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Systematic review of clinical trials on the potential of probiotics for the treatment of Covid-19

Rita Natália Couto Santos[1], Fernando Xavier Ferreira Moreira[1,2], Agostinho Luís Silva Cruz[1,2]
ESS, Instituto Politécnico do Porto, Rua Dr. António Bernardino de Almeida, 400, 4200-072 Porto, Portugal 1
LAQV/REQUIMTE, ESS - Instituto Politécnico do Porto, Rua Dr. António Bernardino de Almeida, 400, 4200-0722

INTRODUCTION & AIM

In recent decades, new deadly coronaviruses (CoVs) have emerged, causing highly infectious diseases in human society, resulting in threats to public health and the global economy (Figure 1).

SARS-CoV November 2002 in Foshan, China → **MERS-CoV** June 2012 in Jeddah, Saudi Arabia" → **SARS-CoV-2** December 2019 in Wuhan, China

Figure 1. Emergence of new coronaviruses up to the major COVID-19 pandemic.

In December 2019, in the province of Wuhan, China, the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) emerged. This infection was classified as the Coronavirus Disease 2019 (COVID-19) pandemic.

Probiotics are live microorganisms, whose administration in adequate amounts has been associated with health benefits for the host, contributing to the treatment and prevention of multiple pathologies.

Objective: To **review the scientific evidence regarding the impact of probiotic treatment on the progression of morbidity caused by SARS-CoV-2.**

METHOD

- The present study is a systematic review (SR) following the PRISMA (Reporting Items for Systematic Reviews and Meta-analyses) guidelines. The research question, was developed using the PICO acronym model (Figure 2).
- The research was performed in the Medline; Web of Science; EBSCO; Clinical Trials; The Cochrane Library and Science Direct
- To assess bias in the study, the Joanna Briggs Institute (JBI) method was used.

Research question
Does the administration of probiotics influence the evolution of SARS-CoV-2?

- **P(Population)** SARS-CoV-2 confirmed diagnosis
- **I(Intervention)** Probiotic administration
- **C(Comparison)** Administration of products without pharmacologically active substances
- **O(Outcome)** Impact on morbidity in SARS-CoV-2 with the use of probiotics

Figure 2. Research question based on the model defined by the PICO acronym.

Inclusion Criteria

- Study period between 2019 and 2023.
- Literature searches: Cochrane Library, Clinical Trials, EBSCO, Medline, Web of Science, and Science Direct.
- Studies on humans, including all age groups with a confirmed diagnosis of SARS-CoV-2.
- Administration of probiotics in the treatment of SARS-CoV-2 in the experimental group.
- Randomized and non-randomized clinical trial studies.
- Administration of placebo and/or multivitamin supplements in the control group.
- Languages: English and Portuguese.

Exclusion Criteria

- Animal studies.
- Exclusion of combined probiotic therapies with other compounds in the treatment of SARS-CoV-2.
- Exclusion of treatments with vaccines, antivirals, or other types of treatment in the control group.
- Exclusion of unexposed control groups.

RESULTS & DISCUSSION

- In the PRISMA flowchart, Figure 3, it is possible to observe the different stages leading to the five results obtained in the systematic review.

