

Probiotics, A Source of Modifying Gut Microbiota to Reduce the Negative Effects of COVID-19; The Study about the Management of Allergic Rhinitis

Kiran Rafiq^{1*}, Shagufta Nesar², Shafaque Mehboob¹, Moona Mehboob³, Muhammad Azhar Mughal⁴, Afshan Khalid⁵, Javeria Iftikhar¹, Sameer Ali¹, Muhammad Usman¹, Muhammad Uzair Noor¹, Sheikh Sami¹

¹Department of Pharmaceutical Chemistry, Institute of Pharmaceutical Sciences, Jinnah Sindh Medical University, Karachi, Pakistan.

²Jinnah College of Pharmacy, Sohail University, Karachi, Pakistan.

³Dow College of Pharmacy, Dow University of Health Sciences, Karachi, Pakistan.

⁴Department of Pharmacology, Jinnah Sindh Medical University, Karachi, Pakistan.

⁵Department of Physiotherapy, Dow University of Health Sciences, Karachi, Pakistan.

ABSTRACT

Background: The current study was designed to investigate the prescribing practice of probiotics to enhance the immunity of patients during COVID-19. Interestingly other than anosmia, nasal obstruction and rhinorrhea are the reported symptoms similar to that of seasonal allergic rhinitis (AR) that led to misdiagnosis and unnecessary anxiety related to invasive diagnostic tests of corona virus.

Objective: The consequent panic can be reduced by strengthening the immunity and addressing the disease having similar signs and symptoms as rhinitis by incorporating the "Probiotics". Nutritional adequacy improves general health and immunity to prevent and assuage infections. Moreover, the adoption will work to improve the fear.

Methodology: The study was conducted through the questionnaire based on International Survey on the Management of Allergic Rhinitis and the targeted population doctors, physicians, nurses and pharmacists were asked about their knowledge of rhinitis and its management via probiotics. In study the patients were also included to respond regarding the management strategies of allergic rhinitis.

Results: The analysis revealed a significant correlation between the experience of healthcare providers and the number of rhinitis patients with moderate to severe symptoms seen per week. However low adoptability was observed among patients for probiotics.

Conclusion: Probiotics, if accepted by the community, can significantly reduce the frequency of allergic rhinitis by strengthening the immune system. There is a strong imperative to raise awareness among the population about the benefits of adopting this remedy for rhinitis.

Keywords

COVID-19, Corona Virus, Probiotics, Rhinitis, ISMAR.

*Address of Correspondence

kiranrafiq@hotmail.com

Article info.

Received: October 10, 2022
Accepted: May 12, 2023

Cite this article: Rafiq K, Nesar S, Mehboob S, Mehboob M, Mughal MA, Khalid A, Iftikhar J, Ali S, Usman M, Noor MU, Sami S. Probiotics, A Source of Modifying Gut Microbiota to Reduce the Negative Effects of COVID-19; The Study about the Management of Allergic Rhinitis. RADS J Biol Res Appl Sci. 2023; 14(1):56-66.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium provided the original work is properly cited.

INTRODUCTION

The hypoalbuminemia is one of the most observed negative outcomes of COVID-19 in elderly. However, the decrease in concentration of albumin in blood is highly

associated with respiratory distress^{1,2} and among these, Allergic rhinitis, a decisive public health issue and has spread beyond the regions, is accountable for indirect

social and economic burden. The data of recent years reveals the high alarming rise of rhinitis cases annually specially when there is a climate change or rough weather³. The disease cause a brutal effect on the health among general population of all ages and gender as prominently declines the immune system and patient may get serious illness that likely to become more worst if there is co-morbidity with other disorders like asthma and sinusitis⁴.

Rhinitis (AR) is an allergic reaction develops due to inhaled moiety as like pollens, cat hairs, common dust or any other factor and that can cause allergic rhinitis (Hay Fever) in health individuals and to specifically those people having unbalanced immune system or having any other health issue like sinusitis and asthma⁵.

The fast economic global change in last decade has highly affected the lifestyles of community and that has directly or indirectly altered the dietary intake of population hence leading the body immunity towards high risk and susceptible for pathogens and allergens. The disease itself causes decline in immunity and weakness, exhaustion in body that in turn contribute for non-social behavior, less participation in smart activities, uncreative intensions with sleep and dietetic intake disturbances^{6, 7}.

In COVID-19 pandemic, due to low immunity level, the rhinitis is observed associated with asthma and accordingly the majority people having asthma are more susceptible to rhinitis and the rhinitis either seasonal or persistence drastically increases the likelihood of asthma as that approximately 40% rhinitis patients are sufferer of asthma presently or will be victim in future⁸.

The high sensitivity of mucosal mast cells present in nasal accountable to respond after the exposure to allergens in couple of minutes and due to cross linking of allergin with immunoglobulin enhance the release of vasoactive hormones like specifically histamine prostaglandin D₂, and cysteinyl, leukotrienes as well in turn develop a multifaceted interface of eosinophils, basophils, mast cells, epithelial cells, T cells, lymphoid cells, along with intense inflammation that persists from hours to days and weeks depending upon the therapy and strength of natural defense system of body. Conclusively allergic rhinitis is not only an uncomplicated acute reaction to allergen exposure,

however, but it is also the outlook as an assemblage of different involved mechanisms^{9, 10}.

