



## RESEARCH ARTICLE

# EFFECTIVENESS AND SAFETY OF *BACILLUS CLAUSII* AS AN ADJUVANT THERAPY IN PAEDIATRIC PATIENTS WITH DIARRHOEA: A RETROSPECTIVE REAL-WORLD EVIDENCE STUDY

\*Dr. Pooja Vaidya, Dr. Aradhana Sinal, Dr. Dattatray Pawar, Dr. Akhilesh Sharma

Medical Affairs Department, Alkem Laboratories Limited, Mumbai

### ARTICLE INFO

#### Article History:

Received 09<sup>th</sup> February, 2025  
Received in revised form  
21<sup>st</sup> March, 2025  
Accepted 19<sup>th</sup> April, 2025  
Published online 30<sup>th</sup> May, 2025

#### Keywords:

Probiotic, Diarrhea, RWE,  
Retrospective study, India

\*Corresponding author: Dr. Pooja Vaidya

Copyright©2025, Pooja Vaidya et al. 2025. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

**Citation:** Dr. Pooja Vaidya, Dr. Aradhana Sinal, Dr. Dattatray Pawar and Dr. Akhilesh Sharma. 2025. "Effectiveness and safety of *Bacillus Clausii* as an adjuvant therapy in Paediatric patients with Diarrhoea: A Retrospective real-world Evidence Study". *International Journal of Current Research*, 17, (05), 33096-33100.

## INTRODUCTION

Diarrheal disease is the third leading cause of mortality and a significant contributor to malnutrition in children under five years of age. It is primarily a clinical manifestation of an infection within the gastrointestinal tract, caused by a diverse range of bacterial, viral, and parasitic pathogens. Transmission occurs *via* ingestion of contaminated food or water, as well as through direct person-to-person contact, often facilitated by inadequate sanitation and hygiene practices.<sup>1</sup> Consequently, the burden of diarrheal disease is disproportionately higher in low- and middle-income countries. Despite being a preventable condition, diarrheal disease remains a major global health concern, responsible for approximately 4,43,832 pediatric deaths annually.<sup>1</sup> A substantial proportion of these fatalities occur in five countries—India, Nigeria, the Democratic Republic of the Congo, Pakistan, and China—accounting for nearly half of all childhood diarrheal deaths.<sup>2</sup> In India alone, the estimated number of diarrheal deaths among children aged 0–6 years is 1,58,209, contributing to 9.1% of total under-five mortality.<sup>3</sup>

Beyond its direct impact on mortality, recurrent diarrheal episodes predispose children to growth faltering, malnutrition, and cognitive impairment, thereby exacerbating long-term health consequences. According to World Health Organization (WHO) guidelines, the cornerstone of diarrheal management involves oral rehydration therapy using an oral rehydration solution (ORS) or a rehydration mixture composed of clean water, sugar, and salt, alongside adjunctive zinc supplementation.<sup>1</sup> These interventions primarily aim to correct dehydration and reduce the duration of illness. However, infectious diarrhea significantly disrupts the gut microbiota, leading to dysbiosis—a state characterized by an imbalance in the composition and function of intestinal microbial communities. This microbial dysregulation, driven by increased intestinal motility and mucosal disruption, can be further exacerbated by frequently prescribed irrational antibiotic therapy, which reduces microbial diversity and depletes commensal bacteria.<sup>4</sup> With unwarranted antibiotics prescription contributing to antimicrobial resistance (AMR), an emerging global crisis (WHO, 2020), complementary therapeutic

