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Role of Probiotics in prevention and cure of diseases in human health

Tabeen Irfan, Aiman Ijaz, Kinza Seher, Sammar Fatima, Mishal liaqat, Maham saeed and Maham riaz

University Institute of diet and nutritional sciences, The University of Lahore, Lahore, **Pakistan**

***Correspondence:** tabeenmalik@hotmail.com **Received 22-04-2021, Revised: 14-08-2021, Accepted: 18-08-2021 e-Published: 25-08-2021**

Probiotics have grown into talk in the advanced period of life which has gathered consideration from wellbeing experts in last several years, due to its importance on the health of animals and humans. Probiotic strains show amazing action in human wellbeing improvement. The fundamental probiotics are Lactobacillus, Bifidobacterium, Pediococcus, Lactococcus, Bacillus furthermore, yeasts strains which are utilized as often as possible.Normally, the food items like kefir, fermented sausages, yogurt, kambucha, sauerkraut, miso, lassi, tempeh, and buttermilk have been playing a significant role in normal diets between various civilizations and nationalities on the globe The usage of probiotics has incited promising results in incalculable very much planned clinical investigations. For instance, as a remedial choice for the treatment, prevention and control of different problems and sicknesses like, gastrointestinal infections, sensitivity, urogenital contaminations, Helicobacter pylori disease, gut disorders also, colon malignant growth. As of now, it has gotten one of the organic product full and alluring examination region as it can forestall and treat transmittable and non-transferable human illnesses. Distinctive clinical study result upholds this thought. The consequences of such widely considered and investigated could exhibit the improvement of wellbeing and personal satisfaction. Their imminent likely application is in useful food varieties for better wellbeing and sustenance of the general public. This review presents all the data on probiotics use in human clinical attributes and their utilitarian application in wellbeing regions all data are introduced. This article traces the at present accessible information on the possible benefits of probiotics for wellbeing

.**Keywords: gut, hypertension, inflammatory diseases, irritable bowl syndrome, ,probiotics ,urogenital diseases**

INTRODUCTION

Globally, probiotics speak to the popular aspect in human dietary choices and are at present the principle center in view of their tremendous human health benefits. Probiotics can be traditionally characterized as a suitable dietary microbial enhancement that influences the host through its impacts on the intestinal tract and an expression of the advanced period, meaning "forever" and is being used as a functional food (Bagchi,2014).Functional foods are substances that are consumed to get a particular outcome and are additionally called as bio-therapeutics and nutraceutical (Begum et al.2017).The historical utilization of live microorganisms in food, specifically the microscopic organisms producing lactic acid, is long to keep up and improve human well-being. A Roman student of history in 76 BC suggested the utilization of milk aging items to treat gastroenteritis. The speculation of Probiotics was framed in the mid-1900s, when Elie Metchnikoff won the Nobel Prize, contending that the utilization of yogurt containing lactobacillus prompted a decrease in the quantity of poison delivering microscopic organisms in the digestive system and, subsequently, builds the host's life

expectancy (Ghasemian et al.2018).Following beginning hiccups, interests in probiotics have increased from last two decades and different experimental studies have done to portrait the benefits of probiotics on heath to cure or prevent chronic diseases. Intestinal gut micro-flora plays a major role in human health. Every individual has more than 100–1000 microbial species in gastrointestinal tract (GIT) (Aziz et al.2013). Human body consist of half of the wet load of colonic material and their numbers surpass by 10-crease. Regularly our body consists of one hundred and three various bacterial species and the absolute microbial population of the colon includes around 1011–1012 cfu/g (Slavin, 2013).

Bacterial organization of the intestinal gut starts during childbirth when infants are first exposed to an aseptic condition. Consequently it changes in a lifetime and continuous transaction between the eating regimens, order of gene and life of a person like anti-infection. Remarkable age-specific compositional movements revealed that gut microbiota composition starts to decrease in individuals more than 60 years. Generally intestinal microflora is stable all through adulthood (Lloyd-Price et al.2016).

Various microorganism species that are often utilized as probiotics are Lactobacillus, Propionibacterium, Peptostreptococcus, Bacillus, Lactococcus, Enterococcus, Pediococcus, Streptococcus, Bifidobacterium, Bacteroides, Akkermansia, and Saccharomyces (Kerry et al.2018).

Probiotic microbes, which dis-engaged from human gastrointestinal microflora, use is very normal in numerous items, for example, matured dairy items (ayran, sharp cream, yogurt and so forth)in child nourishment due to their different wholesome and restorative properties (Kalkan, 2016).

Probiotics is meant to give a medical advantage on the organism, after regulated in satisfactory quantity and it likewise have healthful favorable circumstances. Use of food incorporating probiotics is prescribed to have a positive effect on the number of microflora's present in the intestinal flora. Bifidobacterium and Lactobacillus strains are probiotics found in GIT and supplements, it is exceptionally impressive and different, its creation and number varies. The gut microbiota plays a functional role in human health (Dallal et al.2015).

Probiotics are associated with hindering pathogen development by integrating antimicrobial mixes, delivering lactase, altering gut pH, testing the authoritative of pathogens and receptor destinations just as existing supplements and development factors, and invigorating immunomodulatory cells (Amara & Shibl, 2015).

In spite of the fact that utilizing probiotics for human wellbeing has been considered for very nearly 100 years, intrigue has moved to the counteraction and treatment of various sicknesses, for example, bowel syndrome, hypersensitivities, Helicobacter pylori disease, just as helpful impact of stomach related and invulnerable framework with probiotics. Studies show that standard utilization of items containing probiotic microbes fortifies the human immune system, diminishes malignancy, brings down cholesterol, dispenses with stomach related troubles and prevents gastrointestinal infections (Konuray & Erginkay, 2018;Kobyliak et al.2016).

Furthermore, are additionally useful in battling obesity. Despite of the fact that probiotics have extensive many benefits in nutrition and diseases, significant investigations are needed for the execution of probiotics into wellbeing, so that we can have elaborated guidelines. The purpose of this study is to underline the benefits of consuming probiotics for improvement of human health

Probiotics food products and nutrients profile:

In the worldwide market, above five hundred probiotic food items were introduced in last several years, and amount of probiotic food items is frequently growing (Begum et al.2017).

