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THE ROLE OF PROBIOTICS WITH COVID-19 PATIENTS IN WESTERN REGION, SAUDI ARABIA. A CROSS-SECTIONAL STUDY

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ABSTRACT

The COVID-19 pandemic, declared in 2020, remains a significant global threat with ongoing fatalities despite vaccination efforts. The current study aims to provide a comprehensive analysis of the demographic characteristics, levels of awareness, and practices related to the use of probiotics in managing COVID-19 patients in the Western region of Saudi Arabia. Method: A cross-sectional study was conducted among the population in the western region of Saudi Arabia. A total of 297 participants were included in the study. The data collected for this study were analyzed using R Studio software. Result: The present study found no significant as-sociations between participants' awareness of probiotics and their age or gender. (67.3%) correctly identified probiotics as beneficial live bacteria or yeasts, among individuals with prior COVID-19 infections. (81.9%) reported that probiotics were not part of their treatment or recovery process. Conclusion: The study reveals substantial awareness of probiotics, though usage rates are moderate.

KEYWORDS: Bacteria, COVID-19, Probiotic, GI Symptoms, Public Health, Saudi Arabia.

1. INTRODUCTION

COVID-19, a pandemic that emerged in 2020, has caused a significant number of global deaths. Disease outbreaks persist despite administering millions of vaccine doses worldwide (1). Coronaviruses primarily affect the respiratory system but they can also impact the gastrointestinal tract (2). COVID-19 exhibits a wide range of clinical presentations, ranging from asymptomatic or mild symptoms to severe illness and potential fatality. The most common symptoms include fever, fatigue, dry cough, runny nose, gastrointestinal symptoms, and difficulty breathing. Some patients may experience severe com-plications such as pneumonia, organ dysfunction, and acute respiratory distress syn-drome (1,2).

A substantial proportion of COVID-19 patients present with gastrointestinal symptoms, and growing evidence suggests that the gastrointestinal tract may play a role in the onset of sepsis in these cases. The severity of these symptoms often correlates with the overall severity of the disease (3,4,5,6). The presence of angiotensin-converting enzyme 2 (ACE2) receptors and viral nucleocapsid proteins in gastrointestinal epithelial cells, along with the detection of viral particles in fecal matter, indicates that COVID-19 patients become highly infectious once the virus invades these epithelial cells and is shed through feces (4).

The World Health Organization (WHO) and many countries have cautioned against the use of steroid therapy in COVID-19 patients with comorbidities such as diabetes and hypertension. While suppressing the exaggerated immune response can protect the lungs, an effective immune system is necessary to contain the infection. Therefore, maintaining a balanced host-microbiota relationship could be beneficial in managing COVID-19, particularly in individuals with comorbidities (7,8,9,10). Considering probiotics' immunomodulatory, anti-inflammatory, antioxidant, and antiviral properties, they could be a potential preventive or curative option for COVID-19 (4,5,6).

Probiotics are live, nonpathogenic microorganisms commonly used to restore microbial balance, primarily in the gastrointestinal tract. However, they offer broader benefits to multiple areas of the body. Probiotics typically include Saccharomyces boulardii yeast and lactic acid bacteria such as Lactobacillus and Bifidobacterium species. While they are regulated as dietary supplements and foods, probiotics are known to compete with harmful pathogens, contributing to overall health and well-being (5). Probiotics have many mechanisms to exert their benefit, including lowering intestinal pH, decreasing colonization and invasion by pathogenic organisms, and modifying the host immune response. Generally, they are safe and well tolerated. Systemic infections may rarely occur with critically ill or severely immunocompromised or those with central venous catheters (6,7,8)

Recently, the utilization of probiotics in managing COVID-19 has been considered to boost the immune host response and improve gut microbiota, thus improving symptoms (9,10). By directly opposing harmful bacteria, probiotics strengthen the immune system, improve the function of the mucosal barrier, and prevent bacterial adhesion and invasion of the intestinal epithelium (5). Since the intestinal microbiota increases alveolar macrophage activity and hence plays a protective role in host defense against pneumonia, the gut-lung axis contributes to the pathogenicity of bacterial and viral illnesses (10). Accordingly, the gut-brain-lung axis (3,4), which is supported by current clinical evidence, links the gut, lung, and brain as a single organism through communication mediated by intricate neuronal, immunologic inflammatory, and neuroendocrine networks.