approaches that enhance treatment efficacy, expedite recovery, and restore intestinal microbiota are imperative. To restore gut homeostasis and re-establish a balanced intestinal microbiota, exogenous microbial supplementation through functional foods, dietary supplements, or pharmaceutical formulations has gained increasing scientific interest. Probiotics, prebiotics, and synbiotics have emerged as promising therapeutic strategies to modulate gut microbiota composition, support intestinal barrier function, and enhance immune response.<sup>5</sup> Probiotics, defined as live microorganisms that confer health benefits when administered in adequate amounts, exhibit antimicrobial activity, regulate immune responses, and compete with pathogenic microbes for nutrient uptake and adhesion sites within the gastrointestinal tract.<sup>6</sup> Commercial probiotic formulations predominantly contain bacterial strains from the *Lactobacillus* and *Bifidobacterium* genera, which are integral components of the endogenous gut microbiota. In addition to *Lactobacillus*, the *Bacillus* genus has gained attention for its probiotic potential due to its spore-forming ability, which enhances its stability and resistance to harsh gastrointestinal conditions, including exposure to gastric acid and bile salts.<sup>5</sup> *Bacillus clausii*, a naturally occurring commensal of the human gut, has demonstrated the ability to survive gastrointestinal transit and maintain viability during food and pharmaceutical processing. Clinical trials in adult populations have shown *Bacillus clausii* to be both effective and safe in the management and prevention of acute diarrheal illness. While extensive research has been conducted on *Lactobacillus* and *Bifidobacterium*-containing probiotics, further investigation is warranted to elucidate the therapeutic potential and mechanisms of *Bacillus clausii* in modulating human gut microbiota and improving health outcomes. Despite its probiotic potential, *Bacillus clausii* remains underexplored, with limited clinical adoption and a paucity of real-world effectiveness data. While it is primarily used as an adjuvant therapy to mitigate disease severity and reduce recovery time, there is insufficient evidence regarding its broader clinical applications, prescribing trends, and patient outcomes in routine medical practice. Given the increasing interest in probiotics for gut health and disease management, it is essential to assess the real-world utilization and therapeutic impact of *B. clausii*. This study seeks to address this critical knowledge gap through a multicenter, retrospective, real-world study evaluating prescribing patterns and treatment responses of *Bacillus clausii* spores suspension in clinical settings, thereby providing valuable insights into its effectiveness and potential role in the outpatient management of pediatric gastrointestinal health. By leveraging real-world clinical data, this research aims to provide evidence-based insights to support wider adoption in clinical practice and inform potential updates to treatment guidelines. Strengthening therapeutic strategies for childhood diarrhea is imperative to reducing disease burden, enhancing pediatric health outcomes, and improving healthcare efficiency in India.

## METHODOLOGY

This was a multicenter, retrospective real-world evidence study that analyzed medical records of pediatric outpatients diagnosed with diarrhea and treated with or without probiotic *Bacillus clausii*. As anonymized data from previously treated patients was used, informed consent was not required. Eligible patients included those presenting with diarrhea and other gastrointestinal complaints, treated with or without *Bacillus*

*clausii*, with documented diagnosis, at least one follow-up record, and treatment outcomes available. Patients with incomplete or unavailable medical records were excluded. Investigators extracted demographic details, clinical presentation, disease severity, treatment history, laboratory findings, and clinical outcomes at baseline (Day 0) and follow-up (Day 7 ± 3). An electronic data capture (EDC) platform was used for data entry, review, and verification. Statistical analysis included descriptive statistics, with continuous variables expressed as mean ± SD/SE and categorical variables as percentages. A *p*-value <0.05 was considered statistically significant, and appropriate statistical tests were applied to compare outcomes between treatment groups.

## RESULTS

A total of 1374 patient records meeting the predefined inclusion and exclusion criteria were analyzed. The age distribution ranged from infancy to adolescence, with a minimal representation of infants below one year of age (*n* = 3; 0.22%). Young children between one and three years constituted 4.22% (*n* = 58) of the study population. The majority of patients (*n* = 983; 71.54%) fell within the four to twelve-year age group, forming the largest subset of the study population. Adolescents (aged 13–18 years) comprised 24.02% (*n* = 330) of the total sample. A distinct gender disparity was observed, with a male-to-female ratio of approximately 3:1, as 917 (66.75%) of the patients were male and 457 (33.25%) were female. This distribution as depicted in Figure 1, shows that the male preponderance was consistent across various age groups, suggesting a potential gender-related trend in the disease prevalence within the study population.

