

**IMPACT OF PROBIOTIC (SACCHAROMYCES BOULARDII)  
ADMINISTRATION IN PREVENTION AND MANAGEMENT  
OF CHRONIC DIARRHEA**

**ABSTRACT**

**BACKGROUND**

Diarrheal disease is the second leading cause of death in children under five years old, and is responsible for killing around 525 000 children every year. Though many treatment modalities exist, chronic diarrheal conditions demand a safer alternative modality (with lesser side effects) and thus, role of probiotics in prevention and management of chronic diarrhea merits exploration.

**OBJECTIVE**

To study the impact of probiotic (*Saccharomyces Boulardii*) in prevention and management of chronic diarrhea.

**METHODOLOGY**

This experimental study comprised of a sample of 178 (chosen via non-probability, consecutive sampling) children aged 2 months to 12 years, presenting to the study setting with chronic diarrhea (from November 05, 2019, to May 04, 2020) to the Dept. of Pediatrics at Liaquat University Hospital, Hyderabad. After taking written consent, data was recorded onto a structured questionnaire containing inquiries about the socio-demographic details, diarrheal disease history, medication history and eventual treatment outcome. The study population was divided into 2 equal groups (*S. Boulardii* group & Control Group) of 89 each. The active treatment period was 5 days. All study participants were examined on day 0 (inclusion day) and followed up on day 3 and day 6 during active treatment phase and in the following month thereafter for observation. The data obtained was analyzed through SPSS version 20.

## **RESULTS**

The mean age of the sample stood at 6.5 (SD  $\pm$  1.5) years. Baseline characteristics such as mean age and the average frequency of stools were comparable in *S. boulardii* and control group at the time of inclusion in the trial. By day 3 it reduced to 2.8 and 4.4 stools per day respectively and by day 6 it reduced to 1.4 (*S. boulardii* Group) and 3.7 (control group). The duration of diarrhea was 3.2 days in *S. boulardii* group whereas it was 5.2 day in control group (P = 0.001). In the following month, *S. boulardii* group had a significantly lower frequency of 0.46 episodes as compared to 1.28 episodes in control group.

## **CONCLUSION**

After careful consideration, it can be concluded that average frequency of stools is significantly reduced and brought down to normal in the *S. boulardii* group as compared to the control group. The drug was well accepted and tolerated. There were no reports of the side effects during treatment period.

## **KEYWORDS**

Diarrhea, Probiotic, Normal Flora, Child Health and *S. Boulardii*.

## **INTRODUCTION**

Diarrheal disease is the second leading cause of death in children under five years old, and is responsible for killing around 525 000 children every year. <sup>[1]</sup> In Pakistan, diarrheal diseases cause significant childhood morbidity and mortality, claiming over 45,000 lives of children every year. <sup>[2]</sup> According to other reports, 600 deaths per day in the country are brought about by diarrheal diseases. <sup>[3]</sup> In Pakistan, every child gets, on average, 5-6 episodes of diarrhea per year <sup>[4]</sup> and these repeated and chronic episodes of diarrhea lead to under-nutrition, contributing to debility poor health. <sup>[4]</sup>

Lately, great strides have been made towards better understanding of pathogenesis and management methods of diarrhea. Numerous modalities of interventions have been identified and put to the test around the world, in an attempt to curb this menace and decrease the mortality and morbidity. Among the interventions are oral rehydration salt (ORS), antibiotics, anti-diarrheal, antispasmodics and anti-emetics. However, continued use of most of the aforementioned modalities for persistent diarrhea is not free from side-effects. <sup>[5]</sup> The harmful effects include worsening and increased duration of diarrhea, negative effects on intestinal

motility resulting in paralytic ileus and others. <sup>[6]</sup> Fresher alternatives with potent therapeutic efficacy but fewer side-effects are thus the need of the hour.

Chronic gastrointestinal diseases often result in multitude of adverse consequences, chief among which is the disturbance of the gut's complex ecosystem. The belief that modulating bacterial activity and improving gut microbial function may yield positive results for the gastrointestinal health, has long existed but evidence on this matter is far from adequate. However, despite limited evidence, we have progressed from the use of yoghurt (as a source of various probiotic) in the treatment of diarrhea to using selective probiotics targeted to yield specific positive outcomes. It is, due to this very reason that, now greater recognition is being given to probiotics as a useful means of influencing the composition of gut flora and the gut ecosystem as a whole. Numerous probiotic agents have been studied for this purpose, including Lactobacillus GG, Lactobacillus reuteri, and Saccharomyces Boulardii (S. Boulardii). Amongst these, all are bacteria except S. Boulardii, which is yeast. <sup>[7]</sup>

Many other effective modalities exist to counter acute diarrhea and thus the use of S. Boulardii for acute diarrheal diseases remains limited. However, chronic diarrheal conditions demand a safer alternative modality (with lesser side effects) and thus, we hope to explore the impact of Saccharomyces Boulardii in prevention and management of chronic diarrhea.

