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REVIEW ARTICLE OPEN ACCESS

Probiotic Intervention in the Treatment of Diabetes Mellitus: A Review

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Abstract

Diabetes is a noncommunicable lifestyle condition that impacts millions of individuals worldwide. Diabetes is a physiological illness that affects several different organs in the human body. Several studies have found a direct relationship between gut microbiota and diabetes control. Probiotic intervention in the treatment of diabetes mellitus has been the center of focus in the current scenario. Alteration in composition and metabolic activity of gut microbiota significantly contributes to human health. However, the key mechanism of gut microbiota in the inhibition of diabetes is not fully understood. This review discusses the effect of probiotics on diabetes and the role of gut microbiota. It emphasizes on the pharmacological effects of probiotics on diabetic symptoms like glycemic response, hypercholesterolemia, hypertension, as well as gestational diabetes.

Keywords: Diabetes, Probiotics, Effects of Probiotics, Diabetes, Glycemic Response, Hypercholesterolemia, Hypertension, Gestational Diabetes

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INTRODUCTION

Hyperglycemia is known to cause several metabolic disorders. Diabetes is an amalgamation of insufficient insulin secretion and resistance to insulin caused by genetic and environmental factors. Among many non-communicable diseases which includes cardiovascular respiratory diseases, and cancer, diabetes accounts for about three fourth of deaths globally. According to the IDFGD (international diabetes federation global diabetes) 9th edition, 463 million adults of the age group 20-70 years are estimated to suffer from diabetes and are expected to reach 578 crores population by 2030. Diabetes is clinically classified into four categories Type 1 diabetes mellitus (T1D) -characterized by total lack in production of insulin due to destruction of autoimmune β- cells in the pancreas, type 2 diabetes mellitus T2D develops due to increased resistance for insulin and body fails to overcome the consequence by the large production of insulin), gestational diabetes (GD) (during the process of pregnancy some females shows glucose intolerance), Fourth type of diabetes mellitus is caused by the diseased pancreas function, chemicals/drugs, genetic defect in the action of insulin and beta cells function, which is considered a serious menace to human health.[1-3]

Probiotics are living micro-organisms that exert beneficial effects on humans when consumed in adequate quantity. They are advantageous to humans by their safety profile, economical and reliable properties. Consumption of probiotics impact the intestinal tract by colonization and balanced gut microflora. Clinical trials and animal models are demonstrating the advantages of probiotics for alleviation from diabetes by reducing blood glucose levels, improving insulin resistance, management of intestinal microbiota, and decreasing diabetes symptoms. Although the mechanism by which probiotics affect diabetes is complex. For a greater level of understanding effect of probiotic on diabetes and its action mechanism, we have consolidated latest research on probiotics as a beneficiary supplement.

The practice of a negative lifestyle has undeniably demanded the development of food nutrients and probiotics. The effectiveness of probiotics in promoting health status has been observed, where microbiota has various impacts on human health and diseases. Exposure to antibiotic therapy, toxins, unhealthy lifestyle, and diet affects the microbes in the intestine. There is an interlink between the immune system, disease-causing pathogen, alteration in microbiota, and health. It is observed that pathogenic microbes are dominant in various diseases and disorders like infections, obesity, and auto-immune diseases.

Humans carry about 2Kgs of microbes in the intestine and nearly 1000 species, which are involved in various facets of health, disorder, and disease condition. These disorders include obesity, metabolic syndrome, intolerance to glucose, and insulin resistance and these micro-organisms play important role in maintaining the permeability of gastrointestinal mucosa and immune system. Imbalance in intestinal microflora is a beneficial state for the synthesis of fat, development of adipose tissue, a shift in metabolism of energy leading to disorders/ syndromes related to metabolism. Diabetes is one such disorder associated with imbalance/ dysbiosis of intestinal microbes.