Due to the high figure of rhinitis cases, there is an urgent need of extensive research primarily for the control of rhinitis globally including urbanized and underdeveloped countries equally and specifically in today era of COVID-19 pandemic, when immunity is an essential weapon to fight all around attacking moieties. As after prominent research advancement, probiotics of *Bifidobacterium* and *Lactobacillus* emerged to prevent allergies, their timely reappearance and assuages the intense signs consequently were shoot out for improving the painful conditions of allergic rhinitis. However, the adaptation in medical care practices has not yet been generally accepted widely. Nevertheless, according to the physician response, it is a safer tool of treatment and in USA 93% acceptance by the doctors has been reported for the treatment of gastrointestinal illnesses^{11, 12}.

Probiotics are responsible for altering the gutmicrobiota and modulate the immune system that help to keep body healthy and develop strong immunity against pathogens specifically in the period of COVID, where everyone is at risk of immunity and highly susceptible. The moieties are special microorganisms and gram-positive bacteria that are naturally present in human intestines and protect the body from many diseases, including gastrointestinal infections specifically and hypertension, hypercholesterolemia, tumors and currently has emerged an important shield against antigens causing allergic rhinitis. Furthermore, it also causes the stimulation of short chain fatty acids, that are essential for monitoring haemostatic function and transforming the response stronger enough via decreasing cytokine production, responsible for intestinal inflammation in case of colitis, diarrhea and in allergies. The concept is getting perceptible that the potential diet supplements and probiotics significantly strengthen and regulate the signaling corridor between gut microbes and hypothalamic-pituitary-adrenal (HPA) axis that has insight contribution in modulating the immune system, mood, sexuality, and energy usage additionally other than its fight-or-flight response and cortisol release¹³.

Asthma and all typical allied discriminating immune responses to common allergens are characteristically associated with adaptive immunity. Emerging facts and

data narrates almost for all allergic disorders, the improvement and strengthening of gut microbiome, hence role of oral probiotics may correspond to fruitful targets in gut for cure and management of allergic diseases in which adaptive immune disturbance is a high up feature¹⁴.

For the management of rhinitis ARIA and EAACI guidelines are followed in western countries that recommends a stepwise treatment approach^{15, 16}. Antihistamines are recommended and widely prescribed for the management of mild to moderate disease intranasal steroid, decongestant leukotriene receptor antagonist, non-pharmacological therapy (nasal irrigation). Beside all the conventional and widely practicing therapies, Probiotics are new entity that has entered as strong therapeutic and preventive tool as well for rhinitis. Majority research work on this fact has been done and is going on to prove such hidden ability of probiotics from the beginning of this decade¹⁷. Similar effect of Probiotics were studied through a controlled trial and that assured the reduction in rhinitis nasal and eye symptoms by probiotic therapy for three months because the using up of *Lactobacillus salivarius* probiotic, causes a prominent increase in Interleukin 10 (IL-10), that in turn human cytokine synthesis inhibitory factor (CSIF), that in turn control the Th1 cytokines to enhance the regulatory T cells, hence probiotics work as immuno-regulator along anti-inflammatory response as well to fight antigen challenge in rhinitis¹⁸. Consequently, the innovations and investigations are accompanied with incorporation of probiotics as health care tool as the immune system originates on gut microbiota from birth^{19, 20}.

Among the treatments of anti-histamines, corticosteroids, decongestants, leukotriene inhibitors, probiotic strain called *Lactobacillus paracaesi* LP-33® can be a best choice for the management of Hay Fever or Allergic Rhinitis. *Lactobacillus acidophilus* also reside in intestinal flora with strong *probiotic* distinctiveness and along with Bifidobacterium support metabolic mechanism having high level of phylogenetic property and has been proved as a good remedy for treating gut disorders and as well are found to improve the severity via suppressing the inflammatory cytokines and decreasing the activation of immune cells, myofibroblasts, responsible for producing inflammatory cytokines at the site of wound^{21, 22}.

Current clinical trials support the idea that gut microbiota plays a substantial role in regulating the immune system's

response to allergens. Studies even support the potential future use of live microbes for illness prevention or the treatment of allergies. Variations in patterns of microbial colonization of the gastrointestinal tract, linked with lifestyle or even geographic factors, may be important determinants of the heterogeneity in allergy prevalence throughout the world, according to some theories. These theories are supported by the wide variations in allergy prevalence between different countries, the fact that the prevalence has increased significantly over the last 40 to 50 years, and the role of the microflora in the development of immunity in infants²³. Intestinal microbiota disparities between healthy children in nations with low and high allergy frequency, as well as between allergic and non-allergic infants in both environments, have been identified during the past several years. These studies suggest that changes in the native intestinal flora and gut flora imbalances may have an impact on the immune system's early development and priming^{24, 25}. This might therefore have an impact on the allergy risk. The presence of differences between allergic and non-allergic children would suggest that these differences are not secondary phenomena because they exist before any clinically evident condition²⁶. Probiotics were discovered to be trusted as a safe therapy for the majority of patients, and even 98% of health care professionals advised them for their exceptional role in treating gastrointestinal disorders or symptoms, according to the doctor's comments. Probiotics are currently prescribed by 93% of doctors to treat irritable bowel syndrome in their patients. However, data shows that in some areas, the practice of doctors prescribing probiotics for rhinitis coincides with the usage of evidence-based probiotics²⁷. Antihistamines, corticosteroids, decongestants, and leukotriene inhibitors are frequently used to treat rhinitis. It has been proven in recent years that the probiotic strain *Lactobacillus paracaesi* LP-33 is the best option for treating allergic rhinitis^{28, 29}. Despite recent improvements in medical treatment, childhood atopic illnesses such dermatitis, allergic rhinitis, asthma, and food allergies still necessitate the use of immune modulators called "probiotics" for both prevention and treatment in order to enhance gut flora³⁰.