Probiotic foods

Fruits based probiotics	Vegetables based probiotics	Lactic acid microorganisms	Antioxidants	Grains and lentils based probiotics
Pineapple	Cabbage	L. acidophilus	Kombucha	Sorghum
Cranberry	Carrot root	L. plantarium	Vitamin C	Millet flour
Strawberry	Tomato	L. casei	Vitamin B2	Maize
Sweet lime	Beet root	B. longum	polyphenol	Millet malt
Mango	Onion			Wheat flour
Grapes	Ginger			Finger millet
Cashew apple	Peanuts, etc.			Soya beans
Olives				Rice
Oranges, etc.				Oats

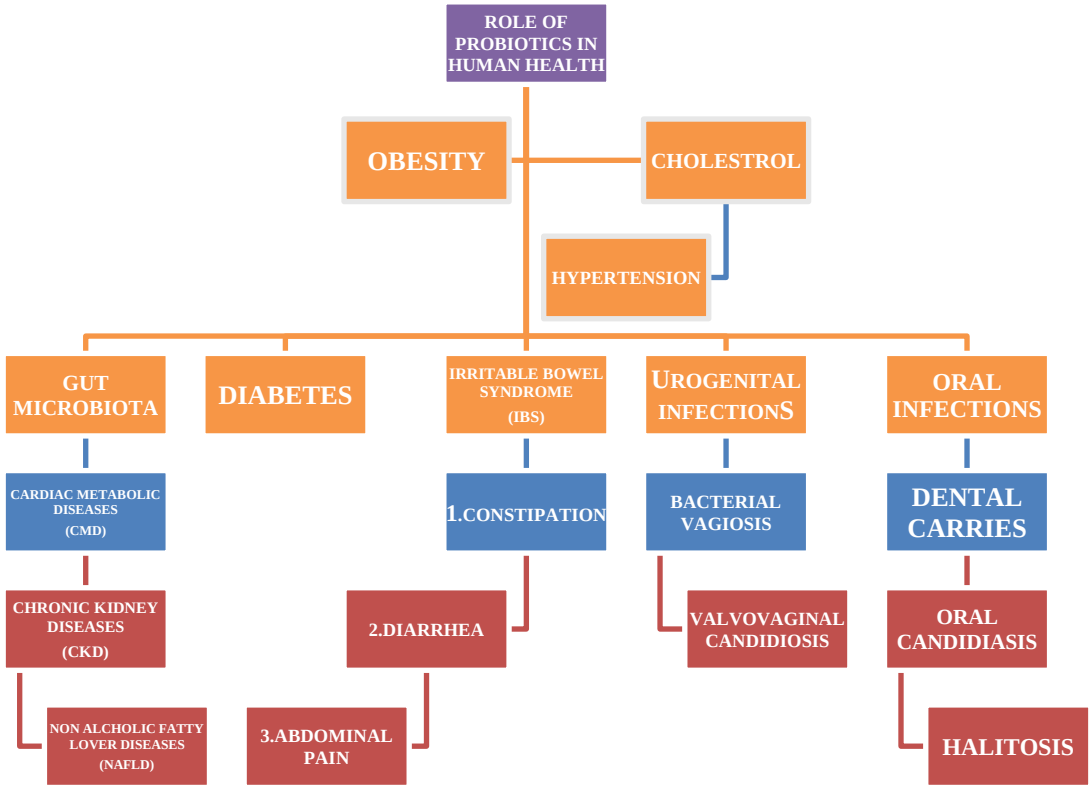

Figure 1: Probiotics in preventing and curing diseases

The lactic acid agitation boosts nutritional amount of items. Kombucha is probiotic liquid that is made by using tea leaves and is high in antioxidants like vitamin C and B2, polyphenols like catechins. Grains and lentils based probiotic food items can be made by utilizing sorghum, millet flour, maize, millet malt, wheat flour, finger millet, soya beans, rice and oat either separately or among multiple blends (Kechagia et al.2013; Panghal et al.2018 ; Markowiak et al.2017)

Mechanism of probiotics:

The probiotics have three stage activity mechanisms:

1. It triggers and restrains safe reaction
2. It standardizes intestinal microflora by secure conquer protection and manages irritable bowel syndrome and more inflammatory bowel disorders
3. The concluding system also have the metabolic impact such as bile salt deconjugation and emission, lactose hydrolysis, decrease in toxigenic and mutagenic reactions in gut, stocking up of nutrients to colon epithelium (Abatenh et al.2018).

Cholesterol-lowering properties of probiotics

Probiotics strains including lactic acid organisms which plays a significant role in lowering cholesterol level. There are two mechanism of lowering cholesterol level by the use of Probiotics. In direct method the denovo synthesis is inhibited or the absorption of cholesterol is decreased. Three ways to decrease the dietary cholesterol are assimilation, binding or degradation. The strains absorb cholesterol for its digestion. By attachment with the cholesterol particles the probiotics strains have the ability for decreasing cholesterol with its catabolic products. The indirect method to decrease cholesterol level involves deconjugating the cholesterol to bile acids. Hypercholesterolemia can also cause CVD. It can be prevented by balancing the level of cholesterol. Lactobacillus pentosus LP05, L. plantarum, L.brevis LB32 and L.reuteri have powerful effect (Bordoni et al.2013; Tomaro-Duchesneau et al.2014; Mojgani et al.2015;Vaishnavi et al.2016).It has been found that when probiotics are supplemented to chicken it shows cholesterol lowering properties

(Getachew, T., 2016).

The probiotic bacteria inhibit the expression of intestinal cholesterol transporter Niemann–Pick C1 in the enterocytes.The use of yeast and probiotic bacteria manage cardiovascular risk and it has beneficial hypocholesterolemia effects. The hypocholesterolemia effects depends upon the state of the host, strains used and the diet to which the probiotics are added (Miremadi et al.2016).

