Probiotics Intake as Adjunct Therapy for Infected Health-Care with SARS COV-2

Anna Surgean Veterini[1], Eighty Mardiyan Kurniawati[2], Hamzah[3], Subijanto Marto Soedarmo[4], Cita Rosita Sigit Prakoeswa[5], Damayanti Tinduh[6]

[1]Anesthesiologist Intensivist, [2]Obstetrician, [3]Anesthesiologist Intensivist, [4]Prof., Pediatrician, [5]Prof. Dermatologist, [6]Medical Rehabilition Specialist of Dr Soetomo General Academic Hospital – Universitas Airlangga, Address: Jalan Prof. Dr. Moestopo 6-8 Surabaya, Indonesia

Abstract

Objectives: We performed this case-control observational study to evaluate the comparison of the length of duration of SARS COV-2 infection and the cycle threshold (Ct) value of reverse-transcriptase polymerase chain reaction (RT-PCR) nasopharynx swab between the probiotics intake (case) group and the non-probiotics intake (control) group.

Materials and Methods: Our study was a case-control study involving 15 cases and 15 controls match for RT-PCR positive results. The participants were healthcare consisted of registrars, consultants, and nurses. Each participant was interviewed by google forms using a structured questionnaire to collect socio-demographic characteristics, diet, therapy from a pulmonologist, and adjunct therapy.

Results: The total participants consisted of 15 males and 15 females. 4 participants in the case group had febrile, 1 participant with anosmia, 1 participant with febrile, nausea, and vomit before they consumed probiotics, and 9 participants without clinical complaints. One participant in the control group had fevered and cough, 14 participants without clinical complaints—1 participant with co-morbidities in the control group. The data of age, duration of infection, and cycle threshold (Ct) value were in the normal distribution. Analysis results using SPSS 21.00 show no significant differences in the course of disease between the case group and the control group. We found 2 participants in the control group had re-infection, while there was no re-infection in the case group.

Conclusion: The present study's finding may imply future care for the viral infection through the immunomodulation mechanism by probiotics consumption.

Keywords*: Probiotics; Immunomodulator; COVID-19*

Introduction

Immediate solutions are needed to deal with the new SARS COV-2 virus that has shocked the world. We must realize immediately about the strategies in the form of prevention and treatment of COVID-19. For example, prevention from the social side, social and physical distancing, wearing masks, avoiding crowds, and washing hands. Meanwhile, vaccines may not give protection in a short time [(1)].

The clinical appearance of COVID-19 varies widely, ranging from asymptomatic, mild symptoms, moderate to critical conditions, mostly needs the ICU treatment. The asymptomatic patient is dangerous for himself and hazardous for others because it causes others to become

Corresponding Author:
Anna Surgean Veterini,
Anesthesiologist Intensivist of Dr Soetomo General Academic Hospital – Universitas Airlangga.
Address: Jalan Prof. Dr. Moestopo 6-8 Surabaya, Indonesia, Email: annasurgeanveterini@gmail.com; annasurgean@fk.unair.ac.id

infected. Critical patients mostly died in the ICU. Transmission of SARS COV-2 is said to be through droplets, but changes in gut stability also contribute to the occurrence of COVID-19 [2]. The previous study detected SARS-CoV-2 ribonukleat acid (RNA) in the gastrointestinal tract and stool samples from patients [3] [4][5], and sewage systems [6]. Coronaviruses, including SARS-Cov-2, can invade enterocytes, thereby acting as a reservoir for the virus [5]. Indeed, extensive clinical studies from China indicate that gastrointestinal symptoms are common in COVID-19 and are associated with disease severity [4][5].

As a result of the SARS COV-2 virus attack, the world seems to have had a monster attack, and we haven't found a weapon to fight back. The group of scientists with various theoretical bases is trying to find a way out of prevention and treatment. The previous literature discussed probiotics' role promotes us to study probiotics' effectiveness against the SARS COV-2 virus. The hypothesis of the inhibition mechanism by probiotic against virus may come from the inhibition of viral entry and/or replication or by suppressing the immunologic response because of the infection (known as cytokine storm).

SARS-CoV-2 can infect the digestive tract and cause inflammation of the absorbing mucosa and sometimes diarrhea. The first US case of COVID-19 showing atypical symptoms, diarrhea, and other gastrointestinal (GI) [7]. Dysbiosis can exacerbate the immune response and the production of systemic inflammatory mediators. Oral probiotics can play a role in the gut and systemic effects of COVID-19. Also, inhaled microorganisms can directly activate the respiratory epithelium and immune system cells that fill them [8].