Probiotics regulating immune response against pathogens by secretion of IgA immunoglobulin, reducing the risk of allergy development, enhancing intestinal mucosal barrier function, modulating the host gene expression, and releasing the functional protein and enzymes which decreases the risk of pathogen adhesion. Thus, probiotics play a vital role in balancing microbes in the gastrointestinal tract by interaction with immune cells.[5] The beneficiary action mode of probiotics is not known completely, but they are multifactorial and the mechanism differs by species (source dependent). *Lactobacillus, Lactococcus,* and *Bifidobacterium* are the most commonly used probiotics in food industries, which possess medicative properties and offer health benefits. In this review we deliberate on gathering latest information on effect of probiotics on diabetes and their parallel effects.[4]

Literature Management

Survey on probiotics and diabetes was conducted to gather related information by using PubMed, Springer, Google Scholar, Web of Science and Wiley Blackwell. Many studies on effect of probiotics on diabetes have been published in

reputed journals like Fitoterapia, Food Chemistry, Journal of Science in Food and Agriculture. Authors also searched for data on probiotics by using diabetes, probiotics, effects of probiotics, glycemic response, hypercholesterolemia, hypertension, gestational diabetes keywords which resulted in gathering most inclined information (Figure).

Health Benefits of Probiotics

Stimulation of immune response

Beneficial microbiota offers influence by regulating immune response against pathogens by secretion of IgA immunoglobulin, which in turn reduces food mediated allergies by enhancing intestinal mucosal barrier function, modulating the host gene expression, releasing the functional protein and enzymes which decreases the risk of pathogen adhesion. Intestinal microflora function along with enhanced adiposity, inflammation, imbalance in β-cells, oxidative stress. Thus, probiotics play a vital role in balancing microbes in the gastrointestinal tract by interaction with immune cells.[5]

Variation in the microbiota of gut effect the synthesis of beneficial hormone-like GLP-1 (glucagon-peptide-1), GLP-1 is produced in the digestive- tract, where it is important in satiety promotion and reducing glucose levels that results in enhanced production of triglycerides, insulin signal inhibition, inflammation, and alteration in energy inflow by pancreatic insulin stimulation and glucagon suppression. According to an evaluation in 2002 by a national health interview survey, about 22% of diabetes patients use probiotics from herbal sources.[6] This has a beneficiary influence on the microbiota of the gut, metabolic condition, diabetic stats. Thus, it is suggested that probiotics enhance insulin sensitivity, and the consumption of probiotics reduces the risk of gestational diabetes.[6]

Probiotic bacteria and its cell wall exhibit a beneficiary effect on human health by inhibiting the growth/adherence of pathogens as probiotics are GI tolerant, and they also compete for the nutrients with pathogens and proliferates. The potential strains of probiotics also have capacity to strike epithelial cells. Where the probiotics *L. casei* CRL 431 and L. para_casei CNCM I-1518, attaches to epithelial cells and stimulates immune system through TLRs (Toll-like receptor). Followed by increased cytokines (IL-6), protein 1 from IECs, macrophage attrahent is also formed without altering intestinal barrier, and observed slight increased migration of mononuclear cells from