Different researches were done to evaluate the efficacy of probiotics in humans and animals to screen probiotic lactic acid bacteria and its cholesterol properties. Total 142 LAB were separated. The Lactic acid bacteria isolates were used in antimicrobial activity. Results showed that seven isolates showed twenty percent reduction in cholesterol (Shehata et al.2016).

To see probiotic effects of Bifidobacterium and Lactobacillus strains on cholesterol levels in obese mice. A female BALB/c 6–8 week's old mice was used for this study. There were eight experimental groups containing 12 mice in one group to test strains of probiotic bacteria. They were fed with fat enriched diet. Results showed that probiotic bacteria and compositions of B. animalis VKL/B. animalis VKB/L. casei IMV B-7280 decreased cholesterol levels in serum were reduced. L. casei IMV B-7280 (separately) and a composition of B. animalis VKL/B. animalis VKB/L. casei IMV B-7280 were also effective at decreasing the cholesterol level and weight of obese mice (Bubnov et al.2017).

Furthermore, positive effects of Enterococcus in lowering cholesterol was investigated, strain of Enterococcus strains separated from B. Infants and Enterococcus faecium WEFA23 were used because of having cholesterol removal capability. Decreased total cholesterol serum lipid level, low-density lipoprotein cholesterol and triacylglycerol's were seen (Zhang et al.2017).

Probiotic consortium and Lactobacillus plantarum results also showed reductions in total cholesterol levels after 2-weeks of supplementing C57BL/6J mice with high fat diet (Michael et al.2017).In Feed Research Centre China 115 isolates has been evaluated and tested to see their probiotic effects in rats fed with high cholesterol diet. Results showed the strain of L. plantarum Lp3 have significant cholesterol-lowering rate (Ding et al.2017).

In China to investigate the effects of probiotics on serum TC. 1971 patients were selected to investigate. Probiotics supplements were given to the patients. Results showed that the serum TC has been reduced in probiotics group (Wang et al.2018). Lactobacillus plantarum and Bacillus coagulans were also proven to be lowering cholesterol in rats (Aminlari et al.2019).

Hence it can be concluded that different strains of probiotics have positive effect on lowering the cholesterol in human beings and rats.

Hypertensive properties of probiotics:

Hypertension is a chronic medical condition that affects more than 20% of adult people in worldwide population. HTN is a factor that increases metabolic diseases such as chronic renal failure, stroke, heart disease, myocardial infarction, dementia and blindness. It is also known as Lifestyle disorder. There are two kinds on HTN. One is primary and the other one is secondary. Primary HTN is defined as high blood pressure due to nonspecific lifestyle and genetic factor. It has been found that 90%-95% cases of HTN are in primary HTN. Secondary HTN occurs due to identifiable cause like Obesity, Cushing's syndrome, and glucose intolerance. While the exact cause of HTN is not clear yet (Borse et al.2018).

The supplementation of probiotics helps in lowering blood pressure during hypertensive conditions. There are many common probiotics which are used against hypertension condition. Some of these are Lactobacillus helveticus, Lactobacillus kefiri, Saccharomyces cerevisiae, Lactobacillus delbrueckii, Lactobacillus rhamnosus GG, Streptococcus thermophiles, Lactobacillus casei, Bifidobacterium breve, Lactobacillus bulgaricus and Lactobacillus rhamnosus (Guo et al.2011; Rerksuppaphol & Rerksuppaphol, 2015).The estimated number of adults suffering from hypertension was 1 billion during the year 2000 and it was predicted to rise to 1.58 billion by the year 2025 (Upadrasta & Madempudi, 2016).

Probiotics regulate inflammation, cholesterol, blood glucose levels and the renin angiotensin system by lowering blood pressure and risk of hypertension. It has been found that 14 manipulating gut microbiota use prebiotics that proved a valuable support to antihypertensive. A meta-analysis indicated that probiotics may lower BP when BP level is increased ,many probiotic species can be used, the time duration is ≥8 weeks and its daily consumption is ≥1011 colony-forming units (Qi et al.2017).To investigate the antihypertensive effect of Lactobacillus plantarum as probiotics strains were examined simultaneously on 653 participants. Lactobacillus plantarum supplementation showed significant effect on improvement of Systolic Blood Pressure (

Lewis-Mikhael et al.2020).

To evaluate the gut microbiota role for the treatment of Hypertension (HTN). A comparative study was done in 22 composition of microbiota between hypertensive rats and increased high salt diet. A control group of rats were taken with normal pressure values. Results showed that Firmicutes/Bacteroidetes was effective in reducing blood pressure which concludes probiotics role as a hypertensive (Yang& Zubcevic, 2017).

Probiotics role in Gut Microbiota:

Probiotics, among other functions, play a significant role in gut microbiota as well. Studies showed that mammals possess a vast variety of unique microorganisms in their GIT (gastro-intestinal-tract). These micro substances make up the microbiome of the intestine. Intestinal-microbiota has been considered as a whole other body organ among humans due to the individuality of substances present in them. Comprehensively, there are around fifteen hundred particular types of microorganisms being recognized acting as the part of the human gut-microbiome.

One of the profound probiotics, Galactosidase has been analyzed for its activity in the improvement of tolerance level and capability of digestion of lactose. Symptoms occurring due to lactose intolerance have been reduced by consuming yogurt and fermented-milk items which contain lactic-acid bacteria and probiotic-bacteria as well (Sánchez et al.2017).

Similarly, in order to assess the function of gut-microbiota in weight loss, the subjects were provided high-fat-diet when treated with probiotics, resulted in various alterations of their gut-microbiome composition. This ultimately led to enhanced insulin signaling-process subsequent to decreased rate of Lipopolysaccharides in the body. Thus, improvement in the insulin signaling-process within liver and muscular cells has been observed. Data exhibits that the subjects who have been given HFD (high-fat-diet) and probiotics tend to be more able to reduce their weight (Bagarolli et al.2017).