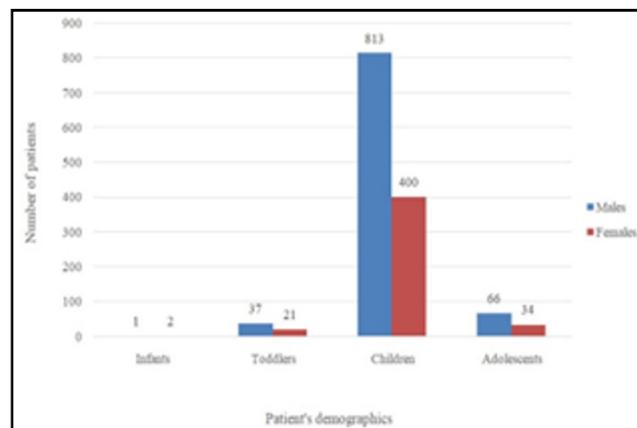


Figure 1. Age-Gender distribution of the patients

The presenting complaints among the 1374 patients were varied, with considerable overlap between different gastrointestinal symptoms (Figure 2). Diarrhea emerged as the most prevalent primary complaint, reported by 1175 patients. Of these, 578 presented with loose stools as their sole symptom, while 17 also reported the presence of blood in their stool. Abdominal pain accompanied loose stools in 409 cases, indicating a frequent co-occurrence of these symptoms. Dehydration was another significant concern, observed as an isolated complaint in 73 patients. However, it also presented as a secondary symptom in patients primarily reporting loose stools (*n* = 75) or abdominal pain (*n* = 289). Vomiting was documented in 80 patients, either as an isolated complaint (*n* = 31) or in conjunction with other primary symptoms such as loose stools, abdominal pain, fever, weakness, and subsequent dehydration.

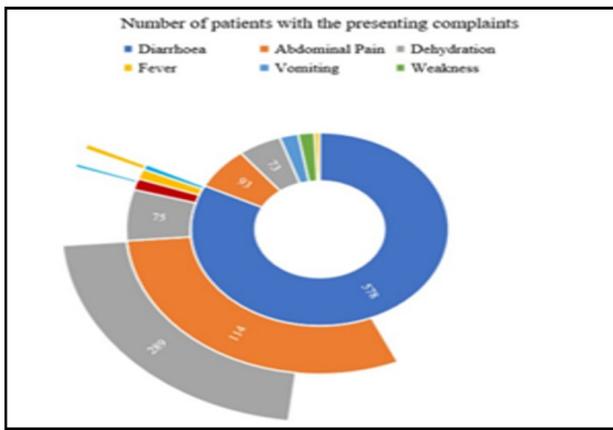


Figure 2. Presenting complaints of the patients

Fever was a relatively uncommon presenting symptom, reported in only 24 cases, while generalized weakness was noted in 30 patients across various symptom combinations. Based on the reported symptoms, diagnoses were established at the discretion of the attending clinicians (Figure 3). The vast majority of patients (n = 1226; 89.22%) were diagnosed with acute diarrhoea, making it the predominant clinical presentation. Acute gastroenteritis (AGE) was the second most common diagnosis, accounting for 7.13% (n = 98) of cases. A similar incidence was observed in patients diagnosed with antibiotic-associated diarrhoea (AAD) (n = 26; 1.89%) and dysentery (n = 17; 1.23%). The remaining cases (n = 7; 0.50%) were classified as acute bacterial diarrhoea.