Probiotics, live microorganisms, interestingly accountable for the healthy response when administered to the recipient. Data facts reveals the growing substantiation

regarding healthy outcomes of probiotic strains and accordingly frequent clinical trials of concerned strains, have been proved positive for improving intestinal infections and diarrheal onsets were found to be reduced. Some other specific strains of probiotics were found optimistic in controlling the urinogenital infections. These all investigations may provide an approach to work further on probiotics for the beneficial use against more diseases specifically rhinitis³¹. The evidence based studies are a source of future advances with strain therapies either single or multiple are on the horizon for the management of a number of debilitating and even fatal conditions and this phenomenon supported the current research to analyze the level regarding implementation and satisfaction for taking probiotics as a preferred line of therapy for rhinitis³².

MATERIALS AND METHODS

Study Design and Duration

The present research was designed to scrutinize the level of concept and adaptation of probiotics for rhinitis in current COVID-19 pandemic among Health Care professionals (HCPs) and a total of 1040 patients and the study duration was of 6 months, i.e., March 2020 to August 2020.

Eligibility Criteria

The present study was designed to focus on health care professionals and their patients during ISMAR study. It included all health care professionals from both public sector and private hospital settings in Karachi, Pakistan.

Research Instrument Development

Through an international transversal investigation, a questionnaire was created in the wake of the ISMAR (International Survey on the Management of Allergic Rhinitis³³). There were three sections to the survey. Information about the demographics of patients and HCPs was included in the first part. The HCPs were initially asked to rate their understanding of probiotics using a Likert scale in section 2. The HCPs were questioned in Section 3 regarding the treatment of rhinitis, and patient responses correlated with their medical histories.

Data Collection and Analysis

The data was collected from both private and public sectors of rural and urban areas. IBM SPSS version 24 was used

to analyze the survey items. The demographic data and replies of the respondents were displayed using descriptive statistics and frequency. The association between the respondents' dependent factors and the independent variables (demographic) was assessed using Pearson's chi-square (X^2) test. $p < 0.05$ was regarded as a significant value.

Statement of Consent and Ethical Consideration

Before data collection, the respondent's verbal consent was obtained. The involvement in the research was voluntary with secrecy without any psychological influence. The ethical approval was taken from Ethical Review committee of Jinnah Sindh Medical University, Karachi.

RESULTS

430 questionnaires were returned out of 500 total. Twenty questionnaires were discovered to be incomplete and were excluded. The present study included 410 questionnaires in total, with an 86% response rate. 41.46% of the 410 HCPs that responded were men and 58.54% were women. 48.78% of the respondents (or just under half) were between the ages of 25 and 30. The majority of them (58.29%) worked in government-run medical facilities. 46.30% of the practitioners were employed by medical college faculties. Nearly twenty percent (21.90%) of them were general practitioners. All came from public and private settings, and the majority are from cities. Tables 1 and 2 respectively contain information about the practice and detailed demographics.

Among the population of patients, most (73.85%) were female. The patients covered from all level of community by profession, however preponderance was of Professional (58.07%) and rest were general labor, self-employed and skilled labor. Patients' characteristics are shown in Table 3.

Patients with allergic rhinitis were found slightly affected whereas majority patients of rhinitis were found to have history of other diseases and that enough to establish the idea of any kind of relation of occurring rhinitis with any specific disease. Similarly, the rhinitis frequency was found devoid of smoking status as 95% rhinitis patients were not smokers. 81% of actual population came across with mild level of rhinitis whereas 43.8% has been victimized of rhinitis for two to four years and 35.05% patients were

fighting with disease for more than five years. Interestingly majority was surveyed to recover within 4 to 6 days from the symptoms of rhinitis (Table 4).

In another part of study, the ISMAR questionnaire analysis was conducted from health care professionals to analyze the understanding about the role and prescribing patterns of probiotics to cure rhinitis. Four hundred and ten HCPs replied and responded (Figure 1) about knowledge regarding management of rhinitis through prescribing Probiotics. Only a small fragment (10.3%) of respondents considered themselves to be very knowledgeable. The

majority (40.0%) considered themselves to have medium knowledge. Most of the practicing doctors who treated the rhinitis patients were above age of 25 years and were working more than a year, interestingly among respondents 58.54% were female healthcare professionals and during their practice most of the rhinitis patients were children and hence a significant level was observed between the health care providers experience and rhinitis patients as according to analysis a prominent figure was observed regarding number of patients per week with moderate to severe symptoms of rhinitis.