Probiotics can also significantly reduce changes in the gut-microbiome resulting in the statement of probiotics that can be used as strategic treatment of CKD (chronic kidney diseases) and CMD (cardio metabolic diseases) (Neto et al.2018).By improving the gut-microbiota through administration of probiotics, migraine can be treated as different studies proved that probiotics can exert positive results both on the recurrence and acerbity of migraine-attacks. Among people who suffer from migraine-headache as well as people suffering from depression/anxiety are linked with a porous gut-environment. Thus, probiotics helps in improving gut-microbiome and inflammation status as well (Yu-Jie et al.2017).

Furthermore to analyze association of gut-microbiota with blood-lipid levels among people suffering from JCP (Japanese cedar pollinosis). Changes in the gut environment are also linked with allergic-diseases along with other diseases. The stools of subjects suffering from Japanese cedar pollinosis have been analyzed before and after treating with and without fermented-milk for ten weeks. It has been concluded that fermented-milk notably led to changes in gut ecosystem after ten weeks. By the end of this study, it has been examined that fermented-milk having probiotics exerted positive influence on the blood-lipid-status and helped fighting against Japanese cedar pollinosis (Harata et al.2017). Intake of probiotics had a distinctive impact on behavior, neural state and microbiome status among healthy subjects (Bagga et al.2018).

Similarly, probiotics' interference has the tendency to improve gut-microbiota and liver-pathology as well. Positive impact has been observed in reducing the development of non-alcoholic-fatty-liver-disease (NAFLD). Thus leading towards the fact that they can decline the continuous growth of this disease via lps/tl4s signaling-process (Xue et al.2017).

Intake of probiotics in the form of supplements has been linked with reduction of disturbances in the gut-microbiome. In this study the analysis of the role of antibiotics on gastrointestinal microbiota was observed. Subjects were studied as the antibiotic group and probiotic group. It was also examined when these medicines were used in a combined form with probiotics. It was concluded that more alterations within the gut-microbiome has been analyzed among the antibiotic group as compared to the group provided with probiotic therapy. Additionally, enhanced rate of antibiotic-resistant substances has been analyzed within the antibiotic group as compare to probiotics' group (Oh et al.2016).rhamnosus NCDC-17 which is also known as the particular strain of lactobacillus when used as a supplement in fermented-milk, consequently led to reduction of body weight, fat-mass, FBG (fasting-blood-sugar) levels, and insulin count as well among mice who were given HFD (high-fat-diet). Yeast being used as a probiotic, when consumed on a daily basis,

resulted in alteration of the formation of gut-microbiota. It consequently enhanced the metabolic status of mice suffering from obesity and diabetes (Davis, 2016).Another significant function of probiotics has been studied which shows that probiotics exhibit a direct regulatory mechanism on the microbiota-balance within the intestine. Its intake reduces the count of gastro-intestinal pathogens, improves stool movements and restores homeostatic processes within the microbiota of the intestine.

Role of probiots in gut micobiome

Probiotics	Roles in Gut-microbiota	References
Galactosidase	Improvement of tolerance level and capability of digestion of lactose.(Sánchez B et al., 2017)	Sánchez B et al., 2017
Probiotics	Alterations of their gut-microbiome composition. Led to weight reduction(Bagarolli RA et al., 2017)	Bagarolli RA et al., 2017
Probiotics	Significantly reduce these changes in the gut-microbiome, thus preventing CKD and CMD(Neto MP et al., 2018)	Neto MP et al., 2018
Probiotics	By improving the gut-microbiota, migraine can be improve (Yu-Jie Dai MD et al., 2017)	Yu-Jie Dai MD et al., 2017
Fermented-milk	Notably changes gut-microbiota thus had a positive influence on the blood-lipid-status and helped fighting against Japanese cedar pollinosis.(Harata G et al., 2017)	Harata G et al., 2017
Probiotics	Distinctive impact on behavior, neural state and microbiome status as well among healthy subjects (Bagga D et al., 2018)	Bagga D et al., 2018
Probiotics	Probiotics' interference has the tendency for the improvement of gut-microbiota and liver-pathology as well (Xue L et al., 2017)	Xue L et al., 2017
Probiotics	Reduction of disturbances as a result of antibiotics intake in the gut-microbiome(Oh B et al., 2016)	Oh B et al., 2016
L. rhamnosus	L.rhamnosus NCDC-17 when used as a supplement in fermented-milk, consequently led to reduction of body weight, fat-mass, fasting-blood-sugar levels, and insulin count as well among mice who were given HFD(high-fat-diet) by altering gut-microbiota(Davis CD et al., 2016)	Davis CD et al., 2016
L. acidophilus or saccharomyces boulardii	Exhibits their preventative function for colorectal-tumorigenesis. It eventually suggested probiotics as one of the remedial approaches for the prevention of hepatic-carcinoma. In mice, alteration within the enteric-flora has been examined as a result of intake of lactobacillus probiotic(Yu AQ et al., 2016)	Yu AQ et al., 2016
Probiotics	By modulating the gut-microbiome, improves the role of the intestine as a barrier and modulates the immune system as well the safest, innovative and affordable approach for the prevention or treatment of hepatocellular carcinoma. (Wan ML et al.,2018)	Wan ML et al., 2018
Probiotics	The treatment with probiotics has been associated with reduction of obesity through changing the microbiome ecosystem of the intestine specifically among mice who were fed with a high sucrose diet.(Kong C et al., 2019)	Kong C et al.,2019

Probiotics' benefits are dependent on their strain. Additionally, various studies show that probiotics are involved in the improvement of gut-barrier function. Another study made it clear that L. acidophilus or saccharomyces boulardii exhibits their preventative function for colorectal-tumorigenesis. It eventually suggested probiotics as one of the remedial approaches for the prevention of hepatic-carcinoma. In mice, alteration within the enteric-flora has been examined as a result of intake of lactobacillus probiotic. Colon-cancer tends to be less prevalent due to this modulation in the enteric-flora (Yu & Li, 2016).