Given the prevalence of Bacteroides sp. in the lung after sepsis, there are signs in both people and animals that the gut microbiota supplies bacteria to the lungs (3,5,7).

Many authors have suggested modulating the gut microbiota and the gut-lung axis with probiotics to prevent and treat COVID-19 (2, 11,12). Improving the gut microbiota through personalized nutrition and targeted supplementation, known to enhance immune function, has been suggested as a potential prophylactic strategy to mitigate the impact of COVID-19(13,14,15). This approach can be carefully administered to COVID-19 patients to help accelerate recovery and improve clinical outcomes by supporting immune resilience and overall health (1, 16,17,18). However, several concerns of probiotic safety should be considered, such as antibiotic resistance and GIT toxicity. However, only rare cases of bacteremia have been observed in immunocompromised patients (19,20). Probiotics can be used as an adjunctive treatment against COVID-19 in the future as a modulator of immune response to de-crease the pathogenic microbiome in the host (21,22,23). The current study aims to provide a comprehensive analysis of the demographic characteristics, levels of awareness, and practices related to the use of probiotics in managing COVID-

19 patients in the Western region of Saudi Arabia.

2. MATERIALS AND METHODS

2.1. Study Design

A cross-sectional study was conducted among the population of the Western region of Saudi Arabia. Participants were randomly selected and invited to complete an electronic questionnaire over a three-month period, from the 10th of January until the 10th of March 2024. Responses were collected anonymously, with no personal or identifying information gathered. All data were treated with strict confidentiality and used solely for research purposes to ensure the privacy and integrity of the participants. The study included adult populations ranging in age from 20 to 80 years any Covid-19 patients. The study excluded cancer patient and immunocompromised. Convenient sample size was used.

2.2. Ethical Approval

The study was approved by the Institutional Research Board of Umm Al-Qura University in Makkah, Saudi Arabia.

2.2.1. Data Collection

The study was conducted using a Google Form and distributed to the target population through social media platforms, including WhatsApp, Telegram, and Twitter. Participants were informed of the study's objectives, with participation being entirely voluntary and without obligation. The survey included 17 multiple-choice questions covering topics such as the indications for probiotic use, perceived benefits, and potential side effects.

2.2.2. Statistical Analysis

The data collected for this study were analyzed using RStudio software, version 4.3.1. Descriptive statistics were utilized to summarize the demographic characteristics of the participants and their awareness, practice, and outcomes related to probiotic use. Categorical variables were presented as frequencies and percentages. Chi-squared tests were employed to assess associations between categorical variables. Specifically, Pearson's Chi-squared test was used when expected cell frequencies were greater than 5, while Fisher's exact test was used for smaller expected frequencies. Statistical significance was set at a p-value less than 0.05.

3. RESULTS

Table 1 shows the demographic characteristics of participants. The total number of participants were 297. The majority of participants were aged between 18 and 24 years, accounting for 147 individuals (49.5%). Gender-wise, the sample was predominantly female, with 243 participants representing 81.8% of the total population.

Table 2 reported that a significant majority, 189 individuals (63.6%), reported being aware of probiotics. Moreover, 200 participants (67.3%) accurately identified probiotics as live bacteria or yeasts beneficial to human health. Regarding probiotic supplementation, 216 participants (72.7%) stated they had never used probiotics, while 81 participants (27.3%) reported having taken them. Among those who had used probiotics, the most common reason cited was managing irritable bowel syndrome, with 20 individuals (24.7%) mentioning this as their primary indication.

Table 3 revealed no significant associations were found between participants' awareness of probiotics and their age ($p = 0.053$) or gender ($p = 0.172$). Similarly, gender was not significantly associated with probiotic use as a dietary supplement ($p = 0.667$). However, a significant association emerged between probiotic use and age ($p = 0.014$).

Moreover, a significant association was found between the use of probiotics as part of the treatment or recovery process and participants' age ($p < 0.001$). In contrast, no significant association was observed between gender and receiving probiotics for treatment or recovery ($p = 0.824$).