Table 1. Demographic information of health care practitioners.

Demographic Information		Frequency
Gender	Male	170
	Female	240
Age	25–30 years	200
	31–35 years	50
	36–40 years	41
	41–50 years	39
	51 and above	80
Organization	Government	239
	Private	171
Designation	General practitioner	90
	Chief medical officer	56
	Head of department	12
	Resident medical officer	55
	Faculty	190
Experience	Less than 5 years	187
	5–10 years	73
	10–15 years	40
	15–20 years	63
	20 and above	47
Number of Rhinitis Patients Per Day		
	1-30	60
	31-60	120
	61-90	80
Locality of Practice		
	Urban	214
	Rural	196

Table 2. Health professional's response regarding management of rhinitis during COVID-19.

Prescribing Approach of Probiotics	Pearson Chi Square Value	Asymptotic Significance
Number of rhinitis patients per week	366.600	0.000
Children come across with rhinitis more frequently	4.786	0.029
Probiotics are mostly prescribed for the management of rhinitis	47.19	0.000
Probiotics work to reduce symptoms of rhinitis	366.600	0.000
Probiotics can be prescribed for children	4.786	0.029
<i>Lactobacillus paracasei</i> LP-33 can replace the other treatments of rhinitis	353.925	0.000
<i>Lactobacillus paracasei</i> LP-33® has side effects	346.32	0.000

Table 3. Demographics of patients.

Demographic Information		Frequency
Gender	Male	272
	Female	768
Occupation	General Labor	188
	Professional	620
	Self employed	176
	Skilled labor	72
Medical history	Allergy	220
	Asthma	52
	ENT disease	80
	Respiratory disease	300
Smoking status	No	988
	Yes	52
Intensity of rhinitis	Mild	844
	Severe	196
Patient of rhinitis	One year	220
	Two to four years	456
	More than five years	364
Duration for symptoms to subside	2-4 weeks	324
	4-6 days	716

Table 4. Patient response summary regarding medical history.

Patient’s Perception about Rhinitis	Pearson Chi Square Value	Asymptotic Significance
Symptoms of rhinitis	33.354	0.000
Intensity of rhinitis	25.461	0.000
Duration required for symptoms to subside	132.25	0.000
The chances of rhinitis to recurrent	67.665	0.000
Anti-allergy or cough syrup is the best therapy for rhinitis	53.487	0.000

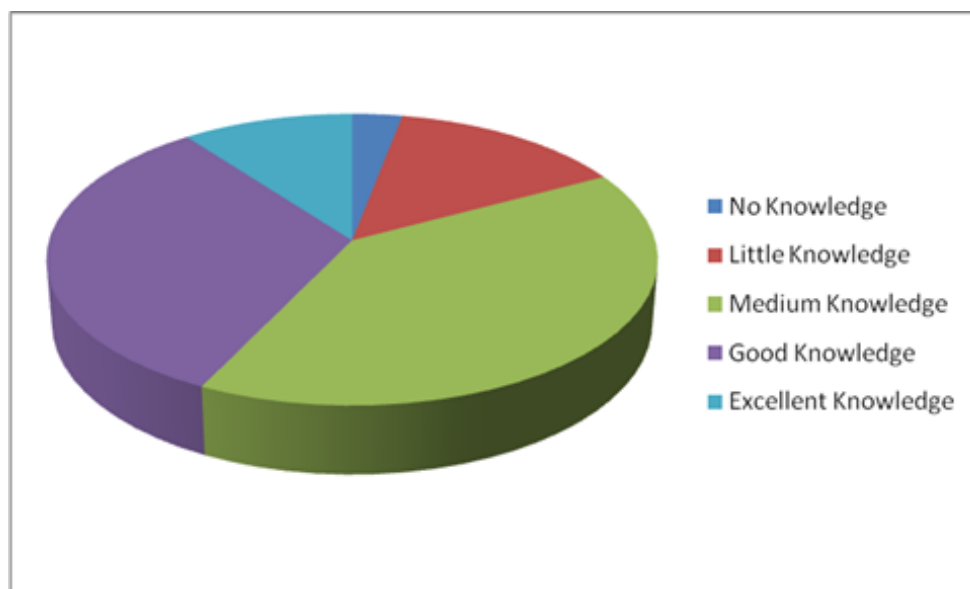


Figure 1. Health care practitioners knowledge about the use of probiotics for the management of rhinitis.

DISCUSSION

A few particles of pollen, cat hairs, common dust or any other factor can cause allergic rhinitis (Hay Fever) to those people having unbalanced immune system. As soon as these particles enter our nose and come in contact to respiratory tract, a series of defensive events start in body. Histamine is released from mast cells. It is autacoid means action is similar to local hormone. It is produced as part of local immune response to foreign particles. Its release is immunologic i.e., IgE antibodies triggers release of Histamine^{34, 35}.