Probiotics have been recommended as the safest, innovative and affordable approach for the prevention or treatment of hepatocellular carcinoma. Probiotics do so by modulating the gut-microbiome, improving the role of the intestine as a barrier and modulating the immune system as well.Alterations in gut-microbiome is associated with HCC (hepatocellular carcinoma) and Probiotics have been playing a therapeutic function for HCC (hepatocellular carcinoma) HCC (Wan & El-Nezami, 2018).

Kong C with his colleagues studied in 2019 determined the impact of probiotics among mice who were given a high-fat content diet and high-sucrose content diet for thirteen weeks. Mice were given probiotics by the last four weeks of the diet and it was observed that body-weight was enhanced among those subjects who ate a high fat diet than those subjects who ate a high sucrose diet. Variety of microbiota was compromised in both groups. It was concluded that administration of probiotics has been proved to be helpful in restoring the amount of bacteria which was negatively influenced during high fat diet and high sucrose diet. The treatment with probiotics has been associated with reduction of obesity through changing the microbiome ecosystem of the intestine specifically among mice that were fed with a high sucrose diet (Kong et al.2019).

Role of probiotics in urogenital infections

Vaginal infections have put a large burden on women's health of reproductive age. One of the urogenital infections is vulvovaginal Candidiasis. This is basically caused by Candida. This is one of the most commonly occurring vaginal-infection. It is characterized by valval discomfortness and pain. Probiotics are largely linked with a significant decreased rate in the recurring infection like VVC (Vulvovaginal Candidiasis)

Quantity of lactobacilli has been observed to be compromised during vaginal infection in women.For example in bacterial vaginosis and vulvovaginal candidiasis. Thus, the lactobacillus category of probiotics has been largely used as intravaginal and consequently it led to many benefits (Li et al.2019).

Vaginal-microbiome and role of antibiotics:

Excessive usage of antibiotic medications, sexual-activities, changes in hormones and contraceptives can lead to disturbances in the vaginal environment due to deficiency of good bacteria. For a healthy and normal vaginal condition, the vaginal-microbiome plays a significant role. As a result, it helps to prevent urogenital infection. The vaginal-microbiome consists of a variety of anaerobically originated substances and aerobiotic substances. Among them, lactobacillus species is abundantly prevalent. It is usually dominated in numbers as well (Borges et al.2016).

Using probiotics might help in prevention of bacterial vaginosis and vulvovaginal candidiasis and their recurrent problems as well.With the help of various mechanisms of action for example; through the competition for nutritional components or through producing antimicrobial components for instance; lactic-acid, H2O2, bacteriocins and bio-surfactants. During some urinary tract infections, the persistent infectious state occurs due to colonization within the bladder from vagina. Thus, introduction of probiotics has been involved in removal of pathogenic compounds from vagina thus ultimately leading to elimination of bladder infection.[50] it has been significantly involved in the reduction of recurring yeast as well as bacterial-pathogens in vagina. Probiotics have also been favorable in normalizing vaginal-flora. It has led to long-term therapeutic treatments for both pregnant women and those who are more vulnerable to urinary tract infections (Raghuwanshi et al.2018).

Lactobacillus acting as a probiotic in vaginal microbiota:

Reproductive systems of healthy pre-menopausal women have at least seventy percent of lactobacillus species which occupy their vaginal ecosystem.A component known as bacteriocin which is locally made via lactobacillus acidophilus KS400. It was concluded that the bacteriocin with its antimicrobial properties works against the relevant urogenital pathogens (Gaspar et al.2018).Anti inflammation takes place within the vaginal due to the presence of lactic acid which

acts as the major metabolic component. This component prevents the receptory substances which are involved in inducing the process of inflammation within the vaginal microflora (Pan, 2019).

Prevention of vaginal infections by Lactobacillus has been assessed. Main aim was the evaluation of alterations in Nugent score in women having moderate vaginal microbiota. Subjects were treated with a mixture of L.acidophilus GLA-14 and L.rhamnosus HN001. When this mixture was combined with bovine lactoferrin for fifteen days.After oral administration of this mixture, the health of vaginal microbiome was supported (Russo et al.2018).

Bacterial vaginosis (BV):

Bacterial vaginosis is considered as the most commonly occurring infection that disturbs the vaginal ecosystem among adult women. In bacterial vaginosis enhanced growth of anaerobic bacteria takes place. This triggers the lactobacilli to deplete and it is linked with increased risk for urogenital-infections and abortion rates. Impact of a yoghurt-drink which consists of lactobacillus strains has been studied. Under this study, thirty six women who have been diagnosed with bacterial vaginosis with age less or equal to eighteen. These subjects were given the oral metronidazole for seven days. They consumed verum (125g yoghurt) two times in a day during four weeks. It was concluded that additional use of yoghurt with probiotic strains enhanced the recovery-rate and symptoms as well. Thus, it eventually leads to improvement of the vaginal microbiota (Laue et al.2015).

Lactobacillus fermentum MG901 and Lactobacillus plantarum MG989 have been observed in the prevention of yeast-growth, this might have been involved in playing a significant function in assessing to remove vulvovaginal candidiasis (Kang et al.2018).

Furthermore, the activity and tolerance rate of an oral product which includes a probiotic strain of lactobacilli Known as Lactobacillus plantarum (P17630) was evaluated. Ninety three females were examined. All of them had a history of repeatedly occurring VVC (vulvovaginal candidiasis infection). These subjects were examined on day forty fifth and 90th. Intake of probiotics clearly enhanced the colonization rate of lactobacillus within the epithelial cells vagina. Thus, introduction of oral-probiotics clearly led towards the improvement of lactic acid bacteria's colonization rate in vagina. Usability of this product has resulted in significant favorable and successful consequences (Vladareanu et al.2018).

The efficiency and safety of Bio-Kult Pro-Cyan was assessed. This product consists of 2 stains of lactobacillus and cranberry extract. It has been used for the prevention of repeatedly occurring urinary tract infections among adult women who are in perimenopause phase. One hundred and fifteen subjects were studied, receiving the product two times in a day for twenty six weeks. Bio-Kult Pro-Cyan has been proved a safe product due to its effectiveness in prevention of repeatedly occurring UTIs among selected subjects (Koradia et al.2019).