A Probiotic is a living microorganism that confers a health benefit on the host when administered in adequate amounts. Evidence is scarce about the relationship between COVID-19 and gut microbiota. Our case-control study about the advantages of using probiotics as one of the therapy modalities in healthcare workers with positive SARS COV-2.

Materials and Methods

Primary outcome

To analyze and compare the duration of infection in healthcare in the two groups of intake (case) and non-intake probiotic (control) during the infection.

Selection of subjects and study design

After passing ethical clearance (Ref.No: 0115/LOE/301.4.2/IX/2020), we collected the data from June to October 2020. We assessed 97 health care (registrars, consultants, and nurses) in Dr. Soetomo General Academic Hospital for eligibility. 67 participants were excluded because they did not fit the inclusion criteria (n =0), participants refused to participate (n = 0) or the data were not complete (n = 67).

We divided 30 eligible participants into two groups (15 cases and 15 controls). Fifteen participants consumed probiotics during the infection phase, while 15 participants never consumed probiotics in the control group. We interviewed and collected the medical records data to detect the clinical complaint and cycle threshold value of Rt-PCR from the nasopharynx swab specimen. This study compared the duration of infection, cycle threshold value, and clinical complaints of the two groups of participants.

Sample collection

The hospital has a schedule to examine healthcare routinely after working in high risk of infection transmission places. After the participant underwent an examination, the research team interviewed each participant with a structured questionnaire. We got the value of laboratory examination results and duration of infection from the medical records.

Viral Load Analysis

We obtain the viral load data from the cycle threshold value of the RT-PCR nasopharynx swab.

Statistical Analysis

Classical descriptive indicators describe the characteristics of the studied samples. Data shows as mean ± Standard Deviation (SD) for continuous variables and as number and percentage for categorical variables. The student's T-test (normally distributed data) compares the duration of infection of the case and control groups. All reported p values are 2-sided, and significantly when $p \leq 0.05$. We performed statistical

analysis with commercially available software (SPSS for Windows version 21.0; SPSS Inc., Chicago, IL, USA).

Results

From June 2020 to October 2020, 30 participants were enrolled (15 consumed probiotics and 15 which no probiotics consumed), and their nasopharynx swab specimens were collected to be analyzed. Table 1 reports participants' characteristics. We found that there were no significant differences in the duration of infection and Ct value in the two groups. From the gender aspect, there was not an important message between the two groups. An essential piece of news came from the information of re-infection events that happened in the control group. But we still can not explain the mechanism of the re-infection event.

Table 1. Characteristics of participants enrolled in this study

Variables	Cases, n (%) n = 15 (50.0)	Controls, n (%) n = 15 (50.0)	p value
Mean age ± SD (years)	34.73 ± 5.612	33.47 ± 3.871	0.21#
Male/female, n (%)	9/6 (60 %/ 40 %)	6/9 (40% / 60%)	0.52~
Re-infection	0	2 (0.13 %)	
Duration of infection	15.20 ±13.078	21.40±14.401	0.22*
Mean Ct value	29.74±5.45	25.32±7.93	0.08*

#Kolmogorov Smirnov

*T-test Unpaired

~Chi-square

Discussion

In much literature, probiotics in the incidence of gastrointestinal disorders are beneficial. According to Xu K et al. (2020), the use of probiotics can reduce secondary infections due to microbial translocation in severe cases of COVID-19. In mild and moderate cases, it can inhibit the progression of COVID-19 [(9)]. But giving probiotics in severe and critical cases needs to be evaluated more deeply [(10)]. We moved to investigate the effects of probiotics in mild to moderate patients of COVID-19, whether symptomatic or not. At this initial stage, we only observed data that was easy to obtain in the field. In the future, we hope that the detailed research comes to strengthen our results in this study.

In this case-control study, we focus on the Lactobacillus strain that is the main compound in the prebiotics. The zero conversion time in the RT-PCR result for SARS COV-2 was the main target after consuming the probiotic. The results show in table 1. There were no significant differences in the duration of infection. An explanation for this result is the sample size of this study was small. The starting of the Ct value between the two groups were not significantly different. It means that the participants have a similar Ct value before consumed probiotics. The excellent information about this study was the re-infection did not happen in the case group. The explanation about this phenomenon was unexplainable. Many works of literature said that probiotics could modify the immune response.