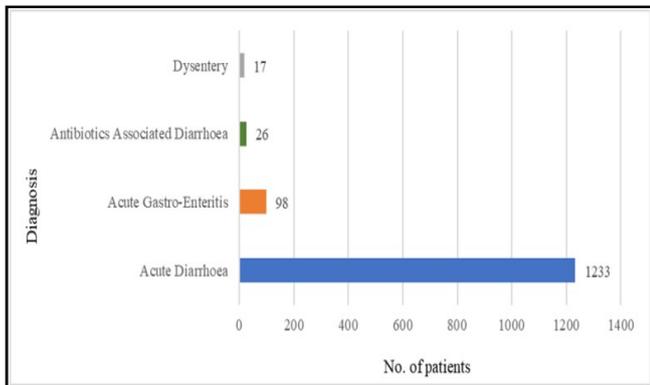


Figure 3. Diagnosis of the patients

A subset of patients had already been exposed to various lines of management before seeking consultation. Among them, 382 patients had received antibiotics, 14 patients had taken probiotics, 10 patients had been administered ORS and 6 patients had used anticholinergics. The remaining 964 patients (70.17%) had no prior history of medication use before their consultation. As illustrated in Figure 4, all prescriptions in the study included *Bacillus clausii* as a probiotic. However, the prescribed dosage regimen varied across patients. The majority of prescriptions (n = 1304) recommended a twice-daily administration, followed by thrice-daily (n = 47), once-daily (n = 19), and, in a rare few cases, four times daily (n = 4). Regarding the duration of therapy, most patients were advised to take *Bacillus clausii* for 2 to 5 days (n = 1209). A smaller subset received prescriptions extending from 5 to 15 days (n = 143), while a rare few (n = 22) were instructed to continue therapy for more than 15 days. (Figure 5).

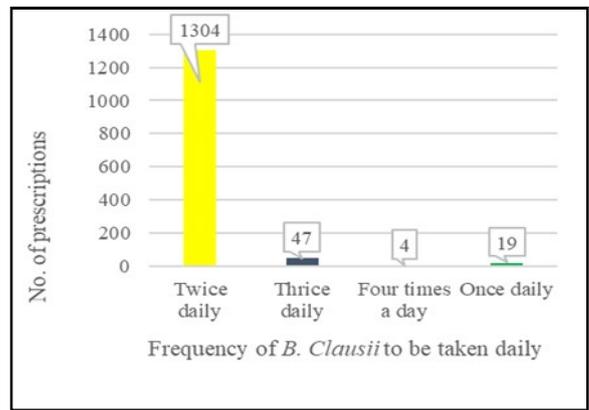


Figure 4. Prescribed daily frequency of B. Clausii

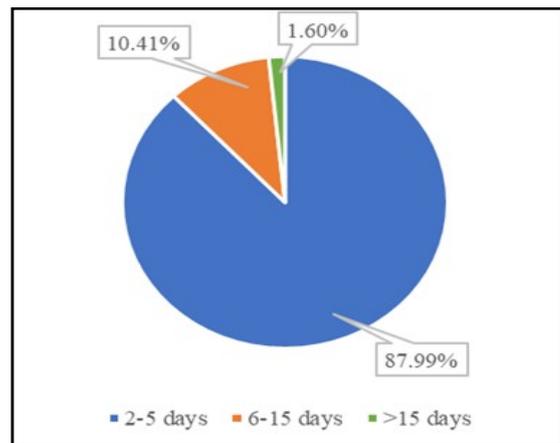


Figure 5. Duration of B. Clausii therapy

A comparative analysis of diarrheal episodes between Day 1 (initial clinical visit) and Day 7 (follow-up visit) was conducted, depicted in Figure 6. On Day 1, the highest frequency of diarrhoea was 4–5 episodes per day, reported by 862 patients. This was followed by 342 patients experiencing more than 5 episodes per day, while 39 patients reported more than 10 episodes daily. Moderate diarrhoea severity (2–3 episodes per day) was observed in 130 patients, and only one patient presented with a single episode of loose stool. By Day 7, stool frequency had significantly declined. By Day 7, majority of patients (n = 744) reported 2–3 episodes per day, while 412 patients experienced only one or fewer episodes. However, 115 patients continued to report 4–5 episodes per day, and 103 patients still experienced more than 5 episodes daily. Notably, no patients reported more than 10 episodes per day at follow-up. Further analysis revealed that 30 out of 39 patients who initially had more than 10 episodes per day reported a reduction to less than 3 episodes after therapy including *Bacillus clausii* probiotic. Additionally, 286 patients out of the 342 patients who had 5–10 episodes before therapy also reported fewer than 3 episodes at follow-up. At the follow-up visit, inquiry regarding stool consistency was also made among the patients. A total of 1,235 patients (89.88%) reported normal stool consistency, while 124 patients (9.02%) continued to experience loose stools. However, 15 patients (1.09%) presented with hard stools. At the Day 7 follow-up visit, 889 out of 1,374 patients were declared cured by their attending clinicians. An additional 114 patients exhibited improvement in their condition. However, 368 patients showed no significant change in their clinical status. Unfortunately, 3 patients succumbed to the illness, resulting in mortality within the study population.