## **METHODOLOGY**

This experimental study comprised of a sample of 178 (chosen via non-probability, consecutive sampling) children aged 2 months to 12 years, presenting to the study setting with chronic diarrhea (from November 05, 2019 to May 04, 2020) to the Dept. of Pediatrics at Liaquat University Hospital, Hyderabad. After taking written consent, data was recorded onto a structured questionnaire containing inquiries about the socio-demographic details, diarrheal disease history, medication history and eventual treatment outcome. The study population was divided into 2 equal groups of 89 each. In S. Boulardii group, patients were managed by WHO-CDD protocol plus S. boulardii (250 mg B.I.D) administered orally diluted in water or other semi-solid food. In the control group patients were managed by WHO-CDD protocol only. The active treatment period was 5 days. Treatment of the subsequent episodes of diarrhea were left to

the discretion of the treating physician. All study participants were examined on day 0 (inclusion day), and followed up on day 3 and day 6 during active treatment phase and in the following month thereafter for observation. The data obtained was analyzed through SPSS version 20.

Qualitative data (e.g. gender and diarrheal symptoms) was expressed as number and percentage (No & %). Quantitative data (age, weight, duration of diarrhea and Bristol stool scores) was expressed as mean & standard deviation ( $X \pm SD$ ). T-Test was used to compare the two groups for respective difference in disease duration. P value  $> 0.05$  was considered statistically non-significant. P value  $\leq 0.05$  was considered statistically significant. Anonymity and confidentiality of the patients shall be protected by assigning codes to the data set, instead of names and keeping the data password protected. The data shall be discarded a set period of time after completion of the project.

### **ELIGIBILITY CRITERIA**

Inclusion Criteria: Children of either gender, aged 2 months to 12 years, presenting to the study setting with chronic diarrhea (more than 3 episodes per day) were included into the study after taking written informed consent from the guardians (parents).

Exclusion Criteria: Children presenting with severe inter-current illnesses, severe diarrhea and dehydration requiring hospitalization and intravenous therapy, and/or presenting with temperature above  $38.5^{\circ}\text{C}$ , who were have been treated by any other anti-diarrheal/antibiotics in last 24 h as well as severely malnourished children shall be excluded from the study sample. Also excluded were children taking systemic anti-mycotic treatment (in the past 6 weeks).

### **RESULTS**

The mean age of the sample stood at 6.5 ( $SD \pm 1.5$ ) years. Baseline characteristics such as mean age, gender and the average frequency of stools were comparable in *S. Boulardii* and control group at the time of inclusion in the trial.

Table 1. Experimental and control group

<b>Variable</b>	<b>Experimental Group</b>	<b>Control group</b>
<b>Age</b>	$6.4 \pm 1.6$	$6.6 \pm 1.4$

<b>Gender</b>	<b>Male</b>	56	61
	<b>Female</b>	33	28
<b>Weight (kg)</b>		17.4	17.1
<b>Frequency of Stool</b>		8.8	9.2

Follow-up statistics (post treatment) were noted on day 3 and 6. The results are tabulated below:

Table 2. Post-treatment statistics

<b>Variable</b>	<b>Day 03</b>		<b>Day 06</b>	
	<b>Experimental</b>	<b>Control</b>	<b>Experimental</b>	<b>Control</b>
<b>Stool Frequency</b>	2.8	4.4	1.4	3.7

The duration of diarrhea was 3.2 days in *S. boulardii* group whereas it was 5.2 day in control group ( $P = 0.001$ ). In the following month, *S. boulardii* group had a significantly lower frequency of 0.46 episodes as compared to 1.28 episodes in control group. The drug was well accepted and tolerated. There were no reports of the side effects during treatment period.

## **DISCUSSION**

*S. Boulardii* is a non-pathogenic yeast first isolated from lychee fruits in Indonesia and used first in France to treat diarrhea, in the beginning of the 1950s. <sup>[8]</sup> Preclinical and experimental studies of *S. Boulardii* have demonstrated an anti-inflammatory, antimicrobial, enzymatic, metabolic and antitoxin activity. <sup>[9]</sup> *S. Boulardii* secretes a 54-KDa protease which has been shown to neutralize certain bacterial toxins; *S. Boulardii* is also able to stimulate an immune response in the intestinal mucosa. It has a trophic effect by enhancing the metabolic function of the mucosa. *S. Boulardii* releases polyamines, which are implicated in stimulating the enzymatic activity of the colonic mucosa. <sup>[10]</sup> It is well tolerated by all, regardless of user's age or disease condition. <sup>[9]</sup>

From 1976 to 2015, 90 randomized controlled trials covering 15 different types of disease conditions have been conducted with *S. Boulardii*. <sup>[11]</sup> The most robust evidence-based efficacy is for the treatment of acute pediatric diarrhea and for the prevention of antibiotic-associated diarrhea. <sup>[12]</sup>

A drop (from 23% to 7.9%) in incidence of diarrhea after administration of *S. Boulardii* was seen among children, as compared to controls in a study by Szajewska et al. [13] Strong evidence is also found for *S. Boulardii* efficacy for the treatment of acute adult diarrhea (75%) [14] and the treatment of inflammatory bowel disease (success rate 75%), [15] but these findings are supported with a fewer number of trials. Other disease indications (*Clostridium difficile* infections, [16] giardiasis, [17] traveler's diarrhea, [18] enteral nutrition-related diarrhea) [19] show promise, but need more studies. A recent meta-analysis shows the success rate of *S. Boulardii* to be 46.4% to 95% in acute pediatric diarrhea, 65% in antibiotic associated diarrhea and up to 100% in diarrhea caused by *C. difficile* infection and *Giardia Lamblia*. [20]

## **CONCLUSION**

After careful consideration, it can be concluded that average frequency of stools is significantly reduced and brought down to normal in the *S. boulardii* group as compared to the control group. The drug was well accepted and tolerated. There were no reports of the side effects during treatment period.

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