Role of probiotics in Irritable bowel syndrome:

(IBS) Irritable bowel syndrome is gastrointestinal chronic disorder. IBS is caused by low intake of dietary fiber (El-Salhy et al.2017) that reduces the life quality. Human microbiome indirectly and directly affects its functions (Harper et al.2018). (IBS) Irritable bowel syndrome illness involve nonadoptive change in microbiota gut that affect the immune systems CNS, balance of neurotransmitters , mucosal barrier function and hormonal balance (Singh et al.2018). By Prebiotic and probiotic treatment, this disorder can be controlled. It is essential to characterize which part of IBS is being talked about while thinking about treatments. IBS can be because of constipation, abdominal pain and diarrhea (Ford et al.2014;Patel &DuPont ,2015)

IBS treatment involves four approaches which are psychosocial, medicine, diet, alternative medicine. Antispasmodics and anti-diarrheal are pharmacological therapies. Pharmacological agents are beneficial in symptoms abdominal pain (AP) function in children. To check the efficacy of non-medicinal treatment by using the probiotics meta-analysis was conducted in children suffering from IBS in which Lactobacillus reuteri significantly improved IBS symptoms (Mearin et al.2016). Fifty-three RCTs of combinations of probiotics strains were given to patients, showed beneficial effects in abdominal pain symptom (Giannetti & Staiano, 2016)

The efficacy of Bifidobacterium infantis 35624 in patients of IBS irritable bowel was assessed. B infantis lowered the IBS symptoms including bloating/distention, abdominal pain and improved bowel frequency (Ford et al.2018).

Therapeutic Probiotics, prebiotics, and low FODMAP diet in gut microbiome also proved to be effective for IBS symptoms. FODMAP short-term restriction in diet can improve IBS symptoms, when

combined with the probiotics strains (Yuan et al.2017).

Furthermore, Efficacy of probiotics was seen on the celiac patients which were on the gluten free diet. With 6-week treatment of probiotics, improvement were seen in the patients having probiotics rather than in non-probiotic group (Ooi et al.2019; Francavilla et al.2019).

Diarrhea is also associated with the intake of antibiotics. With the treatment of probiotics in adults and children, the risk of Clostridium and Diarrhea Associated Difficile was reduced by 64% (Corbitt et al.2018; Goldenberg et al.2017; Szajewska et al.2016).

Hospital-acquired diarrhea are very common. There have been some examination to prevent hospital-acquired diarrhea, and the only one reported successful in LGG method. Supplementation of Bifidobacterium to hospitalized infants has prevented the incidence of diarrhea and hospital acquired diseases. The beneficial effect of Bifidobacterium strain 68% cured infections and hence can be used for the use of probiotics in children with infections (Pattani et al.2013;Wittenberg, 2012 ; Chen et al.2014),

Role of probiotics in Constipation:

Constipation is a common gastrointestinal disorder (Szajewska et al. 2020). chronic constipation involves a multistep process in which unintentional weight loss and rectal bleeding that indicate organic diseases (such as polyps or tumors) and a therapeutic trial with treatments such as dietary changes, lifestyle modifications and over-the-counter laxatives (Dimid et al.2017).

Probiotics were seen to increase stool frequency in Asian children. The randomized controlled trials of probiotics interventions was seen to check stool frequency and consistency. Six studies were investigated and confirmed probiotics treatment was efficacious for constipation in children (Camilleri et al.2017).120 patients suffering from constipation and Parkinson disease were supplemented with a fermented milk, containing multiple probiotic strains and prebiotic fiber, or placebo, once daily for 4 weeks. The consumption of a fermented milk containing multiple probiotic, prebiotic fiber improved constipation in patients with Parkinson Disease (Huang & Hu, 2017)

60 constipated pregnant women were given 300 g of yogurt enriched with Bifidobacterium and Lactobacillus and control group received conventional yogurt for 4 weeks. Consumption of 300 g/day probiotic and conventional yogurt improve the symptoms of constipation during pregnancy and consistency of stool and color of stool were improved significantly (Barichella et al.2016).

A probiotic mixture, including Bifidobacterium was seen to be effective in chronic constipation and safe for the treatment in children (Mirghafourvand et al.2016). Supplementation with products containing Lactobacillus or Bifidobacterium species increases stool frequency and reduces ITT in constipated adults, urban women and children (Russo et al.2017; Miller et al. 2017; Abdullah et al.2019).

Finally effects of guar fiber was also seen to clinically normalize the irritable bowel syndrome. Daily intake of 5 to 10 g/d guar fiber is a natural product in protection of digestive health (de Meij et al.2016), we can conclude that probiotics strains are effective in treatment of IBS patients including children and adults.

Role of probiotics in Obesity:

Extreme and unhealthy deposition of lipids/ fats which will effect health directly usually due to increased energy input ,sedentary life style, and a better regulation of atmospheric temperature, causing a disturbance in energy equilibrium of the body (energy intake and energy expanded).It's been proved that if the microflora from the gut of obese mice are relocated to the germ-free mice they could recreate these obese patterns and can make them much efficient in the process of lipogenesis thus causing obesity (Rao & Quartarone, 2019).

Probiotics have unique physiological attributes which enhances microbes function that effect host health. For example, weight loss happens by the lipolysis and thermogenesis in the body occurred through sympathetic nervous system. Probiotics like Lactobacillus gasseri BNR17 depicts preventive response in the elevation of adipocyte cells, the major resources of adiponectin and leptin, thus decreasing secretion of leptin in body. Several probiotics have shown hypocholesterolemia properties i.e. Bifidobacterium longum, L.casei, Lactobacillus acidophilus (Kobyliak et al.2016).

To determine the effect of probiotics in obesity many researches are done. The research involved nine hundred and fifty seven individuals (sixty three percent women), having average BMI being 27.6 $kgm^{-2,}$ with time interval consisting of three to twelve weeks of interventions. Addition of probiotics helped to have more weight reduction. Low Fat percentage ratio and BMI, in comparison

to placebo; although impact ratio was minimal (Karimi et al.2015).