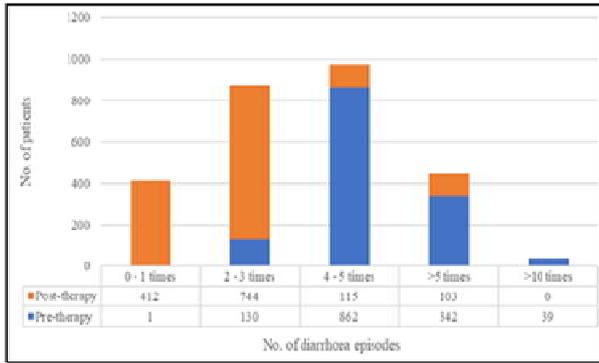


Figure 6. Frequency distribution of no. of diarrhoeal episodes per day

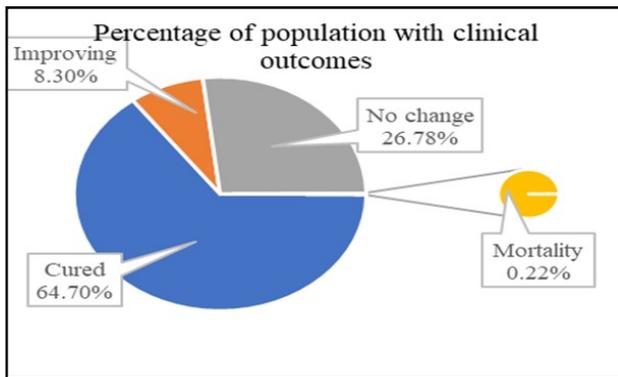


Figure 7. Clinician's perspective on clinical outcomes

## DISCUSSION

This study presents a comprehensive retrospective analysis of paediatric gastrointestinal cases predominantly characterized by acute diarrhoea who were prescribed *Bacillus Clausii*. In this study, the majority of paediatric patients with acute diarrhoea were between 4 and 12 years old (71.54%), followed by adolescents (24.02%). Infants below one year and young children aged 1–3 years were minimally represented. This age distribution aligns with findings from the CODDLE study by de Castro *et al.*<sup>7</sup>, which also reported the highest incidence of diarrhoea among children over three years of age. The mid-childhood peak may be attributed to increased environmental exposure in school settings and maturing immune systems, underscoring the importance of targeted interventions for this age group. A male predominance (66.75%) was noted, with a nearly 3:1 ratio across all age groups. While this could suggest higher male susceptibility, it can also be attributed to sociocultural factors or regional demographics. In contrast, the CODDLE study showed a more balanced ratio (~1.3:1), pointing to regional disparities in healthcare-seeking behaviour and access. Loose stools were the most reported symptom (85.5%), though only 42.1% experienced it in isolation. Common associated symptoms included abdominal pain (29.8%), dehydration (10.7%), and vomiting (5.8%), consistent with symptom overlap seen in de Castro *et al.*<sup>7</sup> and Farzana *et al.*<sup>8</sup> These results highlight the multifactorial nature of paediatric diarrhoeal illness and the importance of comprehensive symptom assessment. Acute diarrhoea was the dominant diagnosis (89.22%), echoing findings from de Castro *et al.*<sup>7</sup> and Ianiro *et al.*<sup>3</sup> Acute gastroenteritis (7.13%) was the next most frequent; AAD (1.89%) and dysentery (1.23%) were rare. Notably, nearly 28% of cases had prior antibiotic exposure, reinforcing the importance of distinguishing AAD. Accurate diagnosis remains key for tailored intervention. Around 30% of patients had received prior treatment, predominantly antibiotics (27.8%), despite unknown stool culture reports. As Lee *et al.*<sup>9</sup> warned, this practice undermines antimicrobial stewardship. Probiotic (1.02%)

