to gastric cancer.<sup>[12-13]</sup>

The Maastricht/Florence Consensus report, which outlines the diagnostic guidelines and treatment strategies for those with *Helicobacter pylori*<sup>[14]</sup> advises individuals with certain risk factors to undergo eradication therapy. In particular, it is recommended that those with functional dyspepsia, undergo the “test and treat” strategy. However, there remains a lack of options for volunteers who are either asymptomatic or experience only mild gastrointestinal symptoms or for patients that have unsuccessfully undergone the standard treatment due to *Helicobacter pylori* antibiotic resistances or those showing low compliance due to massive side effects of antibiotic treatment. Alternative anti-*Helicobacter pylori* treatments are searched for. The *Helicobacter pylori* standard antibiotic therapy fails in about 25–30% of cases, particularly because of the increasing occurrence of resistance to antibiotics. Also, it is associated with side effects and adverse reactions that can cause reduced patient compliance.

The Rapid Urease Test is an indirect test of the presence of *Helicobacter pylori* based on the presence of urease in or on the gastric mucosa. It has an advantage over serology in that it only detects the presence of an active infection. The test requires a sample of gastric mucosa or mucus that is added to a tube, gel, or other device which brings that sample into contact with urea and a method to detect the products of urea hydrolysis, ammonia or carbon dioxide. The sensitivity

of various RUT tests as primary diagnostic tests is high and has been reported to vary between approximately 80% and 100% and specificity between 97% and 99%. Hence, we have used RUT to diagnose patients in our study.

The use of probiotics as monotherapy or, synergistically (in combination with antibiotics) is researched as an alternative way of controlling *Helicobacter pylori* infection and reducing side effects of antibiotic treatment [15-19]. Probiotics have proven to be useful in the treatment of a number of gastrointestinal diseases. Probiotics may compete directly with *Helicobacter pylori*, possibly by interference with adherence or by the production of antimicrobial molecules. *Lactobacillus reuteri* has been shown to inhibit *Helicobacter pylori* in vitro and in vivo, and theoretically may play a role in eradication therapy.[20]

Mechanisms by which probiotics work in this application include suppressive effects against gastrointestinal inflammation and against *Helicobacter pylori* [21]. Probiotics might enhance the production of prostaglandin, mucins, growth factors and anti-inflammatory cytokines, and can stabilize or strengthen the gut mucosal barrier [22-24]. Other mechanisms include production of antimicrobial substances [25] or displacement of *Helicobacter pylori* through competitive binding to adhesion receptors of *Helicobacter pylori* [26]. In this study, spray dried *Lactobacillus reuteri* DSM17648 will be used in the form of capsules which will be given to the patient twice a day for 28 days instead of the standard antibiotic therapy.

## **Methods**

It was an observational study. We included all patients fulfilling inclusion criteria in Krishna Hospital & Medical Research Centre, Karad in this study. It was conducted between December 2019 to June 2021.

### **Inclusion criteria**

- All patients having endoscopic diagnosis of *Helicobacter pylori* gastritis on Rapid Urease test.
- Who have given consent for upper GI endoscopy.
- Age group – 18 to 65 years

### **Exclusion criteria**

- Diagnosed as a case of peptic ulcer disease with complications such as haemorrhage, perforation and obstruction.
- Patients taking other antibiotics during the period of the study.

## **Methodology**

The study was conducted in the Department of Surgery, the patients referred from other Departments of Krishna Institute of Medical Sciences, Karad from December 2019 to July 2021. All patients having diagnosed Acid Peptic Disorder underwent Endoscopic biopsy and Rapid urease test before and after treatment. Only patients who had a positive RUT were included in the study.

- Selecting clinically diagnosed cases of Acid Peptic disease.
- Taking endoscopic biopsy samples for doing a rapid urease test.

- Treating the patients who have a positive Rapid Urease Test with capsules containing spray dried *Lactobacillus reuteri* DSM 17648 twice a day for 28 days.
- Repeating an endoscopic biopsy for doing a rapid urea test.
- Analyzing data: The data regarding demographic information, clinical examination findings, investigation findings were recorded with the help of pre-validated, semi-structured, standard case record proforma.

### **Study design and Statistics**

Patient assessment:

- Full history-taking and clinical examination of all patients was done.
- Upper digestive endoscopy with rapid urease test was done. The rapid urease test, a qualitative assessment of urease activity, was performed using fresh antral and corporal biopsies. Biopsies were impeded on the slides without any contaminating blood and results were classified as negative if no color change from the yellow color for 1 to 3 hours, while sample with color change towards the pink color was considered positive.
- Four weeks after therapy, re-examination was carried out and re-endoscopy was done for a rapid urease test.

### **Statistical analysis**

A sample size of 22 patients was taken.

- The data was entered using MS excel software.
- The data was represented in the form of tables and charts for frequency analysis.
- The data was analysed with the help of SPSS version 22 software.
- P-value less than 0.05 was considered to be statistically significant.