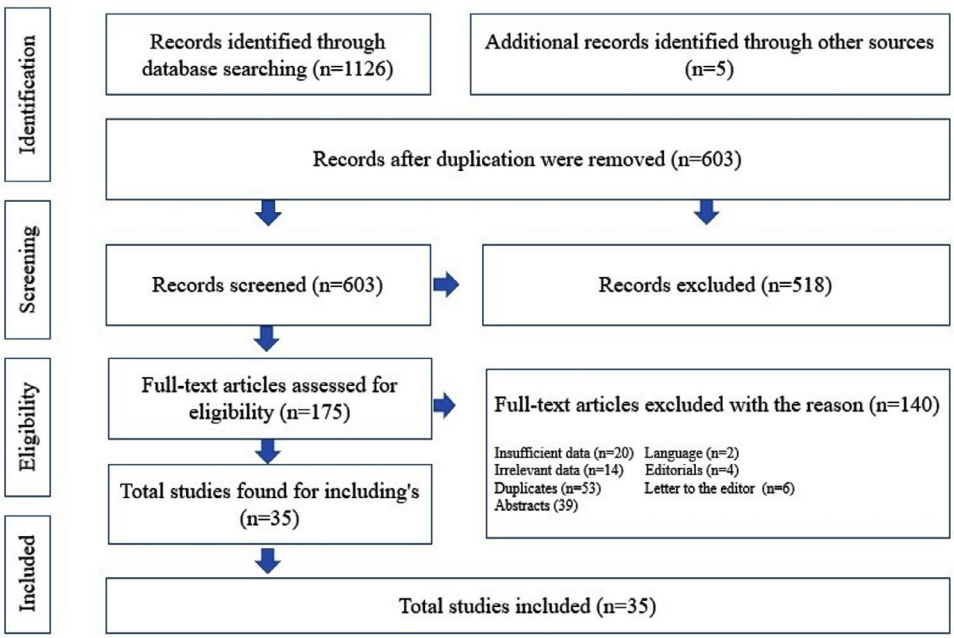

Figure. PRISMA outline followed for literature survey.

small intestine. The study has also observed that the fragments of probiotics also get internalized with IECs, therefore IECs initiates the complex signalling network which is associates with lamina propria to activates immune response, followed by release of cytokines by T cell.

A meta-analysis Tavakoly et al., on consumption of Probiotics and their effect on immune response in athletes. A randamized control trial with 836 participants was reclaimed. Where it is observed that probiotics has reduced lymphocyte t cytotoxicity count evidently (WMD = − 0.08 cells×10^9/L; 95% CI: −0.15 to −0.01; p=0.022), provided with moderate heterogeneity and monocyte count on consumption for span of less than 4 weeks. And significant elevation in leucocyte count was also absorbed on consumption of multi stain probiotics. The study also says that probiotics may also enhance immunological markers, monocytes, cytotoxic t lymphocytes and glucosides in athletes.[7]

Clinical trials on 78 children with celiac autoimmune disease was performed by Hakansson A et al. Where 40 patients were provided with L. plantarum HEAL9 and L. paracasei 8700:2 of 10^{10} CFU/day. And 38 placebo group patients were treated with maltodextrin for a span of 6 months. The blood sample of whole group were drew at 0, 3, 6 months to measure phenotype of peripheral blood lymphocytes, IgA and IgG immunoglobulins against tissue transglutaminase. It is observed that in placebo group naïve CD45RA+ Th cells decreased (p = 0.002), effector and memory CD45RO+ Th cells increased (p = 0.003) and it is also observed that the cells expressing CD4+CD25highCD45RO+CCR4+ increased in placebo group. The changes in the group were absorbed for NK and NKT cells (p = 0.038) and (p = 0.008) respectively. And levels of IgA-tTG was found to be reduced significantly in groups consuming probiotics (p = 0.013) in comparison with placebo group (p = 0.043).[8]

These studies indicates that all different strains of probiotics have a positive effect on stimulating immune responses. But all the studies with the same objective have not ended up with a parallel outcome. However, the probiotics has a positive effect or less effects but no adverse effects are seen in any studies. Further, studies need to be carried out emphasizing auto-immune disease and hypersensitivity, regarding the probiotic's supplementation. A proper amount of immune response generated upon the consumption of probiotics would lead to the validation of the experiments performed.

Lowering the blood pressure

Hypertension is one of the major factors for cardiac arrest and related problems.[8] The effect of probiotics on systolic and diastolic blood pressure was studied by Sun BM et al. Al using preeclampsia rats' model along with intestinal studies. To reduce uterine blood perfusion abdominal operation was performed. The pre operated 40 animals were randomly divided into control and observation group (treated with probiotics), n=20. After intervention on 3rd and 7th day of treatment it was found that along with intestinal microflora the systolic and diastolic blood pressure was found to be normal in observation group. Studies also report the effect of probiotics on patients with blood pressure in grade one hypertension. A human clinical trial with 110 patients performed by dividing whole population into randomized and control groups, and monitored after eight weeks. Where this clinical study postulates that the group treated with probiotics bifidobacterial, streptococcus and lactobacillus has converted the dietary components into active metabolites and these metabolites positively affect function of immune cells which in turn could encourage in lowering of blood pressure.[9]