The intestine performs the critical roles of nutrient acquisition, tolerance of innocuous and beneficial microorganisms, while retaining the ability to respond appropriately to undesirable microbes or microbial products and preventing their translocation to more sterile body compartments. Various components contribute to antimicrobial defenses in the intestine. The mucus layers, antimicrobial peptides and IgA provide the first line of defense, and seek to trap and facilitate the removal of invading microbes. If breached, invading microbes next encounter a single layer of epithelial cells and, below this, the lamina propria with its associated immune cells. The gut immune system has developmental stages, and studies from different species demonstrate that innate capability develops earlier than acquired. In addition, various factors may influence the developmental process; for example, the composition and activity of the gut microbiota, antimicrobials, maternally derived antibodies, host genetics, and various stressors (e.g., feed deprivation)³⁶. Therefore, it is clear that particularly younger (meat-producing) animals are reliant on innate immune responses (as well as passive immunity) for a considerable period of their productive life, and thus focusing on modulating appropriate innate responses should be an intervention^{37, 38}. The gut microbiota is probably the most influential factor for immune development and capability. Interventions (e.g., probiotics, prebiotics, antibodies, etc.) that appropriately modulate the composition or activity of the intestinal microbiota can play an important role in shaping the desired functionality of the innate (and acquired) response. In addition, innate immune mediators, such as toll-like receptor agonists, cytokines, etc., may provide more specific ways to suitably modulate

the response. A better understanding of mucosal immunology, signaling pathways, and processes will provide even more precise methods in the future to boost innate immune capability and minimize any associated costs and barriers³⁹⁻⁴¹.

The present data was obtained from front line health care workers in COVID-19 and patients of rhinitis. According data, the female gender is more prone to disorders as, female mast cells release more inflammatory substances due to activation by allergens leading to a more aggressive immune response such as anaphylaxis and sometimes life-threatening allergic reactions^{42, 43}.

Another interesting thing was observed during the study that the respondent belongs to more urban areas and very little response of doctors and pharmacists from rural areas, although the major population of Pakistan reside in rural areas and accordingly more pharmacists and doctors should be practicing in those areas, that is another aspect and shows the misbalancing of health care system and demands strong attention (Table 1). Among all the cases reported to doctors and pharmacists, children were found more prone to rhinitis, however patients of all ages were preferably treated with antihistamine and according the current data, doctors and pharmacists found it the best therapy for rhinitis. In current study, the probiotics for curing rhinitis, was found at intensity among the majority of doctors and pharmacists as a healthcare professional that belong to specialties like general practitioner, allergist, ENT, pediatrician, hospital and clinical pharmacist choose preferably antihistamine. Furthermore, the phenomenon was appreciably supported by the week response of doctors and pharmacists about the role of probiotics in minimizing the chances of occurring rhinitis in patients of all ages (Table 2).

Lactobacillus paracasei is widely used probiotic and has been approved ranging from a digestive disorders, chronic infectious diseases, obesity, and still under research for other pathological conditions including rhinitis and is also available by brands under the flag of many pharmaceuticals in Pakistan and is prescribed by physicians and doctors in digestive disorders globally but have not been prescribed for the management of rhinitis, however a significant level was observed between the ignorance of this probiotic for rhinitis therapy, although in present study the health professionals were found to have

little knowledge and acceptance for probiotics in the management of rhinitis and consequently the significance of *Lactobacillus paracasei* for replacing the other treatments of rhinitis with no side effects, was observed at low frequency and it was concluded that in Pakistan the doctors and pharmacists are following mostly antihistamine treatment for allergic rhinitis and not have move forward towards the probiotics as taking it not only a therapy rather a preventive tool for seasonal and frequent attacks of disease.

Among targeted population of present study, health care providers were found to have different years of practicing experiences as from one to ten years. Nevertheless, the use of probiotics was observed uncommon for rhinitis in regular practice however according to the analyzed data based on designed queries met the level of uncertainty for taking probiotics as promising remedy in rhinitis with all facets as like minimizing symptoms, preferred prescribing patterns for all aged patients and considering *Lactobacillus paracasei* as choice of treatment.

As mentioned, that the present study covered health professional from both rural and urban areas, however the response rate was very low from rural area, in spite of the fact that in Pakistan major part of population in villages and under privileged area and that indicates the very little provision of health care facilities.

Interestingly the queries asked regarding probiotics were established with the fact of non-significant responses from the doctors and pharmacists and were found to have low confidence. As a future remedy however they found the therapy good and with no after effects for all ages. Similarly, the use of *Lactobacillus paracasei* probiotics could replace the other treatments and method of managements with all its efficacy and no side effects, however the study proved the hypothesis not applicable in Pakistan.

The jeopardy was observed among patients who were professionals as compared to self-employed and housewives (Table 3). This high susceptibility was due to more interaction with outside environment having pollens and allergens and with other individuals may be carrier of the disease^{44,45}. Moreover the data obtained from patients of rhinitis, majority was observed having rhinitis with no medical history as like asthma, respiratory, ENT disease,

allergy and interestingly among the observed symptom like nasal discharge, congestion, runny nose, sneezing and coughing, a significant relationship was analyzed with sneezing as patients having no medical history come across with the symptom mostly (Table 4) as during the mechanism of rhinitis activation of inflammatory cells with vascular dilatation that ultimately accounts for change of glandular activity leading to sneezing and nasal discharge⁴⁶. The study found a strong, statistically significant relationship between patients' rhinitis symptoms, their approach to treatment, and it's usefulness. The likelihood of rhinitis recurring after treatment or remission was also highly significant, with a strong relationship between patients' belief in the effectiveness of anti-allergy or cough syrup and their overall treatment approach (Table 4).