Another research performed to know the positive impacts of consumption of kimchi on 3T3-L1 adipocyte in the reduction of obesity were observe utilizing natural fermented kimchi, a functional kimchi (having green tea), and functional kimchi containing starters (FKS). Functional Kimchi Starters decreased mRNA values of C/EBP-α, PPAR-γ, FAS, which relates in 3T3-L1 cells lipogenesis/adipogenesis.This shows findings that FKS possess anti-fat properties due to elevated lipolysis rate and decreased lipogenesis or adipogenesis of 3T3-L1 adipocytes (Borgeraas et al.2018).

A similar study assessed *Bifidobacterium breve* B-3 in obesity and microbes present in the gut region.80 subjects were randomized to have placebo or *B. breve* B-3 capsules (2×10^{10} CFU/day) regularly up to duration of twelve weeks. Percent body fat and body fat mass was prominently decreased in the B-3 group as in the placebo group on eight and twelve weeks Though there were no prominent changes were seen in blood specification among all groups, but consumption of *B. breve* B-3 lowered TG levels a bit and enhanced HDL above base level (Lee et al.2015).

Another study focuses on assessment of obesity reducing potential of curd containing probiotic having *Lactobacillus casei* NCDC 19 on C57BL/6 mice. Consumption of curd depicts reduction in epididymis fat weight and body weight. In addition to, plasma lipids level, leptin level expression and blood glucose were decreased and caecal *bifidobacteria* levels and expression of adiponectin level was also elevated. So one can say that consumption of curd containing *L. casei* NCDC 19 depicted great obesity reducing properties (Minami et al.2018).

Evaluation of studies showed *Lactobacillus rhamnosus* ATCC 53103 Lactobacillus *gasseri* SBT 2055, and the combination of *L. rhamnosus* ATCC 53102 and *Bifidobacterium lactis* Bb12 might decrease, body weight, adiposity and weight gain. It shows that microbes are useful for obesity management. In addition to this, low level inflammation and short chain fatty acid production was seen as basic mechanism which effects impact weight and metabolism (Rather et al.2014; Mekkes et al.2014).

Furthermore different strains of probiotics 2 bifidobacteria strains, *Bifidobacterium longum* BORI Bifidobacterium *bifidum* BGN4 and, 2 subjects' lactobacillus strains, *Lactobacillus acidophilus*AD031, *Lactobacillus casei* IBS041 was given separately to High Fat Diet-fed mice for eight weeks. *B. longum* BORI prominently reduced weight gain in mouse prior to any change in diet. *B. bifidum* BGN4 and L*. acidophilus* greatly reduced TG levels in liver of mouse whereas B*. longum* BORI prominently decreased overall cholesterol values in liver. *B. bifidum* BGN4 *L. acidophilus* also prohibited serum levels of alanine transaminase and aspartate transaminase. Dietary supplementing by *B. bifidum* BGN4, *L. acidophilus* and *B. longum* BORI effectively enhanced hepatic steatosis and hepatocyte hydropic degeneration. Out of these 4 probiotic subjects, the *B. bifidum* BGN4, bifidobacteria *B. longum* BORI formed in lab, while *L. acidophilus* AD031 depicts extraordinary obesity reducing impacts and reduced lipid accumulation in liver (Sáez-Lara et al.2016).After these studies probiotics have proven to be effective in weight loss.

8. Diabetes:

Diabetes can be defined as chronic multiple disorder, having most symptoms mainly due to glycemic level. As told by the International Diabetes Federation, three hundred and eighty two million have been effected due to diabetes worldwide in year 2013, the count predicted to be increase to five hundred and ninety two million adults by year 2035. Along this, attaining and conserving normal glucose level control in such patients shows a persisting task for them to achieve, which constitutes pharmacologic treatment, dietary modifications and lifestyle changes.

Diabetes and metabolic syndrome are disorders which are needed to be known as of high consideration. Extensive utilization of antibiotics, better sanitation, and adaptation to a more highly processed diet with reduced fiber content and other prebiotics, have changed our natural gut microflora. Also there are many findings which will make think that this changed microflora, or symbiosis, is related to metabolic diseases like diabetes, obesity, hypertension, and dyslipidaemia (Li et al.2016).

A few of researches are given below to understand more about the relation of probiotics and diabetes. These depicts that probiotics could decrease autoimmune reactions and elevate insulin reactivity through regulating gut microbes, thus reducing oxidative stress and inflammatory processes As probiotics effects host through

regulating mucosal immune reaction and intestinal permeability, maintaining consuming practices by appetite-controlling hormones and managing gut endocannabinoid (CBRs) system that is found to be related with inflammation and diabetes. Also, regulating the gut microflora by probiotics manages the individual metabolism through maintaining energy obtaining by food and biochemical production of molecules found in the individual and through microbiota in gut region

(Kobyliak et al.2016).To evaluate the effect of probiotics, *Lactobacillus* strains were utilized. It was seen these microbes shows positive impacts on glucose level management and improved values of, postprandial blood glucose, , insulin resistance, onset of diabetes , fasting plasma glucose level, insulin and glycated haemoglobin (H Rad et al.2017).A similar study, which focuses on evaluating impacts on glucose metabolism in type 2 Diabetes Mellitus in individuals through probiotics depicts the utilization of probiotic greatly altered glycosylated hemoglobin up to -0.54% and fasting plasma glucose up to -15.92 mg/dL in comparison to test group which recommends that consumption of probiotics might be helpful in enhancing glucose metabolism by a slightest rate, with a specifically better results if given for the time period of ≥8 weeks, or more than one strains of probiotics are utilized (Razmpoosh et al.2016).

To consider the impact of dietary supplements having probiotic, in reducing insulin resistance expecting females through diet-assessed GBD (gestational diabetes mellitus) were assessed. Pregnant ladies on the gestation period of twenty fourth to twenty eight weeks, thus randomly assessed to get hold of both probiotic dietary food having a placebo or Lactobacillus and Bifidobacterium each day until 4 continuous weeks.