### **Observations and Results**

Genderwise distribution: We assessed genderwise distribution among the study subjects. Majority of the study subjects were females (54.55%), whereas 45.45% subjects were males. The M:F ratio in the current study was 1:1.2.

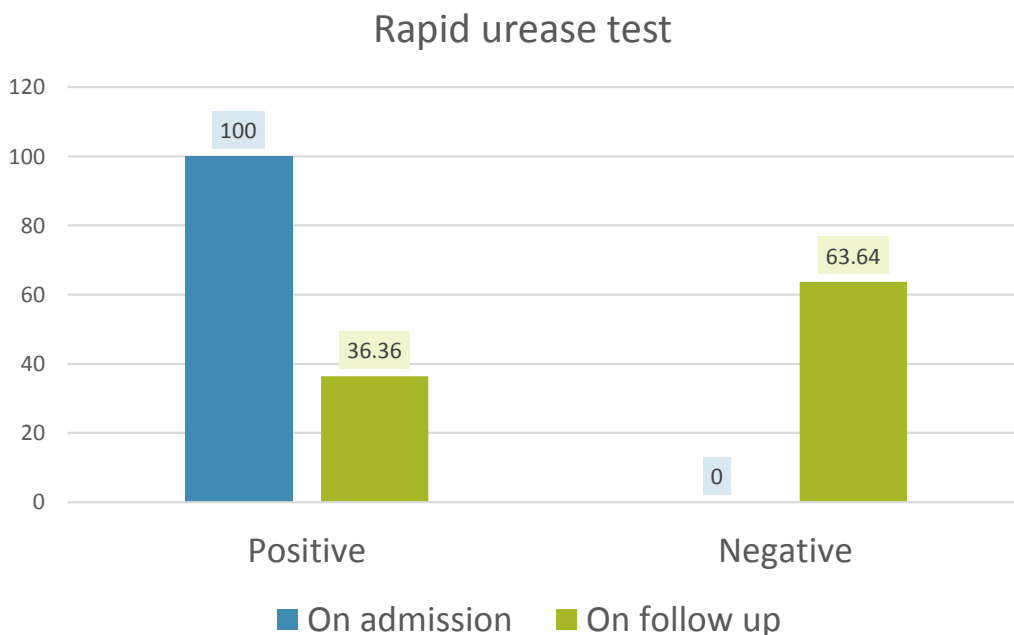
Agewise distribution: We assessed Age distribution among the study subjects. Majority of the study subjects belonged to the age group of 36-45 years (40.91%), followed by 46 to 55 years (22.73%). The mean age of the study subjects was  $41.61 \pm 10.84$  years.

Areawise Distribution: We assessed the type of area of residence among the study subjects. It was observed that 54.55% study subjects belonged to rural area, whereas 45.45% subjects belonged to urban area.

Rapid Urease test results: We assessed Rapid urease test findings on first visit among the study subjects. We only included patients who were positive for *Helicobacter pylori* on Rapid Urease test. Rapid urease test findings on follow up visit among the study subjects were assessed. 63.64% study subjects reported negative on Rapid Urease Test after treatment with spray dried *Lactobacillus reuteri*.

Table 1  
Comparison of Rapid urease test before and after treatment

Rapid urease test	Test conducted on	
	On first visit	On follow up
Positive	22 (100%)	8 (36.36%)
Negative	0 (0%)	14 (63.64%)
Total	22 (100%)	22 (100%)



Graph 1

We observed that on first visit all of the study subjects had rapid urease test positive for *Helicobacter pylori*, whereas after treatment with spray dried *Lactobacillus reuteri*, on follow up visit 63.64% study subjects converted into negative findings for *Helicobacter pylori*.

Table 2

Rapid urease test	Test positivity	
	Before probiotic use	After probiotic use
Positivity	22 (100%)	8 (36.36%)
Significance	t-value: 7.5, p-value: <0.0001	

We evaluated the outcome of treatment of *Helicobacter pylori* patients with spray dried *Lactobacillus reuteri* capsules given twice a day for 28 days. We compared the Rapid Urease Test (RUT) findings on the first visit and on follow up visit after treatment and found that, out of 22 patients, 14 pts (63.64%) were negative on RUT and 8 patients (36.36 %) were positive on RUT. Hence, we observed that

after the treatment, 63.64% study subjects responded to the treatment. The observations are found to be statistically significant, and *Lactobacillus reuteri* has proved to be significantly effective in eradication of *Helicobacter pylori* among the study subjects. (t-value: 7.5, p-value: <0.0001).

## Discussion

There is a casual link between *Helicobacter pylori* infection and acute gastrointestinal symptoms. Hence, it is important to evaluate the patients with symptoms like dyspepsia, abdominal pain etc. *Helicobacter pylori* can cause acute chronic gastritis leading to gastric atrophy and intestinal metaplasia leading to dysplasia and finally leading to gastric cancer. *Helicobacter pylori* has been deemed as a grade 1 carcinogen. Hence, it becomes very important that we use a test and treat approach in any *Helicobacter pylori* infection.