and ORS (0.73%) use was low, reflecting missed opportunities for guideline-based care. The 70.17% without prior treatment represent a key window for proper intervention, including *Bacillus clausii*. The symptom outcome analysis revealed a marked clinical improvement in diarrhoeal frequency and stool consistency over the 7-day observation period, underscoring the therapeutic potential of *Bacillus clausii* in paediatric acute diarrhoea. The significant decline in stool frequency—from over five episodes per day in nearly 25% of patients at baseline to fewer than three episodes in a majority by follow-up—highlights a rapid clinical response. These improvements mirror those observed in the systematic review and meta-analysis by Ianiro *et al.*<sup>3</sup>, which demonstrated that *Bacillus clausii* significantly reduced the duration and frequency of diarrhoea in children with acute infectious gastroenteritis. Among those with more than ten episodes per day (76.9%) improved to fewer than three daily episodes by Day 7. Similarly, 83.6% patients with 5–10 episodes also experienced a marked reduction. These rates are consistent with the findings of de Castro *et al.*<sup>7</sup> in the CODDLE study, where a high percentage of paediatric patients achieved symptom resolution within a week of initiating *Bacillus clausii* therapy. Their study similarly emphasized rapid symptom improvement, particularly in cases of acute diarrhoea and acute gastroenteritis, aligning closely with the patterns observed in our cohort.

All patients in this study received *Bacillus clausii*. By Day 7, diarrhoeal episodes had reduced markedly, with nearly 90% showing normalized stool consistency. These findings align with Ianiro *et al.*<sup>3</sup>, who confirmed efficacy of *Bacillus clausii* in reducing diarrhoea duration and frequency. The small proportion of patients reporting hard stools (1.09%) may suggest overcorrection or unrelated changes in bowel habit, warranting individual follow-up. In terms of overall clinical outcomes, 64.7% of patients were deemed cured and 8.3% showed improvement, reflecting a combined therapeutic success rate of over 70%. These outcomes are in line with the review by Acosta-Rodríguez-Bueno *et al.*<sup>6</sup>, which emphasized immunomodulatory properties of *Bacillus clausii*, its ability to restore epithelial integrity, and its compatibility with concurrent antibiotic use—all of which likely contributed to the favorable outcomes in our study. Moreover, the lack of reported adverse events echoes findings from both Ianiro *et al.*<sup>3</sup> and Acosta-Rodríguez-Bueno *et al.*<sup>6</sup>, further affirming the probiotic's safety in paediatric populations. Collectively, these findings add to a growing body of evidence supporting *Bacillus clausii* as a safe, effective adjunct in the management of paediatric diarrhoea. When contextualized alongside findings from other above-mentioned studies from the past few years, the symptom outcome data from our study reinforce the global relevance of probiotic therapy, while also highlighting the need for prudent antibiotic stewardship and continued monitoring of treatment responses. Additional evidence from Lahiri *et al.*<sup>10</sup> showed that combining *Bacillus clausii* with ORT and zinc significantly shortened diarrhoea duration. The Asian Expert Consensus (2020)<sup>11</sup> also supports its use across various paediatric diarrhoeal conditions. These collective findings reinforce *Bacillus clausii* as a safe and effective adjunct in pediatric gastroenterology.

## CONCLUSION

This retrospective analysis, grounded in clinicians' direct observations and treatment records, highlights the practical efficacy of *Bacillus clausii* as an adjunct in managing paediatric diarrhoea in outpatient settings. The notable improvement in stool frequency and consistency observed across a majority of cases, reflects positive therapeutic responses routinely seen in clinical practice. *Bacillus clausii*, when integrated appropriately into treatment regimens, can enhance recovery and reduce disease burden. Public health initiatives must prioritize awareness campaigns and healthcare provider training to promote timely, appropriate interventions and discourage antibiotic misuse. Expanding access to affordable probiotic therapies like *Bacillus clausii* could further reduce illness duration and prevent complications, ultimately contributing to lower morbidity and mortality rates among children affected by diarrhoeal illnesses.