Table 4 revealed that 203 participants (81.9%) stated that probiotics were not part of their treatment or recovery, while 45 participants (18.1%) reported using probiotics during this period. For participants who had not been diagnosed with COVID-19, 26 individuals (53.1%) indicated they would not consider taking probiotics as a preventive measure, while 23 participants (46.9%) expressed a willingness to do so.

Table 5 shows the Characteristics and outcomes of probiotic use among the 45 participants who reported using probiotics during their COVID-19 infection, the majority of 33 individuals (73.3%) used probiotics under medical supervision. The most commonly used probiotic was Enterogermina, reported by 28 participants (63.6%), followed by Dicoflor, used by 13 participants (29.5%). A significant portion of probiotic users experienced improvements in fatigue (80.0%) and respiratory symptoms such as coughing and sneezing (84.4%). Notably, 31.1% of participants continued using

probiotics after recovering from COVID-19. Most reported improvements in allergic rhinitis (84.4%), digestive issues like diarrhea and constipation (80.0%), and sleep quality (73.3%) due to continued probiotic use.

4. DISCUSSION

The findings of the present study provide insights into the demographic characteristics, awareness, and practices related to probiotic use with COVID-19 patients among participants. The majority of the participants (49.5%) were aged between 18 to 24 years. Regarding awareness of probiotics, the majority of participants (63.6%) reported being aware of probiotics, and a similar proportion (67.3%) correctly identified probiotics as beneficial live bacteria or yeasts. These findings suggest a relatively high level of awareness and knowledge about probiotics found among the participants. However, despite the high awareness, only 27.3% of participants reported having taken probiotics as a dietary supplement. Among those who used probiotics, the primary reasons included managing constipation (25.9%), irritable bowel syndrome (24.7%), and intestinal gases and bloating (19.8%). These findings align with an existing study that highlights gastrointestinal health as a common motivation for probiotic use (7). The study also examined associations between demographic characteristics and utilization of probiotics and found no significant association between their age ($P = 0.053$) or gender ($P = 0.172$). This indicates that awareness is relatively uniform across different age groups and between genders. However, a significant association was identified between age and the receipt of probiotics as a dietary supplement ($P = 0.014$). Interestingly, the result of the study revealed that the likelihood of probiotic use increased with age, with the highest usage reported among individuals aged between 31 to 40 (58.8%) and over 40 (38.1%). This trend could be attributed to heightened health concerns or a higher incidence of gastrointestinal issues among older adults, prompting their interest in probiotic supplements. Moreover, increasing evidence supports the potential of probiotic supplementation to alleviate age-related shifts in gut microbiota diversity and composition, potentially improving health outcomes for elder individuals (8,9).

There is no specific antiviral recommended for the treatment of COVID-19, and the currently available vaccine is a few numbers. Only supportive care and personal protection are available [24,25]. With the increased number of users of herbal products and dietary supplements, many studies have documented that they are safer than prescription medications and are of good quality to prevent most chronic diseases or increase health [26,27,28].

A notable aspect of the study was the exploration of probiotic use in relation to COVID-19. The current study found that the majority of participants, 248 individuals (83.5%), reported that either they or someone they knew had been diagnosed with COVID-19. The intake of probiotics during the COVID-19 outbreak was low, as 81.9% of participants did not receive probiotics as part of their treatment and recovery process, and only 18.1% of participants used probiotics as part of their treatment process. This result is consistent with another study conducted in Saudi Arabia, which indicated a low prevalence of probiotic use during the COVID-19 outbreak, and the prevalence of probiotic use did not significantly change before and after the outbreak (10). However, 46.9% of participants stated that they would consider taking probiotics as a preventive measure for COVID-19. The study explored the characteristics and outcomes associated with probiotic use among individuals who reported using probiotics during their COVID-19 infection. Among these participants, a significant majority (73.3%) reported using probiotics under medical supervision, primarily choosing Enterogemina (63.6%) and Dicoflor (29.5%). This may indicate that healthcare providers have prior knowledge of probiotics' potential anti-viral effects. Previous research suggested that probiotics exert these effects through direct virus interaction or immune system stimulation. Despite supporting evidence for probiotics in respiratory illnesses, their specific effects on different viruses remained insufficiently studied (11). However, recent research has demonstrated that probiotic use in COVID-19 patients significantly reduces mortality risk by 60% and shortens hospital stays and recovery times (12).