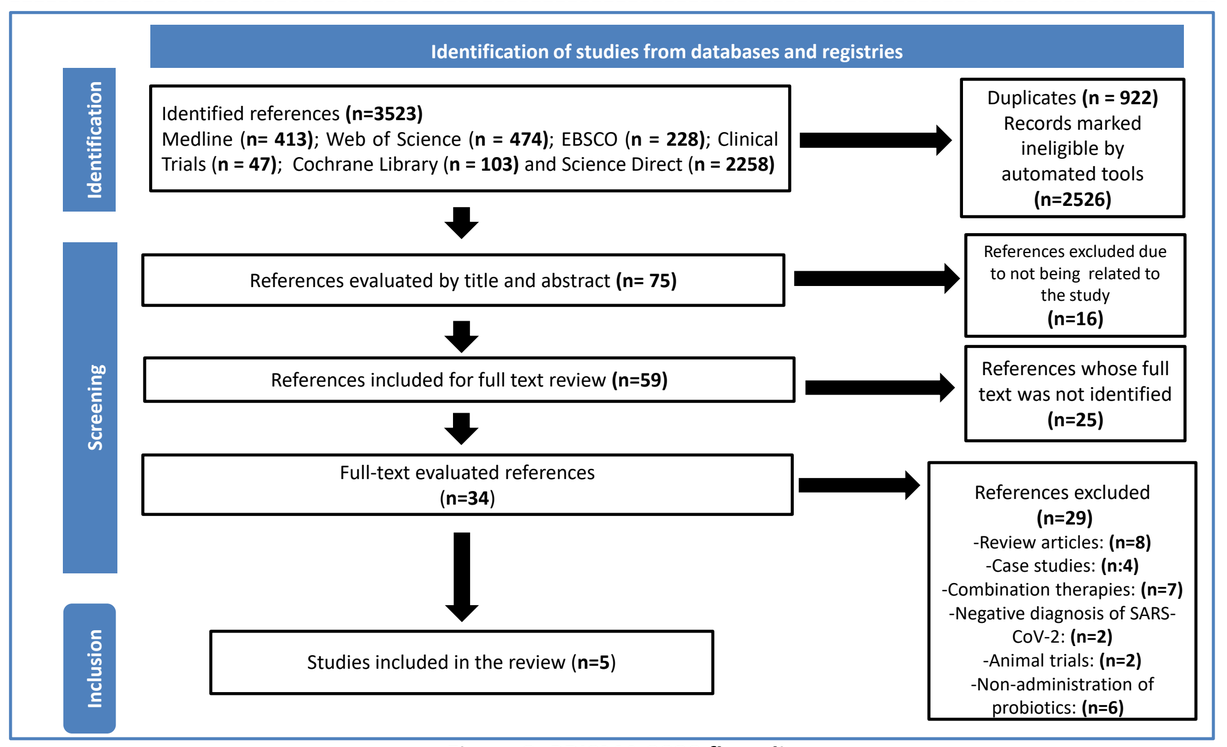

Figure 3. PRISMA 2020 flow diagram.

- A total of 26 participants from experimental groups and a total of 26 participants from control groups dropped out of the studies. Among the participants who completed the clinical trials, 242 belonged to the experimental group and 231 to the control group.
- The adverse effects detected in the studies were mainly abdominal pain, facial pain and discomfort, fever, cough, nausea, mild constipation and myalgia.

Table 1. Included studies and main features regarding intervention in experimental and control groups and mains results and/or conclusions.

Reference	Intervention in the Experimental Group	Intervention in the Control Group	Main Results/Conclusions
Kolesnyk et al., (2024)	One capsule a day containing Bifidobacterium (B.) lactis; B. longum, Lactobacillus(L). rhamnosus, L. casei, L. Acidophilus, for 28 days.	One capsule a day of placebo (consisting only of excipients and no probiotics), for 28 days.	Probiotics improved acute and post-illness symptoms. There was also a significant improvement in the humoral immune response to viral antigens.
Endam et al.,(2021)	Two nasal irrigations a day, with buffered isotonic solution with Lactococcus Lactis, for 14 days.	Two nasal irrigations a day with buffered isotonic solution (without probiotics) for 14 days.	The administration of probiotics increased intensity of symptoms of facial pain and discomfort; but was also a potential association with reduced intensity of symptoms of fatigue, loss of smell and shortness of breath.
Gutiérrez-Castrellón et al.,(2022)	One capsule per day containing Lactiplantibacillus (L.) plantarum KABP033, L. plantarum KABP022, L. plantarum KABP023, Pediococcus acidilactici KABP021, for 30 days.	One capsule a day of placebo (consisting only of excipients and no probiotics), for 30 days.	Probiotic administration resulted in a reduction in nasopharyngeal viral load, pulmonary infiltrates and the duration of digestive and non-digestive symptoms compared to placebo. There was no significant change in the composition of the fecal microbiota between the groups, but a significant increase in IgM and IgG in the probiotic group against SARS-CoV-2.
Navarro-López et al.,(2022)	One capsule a day containing Lactobacillus rhamnosus and Kluyveromyces marxianus, for 30 days.	The control group received no intervention.	Total reduction of digestive and general symptoms with probiotic treatment.
Di Pierro et al.,(2022)	Two tablets a day containing Streptococcus salivarius for 14 days.	Standard treatment according to hospital guidelines.	Improvement in the probiotic group in terms of biochemical parameters (CRP, D-Dimer; Ferritin, LDH), fever, oxygen saturation level, need for and duration of oxygen therapy, rate of ICU progression and death.

CONCLUSION/FUTURE WORK

The administration of probiotics possibly has an impact on the evolution of SARS-CoV-2 morbidity. The results analyzed indicate an improvement in symptoms, an increase in the immune response to viral antigens, a significant reduction in inflammatory markers and an improvement in the rate of progression in hospitalized patients and survival in groups treated with probiotics. **Future research will analyze intranasal probiotics as a new immunomodulatory therapy in the treatment and prevention of SARS-CoV-2.**

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