Interestingly patients having no medical history were observed to face mild type of rhinitis and according to Pearson chi square calculations a strong and significant correlation was found with the low intensity of disease.

According the data a smart relation with significant p value was observed between the duration of rhinitis condition as patients with no medical history comes to normal within 4 to 6 days and the chances of recurrence of disease was estimated twice a year and regarding treatment anti-allergy was observed to adopted among 51% of population and estimated for having significant relation for treatment among the patients of rhinitis and with no related medical history.

In present study, the targeted population who suffers from rhinitis, was found devoid of smoking as 95% were nonsmoker and statistical analysis reveals a positive significance between these two frequencies and strongly established the fact that allergic rhinitis occurring frequency has no interlink with smoking or in other words smoking practice cannot be responsible for the aggravation of severe rhinitis symptoms, however smoking could be allied with high risk of developing airway modifying and declining lung function in rhinitis patients⁴⁷ and similarly the symptoms and intensity of rhinitis were statistically found significant among the smokers as like nonsmokers and similar chances of recurrence was observed. Furthermore, the use of anti- allergy to treat rhinitis among smokers was significant as like nonsmokers⁴⁸. However, among 450 patients, it was scrutinized that in all cases the probiotics

use was negligible and patients were found to have very little knowledge as approximately only 4% of total population rely on the use of probiotics for rhinitis, whereas 30% recovered themselves through home and herbal remedies and 30% patients take antihistamine and cough syrups. Interestingly 20% patients wait for the symptoms to be subside via self-immune response^{49, 50}.

As most of the population either health professional or patients have no idea about the probiotics and further, they all were found unwilling for the adaptation of mentioned therapy as accordingly were not found to support the beneficial role of probiotics for the symptomatic relief of rhinitis. However interestingly among children, a slight positive response from doctors and pharmacists was recorded regarding the probiotics therapy that showed the phenomenon of misconception regarding the efficacy and therapy with probiotics among adults that need to be addressed.

CONCLUSION

It is figure out that allergic rhinitis has been recognized as a devastating illness globally that prominently affects the normal life and results in below the standard output. It is essential to combat the disease specifically in the period of COVID-19, because the deadly virus already has altered the immunity as it induced stress, anxiety and unhealthy lifestyle. According the epidemiological facts obtained in present study showed high prevalence of the disease in Pakistan especially in rural areas, however the adaptation of Probiotics for both therapeutic and management purpose was obtained negligible. At the stage, when the new insight for improvement and implementation of current research on the management of individual diseases are following globally, the ignorance of novel strategies can lead to more verse scenario regarding allergic rhinitis although the Probiotics, provided that if accepted in community, can work significantly to minimize the frequency of allergic rhinitis in pandemic either as a first line of therapy or as a blanket by strengthening the immune system.

CONTRIBUTOR STATEMENT

All authors contributed equally in preparation and evaluation of the manuscript.

CONFLICT OF INTEREST

No conflict of interest.

FUNDING SOURCE

No funding sources.

ACKNOWLEDGEMENT

KR is grateful to the students of who collected data for the present study.

LIST OF ABBREVIATION

ISMAR	International Survey on the Management of Allergic Rhinitis
HPA	Hypothalamic-Pituitary-Adrenal
EAACI	European Academy of Allergy and Immunology
ARIA	Allergic Rhinitis and it's Impact on Asthma
HCPs	Health Care Professionals

REFERENCES

1. Mehta S. Nutritional Status and COVID-19: An Opportunity for Lasting Change? *Clin Med.* 2020; 20:270-273.
2. Laviano A, Koverech A, Zanetti M. Nutrition Support in the Time of SARS-CoV-2 (COVID-19). *Nutrition* 2020; 74:110834.
3. Mims JW. Epidemiology of allergic rhinitis. *Int Forum Allergy Rhinol* 2014; 4(Suppl 2): S18-20. doi: 10.1002/alr.21385.
4. Brown T. Diagnosis and Management of Allergic Rhinitis in Children. *Pediatr Ann* 2019; 48(12): e485-e488. doi: 10.3928/19382359-20191111-01.
5. Wallace DV, Dykewicz MS. Seasonal Allergic Rhinitis: A focused systematic review and practice parameter update. *Curr Opin Allergy Clin Immunol.* 2017; 17(4):286-294. doi: 10.1097/aci.0000000000000375.
6. Cox L. Approach to Patients with Allergic Rhinitis: Testing and Treatment. *Med Clin North Am* 2020; 104(1):77-94. doi: 10.1016/j.mcna.2019.09.001.
7. Eifan AO, Durham SR. Pathogenesis of rhinitis. *Clin Exp Allergy* 2016; 46(9):1139-1151. doi: 10.1111/cea.12780.
8. Agnihotri NT, McGrath KG. Allergic and nonallergic rhinitis. *Allergy Proceeding*, 2019; 40(6):376-379. doi: 10.2500/aap.2019.40.4251.