Intervention element	No of subjects	Duration	Effect of intervention	References
Lactobacillus acidophilus NCFM (T1) or Lactobacillusrhamnosus Lr-32 (T2)supplemented with cheese To reduce oral candida	60 denture rats	8 weeks	Regular intake of supplemented cheese reduced the colonization of oral Candida.	Miyazima et al.,2017)
Bifidobacterium and Lactobacillus in form of supplements For diabetes	57 patients	4 weeks	Glucose levels and increased insulin sensitivity was improved in the females with diet-controlled gestational diabetes in the late second and early third trimester.	Kijmanawat A et al.,2019)
B. breve B-3 capsules (2×10^{10} CFU/day) daily for obesity	80 participants	12 weeks	Body fat percentage and BMI were significantly lower by the supplementation of probiotics hence is beneficial in obesity.	Minami J et al.,2018)
Functional constipation probiotic (Lactobacillus plantarum IS 10506) administration	73 participants	3 weeks	Probiotics consumption improved constipation symptoms in urban women.	Abdullah M et al.,2019).
Celiac Disease patients with IBS-type symptoms treated with probiotic treatment	109 patients probiotics	6 weeks	The severity of IBS-type symptoms, in celiac disease patients on strict gluten free diet improved and altered gut microbiota, by increasing Bifidobacterium.	Francavilla R et al.,2019)
L. plantarum P17630 (5x109 CFU/capsule) administrated orally in vulvovaginal candidiasis infection	93 women	90 days	Administration of probiotics successfully prevented vulvovaginal candidiasis.	Vladareanu R et al.,2018).
Yoghurt-drink which consists of lactobacillus strains 125g yogurt twice a day in Bacterial Vaginosis	36 women	7 days	Hence concluded that use of yoghurt with probiotics increases the recovery-rate. Thus it ultimately helps the vaginal microbiota.	Laue C et al.2018).
Japanese cedar pollinosis treated with LGG–TMC0356-fermented milk	25 fecal samples of patients(n = 14) and without (n = 11)	10 weeks.	The altered gut microbiota through supplementation of fermented milk containing the probiotic improves and protects against JCP disease.	Harata G et al.2017)
Bacillus coagulans, Lactobacillus plantarum supplementation to improve serum lipid profile	28 male Wistar rats	50 days	Supplementation of probiotics improved serum lipid profile.	Aminlari L et al.2019)

After giving supplements containing probiotics for 4 weeks to females having Diet-induced GDB during the end of second and starting of third trimester accelerated insulin sensitivity and reduced fasting glucose. These supplements might also regard as low-level cure in controlling glycemic levels in females (Zhang et al.2019; Kijmanawat et al.2019).

Role of probiotics in oral infections

Probiotics shows promising effects for the containment of bacterial infections of the oral cavity. Probiotics have emerged as each preventive and therapeutic tactics for oral infections related with macrobiotic imbalance, such as dental caries, periodontal diseases, and halitosis. Dental caries, the most important reason of oral ache and enamel loss, is an infectious disorder precipitated by way of cariogenic microorganism (such as S. mutans) that ferment carbohydrates and produce natural acids (Bustamante et al.2020)

Probiotics helps to fight the microbes in the oral cavity preserves healthful gums and teeth. Since probiotics is a natural cure it have no harmful effects. Lactobacillus acidophilus and Bifidobacterium lactis have antifungal property (Chitra,2013; Dhawan& Dhawan, 2013).

Short-term every day consumption of probiotic pill (twice a day, for a 4-week period) with LGG and Bifidobacterium lactis BB-12 decreased drastically the gingival index in probiotic consuming group in contrast to the other group which was not consuming probiotics. In addition, A. actinomycetemcomitans and P. gingivalis in the saliva and biofilm was decreased with probiotics (Lesan et al.2017).

Probiotics and Halitosis:

Halitosis is when the breath has disagreeable odor. It can be because of many reasons, for example, intake of fast foods, metabolic disorders and respiratory tract infections. Streptococcus salivarius act as a commensal probiotic of the oral cavity. The utilization of gum or drugs containing S. salivarius K12 diminished degrees of unstable Sulphur compounds amongst sufferers identified to have halitosis. Take a probiotic complement regularly. There is proof it helps in stopping the growth of hazardous bacteria. S. salivariu, L. salivarius, L. reuteri, L.casei and W. Cibaria was once used for administration option (Alanzi et al.2018; Khodaii et al.2017).

Oral candidiasis:

Oral candidiasis is one of the most frequent infections of the oral cavity, providing one-of-a-kind medical manifestati ons with various diagnostic and therapeutic approaches (Quindós et al.2019).

To evaluate the impact of intake of cheese supplemented with probiotics on the oral colonization of Candida in denture wearers. The study group was supplemented with cheese L. acidophilus or L. rhamnosus day by day for eight weeks and confirmed reduction in the Candida levels in contrast to the group (cheese except probiotics) (Miyazima et al.2017).

CONCLUSION

So the review clearly shows that probiotics plays a significant part in decreasing the prevalence of a lot of disorders in humans. It has been tested as an effective item in reducing the risk of high cholesterol level, hypertension, diabetes and oral infections including halitosis. It strengthens the immune system while treating irritable bowls syndrome and constipation. Mammals carry an extensive range of microorganisms in their gastrointestinal tract which make up the microbiome in the intestine helping in reducing body weight, reducing the occurrence of cardio metabolic disease and chronic kidney disease. It also neutralizes the gut environment which then shows positive effect on people suffering from migraine attacks, depression, anxiety issues and allergies. Probiotics also helps in curing the urogenital infections which includes balancing the pH of vagina.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

AUTHOR CONTRIBUTIONS

All the data was collected by tabeen irfan,kinza seher, sammar Fatima ,mishal liaqat.maham saeed,maham riaz.Supervised by aimen ijaz Compiled and designed by tabeen irfan Proofread by kinza seher

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