In developing countries, treatment of *Helicobacter pylori* infection is has become a very relevant issue. There are various treatment regiments available for *Helicobacter pylori* eradication. All these regimens are antibiotic therapies. But the antibiotic treatment regimen failure is a very growing problem in the current scenario. Most important factors that act in treatment failure are antibiotic resistance, side effects and reduced patient compliance.

Probiotics are defined as live microorganisms which when administered in adequate amounts confer a health benefit to the host (FAO/WHO). *Lactobacillus reuteri* DSM17648 showed a significant decrease of *Helicobacter pylori* stomach colonization in vivo study. In our study we have used the probiotic, *Lactobacillus reuteri* DSM17648 in the form of capsules to treat *Helicobacter pylori* infection.

Maria Pina Dore et al in their pilot study used *Lactobacillus reuteri* plus pantoprazole twice a day and cured 13.6%. They concluded that *Lactobacillus reuteri* may have a potential role in *Helicobacter pylori* eradication therapy if the cure rate can be improved by changes in dose, dosing interval, or duration of therapy. [27]

Caterina Holz et al in their study revealed that *Lactobacillus reuteri* strain DSM17648 has unique properties as it specifically aggregates with planktonic *Helicobacter pylori* in the stomach. The spray dried cells remain active as nonviable cell preparation. This strain acts against *Helicobacter pylori* in stomach by specifically binding and co-aggregating with *Helicobacter pylori*. Binding of *Lactobacillus reuteri* masks the surface structures of *Helicobacter pylori* and severely impedes its motility. The aggregated *Helicobacter pylori* can no longer adhere to the gastric mucosa and the *Lactobacillus/ Helicobacter* complexes are flushed out of the stomach. [28]

Imase K et al in their study concluded that administration of *Lactobacillus reuteri* Tablets significantly decreased UBT in *Helicobacter pylori*-positive subjects, demonstrating that *Lactobacillus reuteri* suppresses *Helicobacter pylori* density. The overall decrease in UBT due to medication with *Lactobacillus reuteri* Tablets was 69.7±4.0% (p<0.05). [29]

Iulia Antonia Pop Muresan et al in their study observed that the group on Lactobacillus reuteri plus Pantoprazole presented 65.22% eradication rate compared to 73.91% cure rate in the group that received the Pantoprazole and Amoxicillin and Clarithromycin therapy, with no statistically significant difference in eradication rate between the two groups ( $p=0.75$ ).<sup>[30]</sup>

Unfortunately, in our country there are no data on Helicobacter pylori antibiotic resistance or sensitivity. Therefore, using probiotics for Helicobacter pylori eradications seems to be attractive. In the recent times, the efficacy of probiotics for Helicobacter pylori eradication has been tested to avoid antimicrobial resistance, allergies or other antibiotic side effects. Hence the current study was conducted to study the effectiveness of spray dried Lactobacillus reuteri in treatment of Helicobacter pylori infection at tertiary healthcare institute.

In our study we assessed Rapid urease test findings on first visit among the study subjects. We only included patients who were positive for Helicobacter pylori on Rapid Urease test. All patients were treated with spray dried Lactobacillus reuteri capsules twice a day for 28 days. We assessed Rapid urease test findings on follow up visit among the study subjects. We found that on first visit all the study subjects had rapid urease test positive for Helicobacter pylori, whereas after treatment with spray dried Lactobacillus reuteri, on follow up visit 63.64% study subjects converted into negative findings for Helicobacter pylori.

The observations were found to be statistically significant, and probiotics, in our case Spray dried Lactobacillus reuteri DSM17648 have proved to be significantly effective in eradication of Helicobacter pylori among the study subjects. (t-value: 7.5, p-value:  $<0.0001$ ). In our study, we observed that 63.64% study subjects responded to the treatment with Lactobacillus reuteri capsules. The results are comparable to the other studies which show that Lactobacillus reuteri (Probiotics) are useful in the Helicobacter pylori infection treatment.

Probiotics are an effective and a newer treatment in Helicobacter pylori infection eradication. Our study shows that probiotics can be used effectively. The conversion rate after treatment with spray dried Lactobacillus reuteri was found to be 63.64%. The results demonstrated that Lactobacillus reuteri DSM17648 has the potential to suppress Helicobacter pylori infection, and may lead to an improvement of Helicobacter pylori-associated gastro intestinal symptoms.

## **Conclusion**

Lactobacillus reuteri can be used as a potential treatment modality for Helicobacter pylori infection eradication. It can be a very important part of treatment to avoid use of antibiotics. It has a potential to suppress the infection and reduce symptoms along with no side effects and a good safety.

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