## ACKNOWLEDGEMENT

We extend our sincere appreciation to the clinicians whose valuable contributions and support in providing access to anonymized medical records were instrumental in establishing a robust dataset for this study. Their commitment to accurate documentation and patient care has been vital to the integrity of our findings. We are especially grateful to the patients and their families; although their identities remain fully protected, their medical information has significantly advanced our understanding of the clinical application and therapeutic impact of *Bacillus clausii* in pediatric diarrhoeal management.

## REFERENCES

- Acosta-Rodríguez-Bueno CP, Abreu y Abreu AT, Guarner F, Guno MJ, Pehlivanoğlu E, Perez III M. *Bacillus clausii* for gastrointestinal disorders: A narrative literature review. *Advances in Therapy*. 2022 Nov;39(11):4854-74.
- de Castro JA, Guno MJ, Perez MO. *Bacillus clausii* as adjunctive treatment for acute community-acquired diarrhea among Filipino children: a large-scale, multicenter, open-label study (CODDLE). *Tropical diseases, travel medicine and vaccines*. 2019 Dec;5:1-9.
- De Castro JA, Kesavelu D, Lahiri KR, Chajjitraruch N, Chongsrisawat V, Jog PP, Liaw YH, Nguyen GK, Nguyen TV, Pai UA, Phan HN. Recommendations for the adjuvant use of the poly-antibiotic-resistant probiotic *Bacillus clausii* (O/C, SIN, N/R, T) in acute, chronic, and antibiotic-associated diarrhea in children: consensus from Asian experts. *Tropical diseases, travel medicine and vaccines*. 2020 Dec;6:1-5.
- Ghosh K, Chakraborty AS, Mog M. Prevalence of diarrhoea among under five children in India and its contextual determinants: A geo-spatial analysis. *Clinical Epidemiology and Global Health*. 2021 Oct 1;12:100813.
- Hamid F, Quaium SM, Rahman A. Comparative study of *Bacillus clausii* and multistrain probiotics in the management of acute diarrhoea in children. *International Journal of Research in Medical Sciences*. 2019 Apr; 7(4): 1156-1160
- Iancu MA, Profir M, Roşu OA, Ionescu RF, Cretoiu SM, Gaspar BS. Revisiting the intestinal microbiome and its role in diarrhea and constipation. *Microorganisms*. 2023 Aug 29;11(9):2177.
- Ianiro G, Rizzatti G, Plomer M, Lopetuso L, Scaldaferrì F, Franceschi F, Cammarota G, Gasbarrini A. *Bacillus clausii* for the Treatment of Acute Diarrhea in Children: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Nutrients*. 2018 Aug 12;10(8):1074.
- Lahiri KR, Singh R, Apte M, Patil M, Taksande A, Varona R, Chatterjee G, Verma M, Brette S, Perez MI. Efficacy and safety of *Bacillus clausii* (O/C, N/R, SIN, T) probiotic combined with oral rehydration therapy (ORT) and zinc in acute diarrhea in children: a randomized, double-blind, placebo-controlled study in India. *Tropical diseases, travel medicine and vaccines*. 2022 Apr 10;8(1):9.
- Lakshminarayanan S, Jayalakshmy R. Diarrheal diseases among children in India: Current scenario and future perspectives. *Journal of natural science, biology, and medicine*. 2015 Jan;6(1):24.
- Lee NK, Kim WS, Paik HD. *Bacillus* strains as human probiotics: characterization, safety, microbiome, and probiotic carrier. *Food science and biotechnology*. 2019 Oct;28:1297-305.
- World Health Organization: WHO. Diarrhoeal disease [Internet]. March 2024. Available from: <https://www.who.int/news-room/factsheets/detail/diarrhoeal-disease>

\*\*\*\*\*