The majority of probiotic users reported improvements in fatigue resulting from COVID-19 infection (80.0%) and respiratory symptoms such as coughing and sneezing (84.4%). Most participants reported they responded favorably to probiotics with a rating of 7 or 8 out of 10 (22.2%), suggesting that the use of probiotics may have had a beneficial impact on the management of both systemic and respiratory manifestations of COVID-19. These outcomes are particularly relevant in the context of a recent study that has indicated that probiotics can modulate the gut-lung axis, potentially enhancing immune responses and reducing the Incidence, prevalence, and duration of respiratory infection symptoms were

significantly lower in the probiotic user's patients (12). Interestingly, 31.1% of participants continued using probiotics even after recovering from COVID-19. This sustained usage suggests ongoing perceived benefits, which may extend beyond acute illness recovery. For instance, 84.4% of participants reported improvements in allergic rhinitis, these consistent findings across multiple studies support the hypothesis that probiotics may modulate the immune response in a way that alleviates the symptoms of allergic rhinitis. The mechanism is thought to involve the modulation of gut microbiota, which in turn in-fluences systemic immune responses, potentially reducing the hypersensitivity reactions associated with allergic rhinitis (13, 29). While 80.0% experienced relief from diarrhea and constipation, respectively, probiotics are known to enhance gut health by balancing the gut microbiota, increasing short-chain fatty acid production, and enhancing gut barrier function (14). The improvement in sleep quality observed in 73.3% of participants is consistent with findings from other research, these consistent results across multiple studies reinforce the high percentage of participants reporting improved sleep quality highlights the potential of probiotics as a non-pharmacological intervention for sleep disorders. Given the prevalence of sleep disturbances and their impact on overall health, probiotics could offer a safe and accessible option for individuals seeking to improve their sleep (15, 30).

The analysis showed significant associations between probiotic use during COVID-19 treatment or recovery and participants' ages ($P < 0.001$). Specifically, the data demonstrated a marked trend where younger age groups had a higher proportion of pro-biotic use: 36.5% in participants under 18 years old, compared to only 10.9% and 4.5% in the 18 to 24 and 25 to 30 age groups. This trend is supported by findings from Başar Gunes et al., which highlighted that a significant proportion of healthcare providers -59.6% of physicians and 54.6% of pharmacists- are more likely to recommend probiotics for individuals aged 0-18 years compared to other age groups (16, 31). Conversely, gender did not show a significant association with probiotic receipt ($p = 0.824$), indicating that the administration of probiotics is not influenced by this demographic factor. This neutrality in gender association suggests that probiotic treatment decisions are uniformly applied across male and female patients.

Hundreds of clinical studies have demonstrated associations between the human microbiome and disease, yet fundamental questions remain on how we can generalize this knowledge. Results from individual studies can be inconsistent, and comparing published data is further complicated by a lack of standard processing and analysis methods (28,29,30).

This study has a number of shortcomings, including the cross-sectional survey design and small sample size preclude the inference of causal relationships between the research variables. We were unable to accurately compare our findings to those from other nations, including Saudi Arabia, due to the paucity of population-based studies on the effectiveness of dietary supplements and herbal products in the prevention and treatment of COVID-19 infection. Additionally, using an online survey to collect data increases the danger of data fraud and the exclusion of some vulnerable populations. Because all of the participants were from Western Saud Arabia, the study's regional dispersion was constrained. It is necessary to carry out extensive prospective studies in order to ascertain the prognostic significance of these findings.

5. CONCLUSIONS

The study concluded that probiotics are still not widely used as dietary supplements, despite the participants' high level of awareness about them, according to the data. Interestingly, there was a substantial age difference in the use of probiotics: elderly individuals were more likely to take them routinely, while younger people tended to take them more often during a COVID-19 infection. The necessity for focused initiatives to promote the advantages of probiotics for people of all ages is highlighted by these findings. Given their potential health advantages, future research should concentrate on identifying constraints to probiotic uptake and devising tactics to enhance their use.

Institutional Review Board Statement: The study was approved by the Institutional Research Board of Umm Al-Qura University in Makkah, Saudi Arabia. Approval Number is: HAPO-02-K-012-2024-10-988.
Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.
Conflicts of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.
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