9. Hoyte FCL, Nelson HS. Recent advances in allergic rhinitis. *F1000Res* 2018; 7. doi: 10.12688/f1000research.15367.1.
10. Bousquet J, Vignola A, Demoly P. Links between rhinitis and asthma. *Allergy* 2003; 58(8):691-706.
11. Okubo K, Kurono Y, Ichimura K, Enomoto T, Okamoto Y, Kawauchi H, *et al.* Japanese guidelines for allergic rhinitis 2017. *Allergol Int* 2017; 66(2):205-219. doi: 10.1016/j.alit.2016.11.001.
12. Seidman MD, Gurgel RK, Lin SY, Schwartz SR, Baroody FM, Bonner JR, *et al.* Clinical practice guideline: Allergic rhinitis. *Otolaryngol Head Neck Surg* 2015; 152(1 Suppl):S1-43. doi: 10.1177/0194599814561600.
13. Humbert M, Bousquet J, Bachert C, Palomares O, Pfister P, Kottakis I, *et al.* IgE-Mediated Multimorbidities in Allergic Asthma and the Potential for Omalizumab Therapy. *J Allergy Clin Immunol Pract*. 2019;7(5):1418-1429. doi: 10.1016/j.jaip.2019.02.030.
14. Islam SU. Clinical Uses of Probiotics. *Medicine (Baltimore)*. 2016;95(5):e2658. doi: 10.1097/md.0000000000002658.
15. La Fata G, Weber P, Mohajeri MH. Probiotics and the Gut Immune System: Indirect Regulation. *Probiotics Antimicrob Proteins*. 2018;10(1):11-21. doi: 10.1007/s12602-017-9322-6.
16. Anjum N, Maqsood S, Masud T, Ahmad A, Sohail A, Momin A. *Lactobacillus acidophilus*: characterization of the species and application in food production. *Crit Rev Food Sci Nutr*. 2014;54(9):1241-1251. doi: 10.1080/10408398.2011.621169.
17. Bull M, Plummer S, Marchesi J, Mahenthalingam E. The life history of *Lactobacillus acidophilus* as a probiotic: a tale of revisionary taxonomy, misidentification and commercial success. *FEMS Microbiol Lett*. 2013;349(2):77-87. doi: 10.1111/1574-6968.12293.
18. Adak A, Khan MR. An insight into gut microbiota and its functionalities. *Cell Mol Life Sci*. 2019;76(3):473-493. doi: 10.1007/s00018-018-2943-4.
19. Jin Y, Wu S, Zeng Z, Fu Z. Effects of environmental pollutants on gut microbiota. *Environ Pollut*. 2017;222:1-9. doi: 10.1016/j.envpol.2016.11.045.
20. Milani C, Duranti S, Bottacini F, Casey E, Turrone F, Mahony J, *et al.* The First Microbial Colonizers of the Human Gut: Composition, Activities, and Health Implications of the Infant Gut Microbiota. *Microbiol Mol Biol Rev*. 2017;81(4). doi: 10.1128/membr.00036-17.
21. Ianiro G, Tilg H, Gasbarrini A. Antibiotics as deep modulators of gut microbiota: between good and evil. *Gut*. 2016;65(11):1906-1915. doi: 10.1136/gutjnl-2016-312297.
22. Vemuri R, Shinde T, Gundamaraju R, Gondalia SV, Karpe AV, Beale DJ, *et al.* *Lactobacillus acidophilus* DDS-1 Modulates the Gut Microbiota and Improves Metabolic Profiles in Aging Mice. *Nutrients*. 2018;10(9). doi: 10.3390/nu10091255.
23. Goldstein EJ, Tyrrell KL, Citron DM. *Lactobacillus* species: taxonomic complexity and controversial susceptibilities. *Clin Infect Dis*. 2015;60(Suppl 2):S98-107. doi: 10.1093/cid/civ072.
24. Homayouni A, Bastani P, Ziyadi S, Mohammad-Alizadeh-Charandabi S, Ghalibaf M, Mortazavian AM, *et al.* Effects of probiotics on the recurrence of bacterial vaginosis: a review. *J Low Genit Tract Dis*. 2014;18(1):79-86. doi: 10.1097/LGT.0b013e31829156ec.
25. Salim A, Nadri S, Hosseini MJ, Rokni-Zadeh H, Mohseni M. Protective effect of probiotic *Lactobacillus acidophilus* against the toxicity of beauvericin mycotoxin on the Caco-2 cell line. *Nutrients*. 2018;10(9). doi: 10.3390/nu10091255.
26. Nishida A, Inoue R, Inatomi O, Bamba S, Naito Y, Andoh A. Gut microbiota in the pathogenesis of inflammatory bowel disease. *Clin J Gastroenterol*. 2018;11(1):1-10. doi: 10.1007/s12328-017-0813-5.
27. Alavi Foumani A, Ganjeh Khosravi H, Melli LC, do Carmo-Rodrigues MS, Araújo-Filho HB, Solé D, *et al.* Intestinal microbiota and allergic diseases: A systematic review. *Laryngoscope*. 2016;126(2):177-188. doi: 10.1002/lary.27858.
28. Güvenç IA, Muluk NB, Mutlu F, Eşki E, Altıntoprak N, Oktemer T, *et al.* Do probiotics have a role in the treatment of allergic rhinitis? A comprehensive systematic review and meta-analysis. *Am J Rhinol Allergy*. 2016;30(5):157-175. doi: 10.2500/ajra.2016.30.4354.
29. Du X, Wang L, Wu S, Yuan L, Tang S, Xiang Y, *et al.* Efficacy of probiotic supplementary therapy for asthma, allergic rhinitis, and wheeze: a meta-analysis of randomized controlled trials. *Allergy Asthma Proc*. 2019; 40(4):250-260. doi: 10.2500/aap.2019.40.4227.
30. Hernandez L, Papalia S, Pujalte GG. Anaphylaxis. *Prim Care*. 2016; 43(3):477-485. doi: 10.1016/j.pop.2016.04.002.
31. Hostoffer RW, Joseph N. Immunoglobulin E. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing Copyright © 2021, StatPearls Publishing LLC; 2021.
32. Shi N, Li N, Duan X, Niu H. Interaction between the gut microbiome and mucosal immune system. *Mil Med Res*. 2017;4:14. doi: 10.1186/s40779-017-0122-9.
33. Baena-Cagnani CE, Canonica GW, Zaky Helal M, Gómez RM, Compalati E, Zernotti ME, *et al.* The international survey on the management of allergic rhinitis by physicians and patients (ISMAR). *World Allergy Organ J*. 2015;8(1):10. doi: 10.1186/s40413-015-0057-0.