Although our study did not show the analysis results of the response time to clear the infection faster than the control group, several previous theories still accepted to be proven by a better number of cases than we have done. The study we conducted showed that there was no re-infection in the case group. This phenomenon may

support the article published by Baud et al. (2020) that probiotics can flatten the case curve of COVID-19 [1].

Effects on Virus Titres Reduction

The results of our observation show that the average day of rt-PCR zero conversion in the case group was 15.20 ± 13.078 days. We could not show the real result of the length of duration infection because the hospital examined the healthcare on a fixed schedule (checked 7 days after the first positive result, then multiplies 7 days).

Study of Gender

Our study shows that 50 % positive for SARS COV-2 are male, while 50 % are female. This data did not support the previous data that mention males bigger than female patients.

Study of Age

The mean age of the subject in the case group was 34.73 ± 5.612 years old (table 1). The young generation of participants may cause an improvement of clinical appearance in our study. Much previous literature said that older age gives a lousy prognosis.

Study of RT-PCR Results

A Ct value < 40 cycles denotes a positive result for SARS-CoV-2, whether a lower value indicating a larger amount of viral RNA was a basic policy to adjust someone positive COVID-19.

Limitation of The Study

The sample size in this study was small, and the dose of probiotics did not record. We did not examine the RT-PCR every day, so we can not obtain the infection's actual duration.

Conclusion

The study considered consuming probiotics for the prevention and treatment of COVID-19—further research based on the data we have obtained highly expected to solve the COVID-19 problem worldwide.

Ethical Clearance: Ethical clearance was taken from Health Research Ethics Committee Dr Soetomo General Academic Hospital

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References

1. Baud D, Dimopoulou Agri V, Gibson GR, Reid G, Giannoni E. Using Probiotics to Flatten the Curve of Coronavirus Disease COVID-2019 Pandemic. Front Public Heal. 2020;8:186.
2. Ng SC, Tilg H. COVID-19 and the gastrointestinal tract: more than meets the eye. Gut [Internet]. 2020 Jun 1;69(6):1–2. Available from: http://gut.bmj.com/content/69/6/973.abstract
3. Pan Y, Zhang D, Yang P, Poon LLM, Wang Q. Viral load of SARS-CoV-2 in clinical samples. Lancet Infect Dis [Internet]. 2020;20(4):411–2. Available from: http://dx.doi.org/10.1016/S1473-3099(20)30113-4
4. Jin X, Lian J-S, Hu J-H, Gao J, Zheng L, Zhang Y-M, et al. Epidemiological, clinical and virological characteristics of 74 cases of coronavirus-infected disease 2019 (COVID-19) with gastrointestinal symptoms. Gut [Internet]. 2020 Jun 1;69(6):1–8. Available from: http://gut.bmj.com/content/69/6/1002.abstract
5. Lin L, Jiang X, Zhang Z, Huang S, Zhang Z, Fang Z, et al. Gastrointestinal symptoms of 95 cases with SARS-CoV-2 infection. Gut [Internet]. 2020 Jun 1;69(6):1–5. Available from: http://gut.bmj.com/content/69/6/997.abstract
6. Wu F, Xiao A, Zhang J, Gu X, Lee WL, Kauffman K, et al. SARS-CoV-2 titers in wastewater are higher than expected from clinically confirmed cases. medRxiv [Internet]. 2020 Jan 1;2020.04.05.20051540. Available from: http://medrxiv.org/content/early/2020/04/07/2020.04.05.20051540.abstract
7. Holshue ML, DeBolt C, Lindquist S, Lofy KH, Wiesman J, Bruce H, et al. First case of 2019 novel coronavirus in the United States. N Engl J Med. 2020;382(10):929–36.
8. Infusino F, Marazzato M, Mancone M, Fedele F, Mastroianni CM, Severino P, et al. Diet Supplementation, Probiotics, and Nutraceuticals

in SARS-CoV-2 Infection: A Scoping Review. Nutrients. 2020 Jun;12(6):1718.

9. Kaijin X, Hongliu C, Yihong S, Qin N, Yu C, Shaohua H, et al. Management of corona virus disease-19 (COVID-19): the Zhejiang experience. J Zhejiang Univ. 2020 Feb 21;49(2):147–57.
10. Didari T, Solki S, Mozaffari S, Nikfar S, Abdollahi M. A systematic review of the safety of probiotics. Expert Opin Drug Saf. 2014 Feb;13(2):227–39.