34. Thaïss CA, Zmora N, Levy M, Elinav E. The microbiome and innate immunity. *Nature*. 2016;535(7610):65-74. doi: 10.1038/nature18847.
35. West AP, Shadel GS. Mitochondrial DNA in innate immune responses and inflammatory pathology. *Nat Rev Immunol*. 2017;17(6):363-375. doi: 10.1038/nri.2017.21.
36. Butel MJ. Probiotics, gut microbiota and health. *Med Mal Infect*. 2014;44(1):1-8. doi: 10.1016/j.medmal.2013.10.002.
37. Plaza-Diaz J, Ruiz-Ojeda FJ, Gil-Campos M, Gil A. Mechanisms of Action of Probiotics. *Adv Nutr*. 2019;10(suppl_1):S49-S66. doi: 10.1136/bmjopen-2019-031339 10.1093/advances/nmy063.
38. Peng Y, Li A, Yu L, Qin G. The role of probiotics in prevention and treatment for patients with allergic rhinitis: A systematic review. *Am J Rhinol Allergy*. 2015;29(4):292-298. doi: 10.2500/ajra.2015.29.4192.
39. Nagaraju K. Probiotics and allergic rhinitis. *Indian Pediatr*. 2013;50(2):195-196. doi: 10.1007/s13312-013-0051-y.
40. Jalali MM, Soleimani R. Add-on probiotics in patients with persistent allergic rhinitis: A randomized crossover clinical trial. *Laryngoscope*. 2019;129(8):1744-1750. doi: 10.1002/lary.27858.
41. Paturi G, Phillips M, Jones M, Kailasapathy K. Immune enhancing effects of *Lactobacillus acidophilus* LAFTI L10 and *Lactobacillus paracasei* LAFTI L26 in mice. *Int J Food Microbiol*. 2007;115(1):115-118.
42. D'amato G, Cecchi L, Bonini S, Nunes C, Annesi-Maesano I, Behrendt H, *et al*. Allergenic pollen and pollen allergy in Europe. *Allergy*. 2007;62(9):976-990.
43. Asam C, Hofer H, Wolf M, Aglas L, Wallner M. Tree pollen allergens—an update from a molecular perspective. *Allergy*. 2015;70(10):1201-1211.
44. Leynaert B, Neukirch C, Kony S, Guénégou A, Bousquet J, Aubier M, *et al*. Association between asthma and rhinitis according to atopic sensitization in a population-based study. *J Allergy Clin Immunol*. 2004;113(1):86-93.
45. Sur DK, Plesa ML. Treatment of Allergic Rhinitis. *Am Fam Physician*. 2015;92(11):985-992.
46. Incorporaia C, Cavaliere C, Frati F, Masieri S. Allergic rhinitis. *J Biol Regul Homeost Agent*. 2018;32(1):61-66.
47. Kim SK, Guevarra RB, Kim YT, Kwon J, Kim H, Cho JH, *et al*. Role of Probiotics in Human Gut Microbiome-Associated Diseases. *J Microbiol Biotechnol*. 2019;29(9):1335-1340. doi: 10.4014/jmb.1906.06064.
48. Tabatabaian F, Casale TB. Allergic rhinitis management: what's next? *Expert Rev Clin Immunol*. 2018;14(3):191-196. doi: 10.1080/1744666x.2018.1438270.
49. Butel MJ. Probiotics, gut microbiota and health. *Med Mal Infect*. 2014;44(1):1-8. doi: 10.1016/j.medmal.2013.10.002.
50. Bousquet PJ, Cropet C, Klossek JM, Allaf B, Neukirch F, Bousquet J. Effect of smoking on symptoms of allergic rhinitis. *Ann Allergy Asthma Immunol*. 2009;103(3):195-200.