The meta-analysis on probiotics for antihypertensive effect from fermented milk has shown a significant effect on systolic and diastolic blood pressure (BP),[10] but during the process of investigation it is observed that the supplemented probiotics significantly affect systolic blood pleasure in patients with hypertension and diabetes, and effect on diastolic blood pressure was observed in patients with only hypertension for short period (8-10) weeks on comparing with the control group.[11] The study by Lewis et al., has supported the use of probiotics supplements for lowering systolic BP -1.58 mmHg, and diabolic BP -0.92 mmHg.[12]

On comparing different studies, it is observed that reduction in systolic BP and diabolic BP is not constant. Further, as the results are found

to be positive in decreasing blood pressure studies has to performed concentrating on dose and span of treatment to get the linear outcome. However, the slight decrease in Blood pleasure decreases the risk of myocardial infarction and stroke.

Reducing the oxidative stress

The disturbance in the produced reactive oxygen species (free radicals) and defensive antioxidants leads to oxidative stress. Probiotics are exogenous and beneficiary micro-organisms which can be considered for its ability to modulate the oxidative stress in the host.

An animal study by El-Khadragy et al. 2019. By infecting mice with *Schistosoma mansoni* which is a causative agent for liver fibrosis and further liver cirrhosis. Followed by oral treatment of probiotics has shown a significant reduction in oxidative stress markers, which were induced by *Schistosoma mansoni* infection. And the concentration of some antioxidants like glutathione peroxidase, glutathione reductase, catalase and superoxide dismutase were drastically enhanced. And also, the treatment with probiotics have also inhibited the process of apoptosis in hepatic tissues, which mainly induced the expression of caspases-3 in liver tissues. And almost same results were observed in study by Tang et al., in neonatal rats.[13,14]

Riane K et al.[15] through his investigation has showed the effect of probiotics supplementation on oxidative stress markers in rats with diclofenac hepatotoxicity. Mice after treating with probiotic (Streptococcus salivarius) of concentration 10^9 CFU for seven successive days and then single treatment of diclofenac overdose with distilled water was given. On investigating the liver transaminases, histology, MDA (malondialdehyde) and GSH (glutathione), it shows that the pre-treatment of mice with probiotics has reduced the diclofenac induced hepatotoxicity by enhancing hepatic markers, regulation of antioxidant expressions and their activities.[15]

A study by Shang et al., has investigated the effect of probiotics on mercury (Hg), which is a poisoning agent in both animal and fishes. Mercury is a potential oxidative stress inducer, as it exerts high toxicity against enzymes involved in antioxidants regulation. The viability of enzymes inhibited by Hg can be reactivated by supplementing with Selenium (Se). Bacillus subtilis probiotics is found to be used widely IN aquacultures as it has an adoption capacity with heavy metals. In this study, the Se-rich B. subtilis of 10^5 CFU/g to a span of 30 days was used in treating fishes that were exposed to Hg (0.03 mg/L). On sampling the treated fishes for its antioxidant and intestinal damage repair, it was observed that Se-rich B. subtilis has a capacity to protect the intestine from mercury induced morphological changes and parallel treatment has also decreased the activities of CAT, SOD and FSH-PX and increased activity of MDA, GSH and GST with $P < 0.05$. But here it is not clearly mentioned that the antioxidant activity observed in fishes is due to treatment with probiotics or it is a synergy of selenium and B. subtilis.[16]

Chen Y et al.,[17]. Analyzed the effect of probiotics on fasting blood glucose levels, hs-CRP High sensitivity C reactive protein, GHS (total glutathione), MDA (malonaldehyde), and levels of nitric acid in a patient with gestational diabetes and observed reduced FBG (fasting blood glucose levels), hs-CRP, MDA but no significant reduction of GSH. Thus, in comparison with other methods of treating GD the treatment with probiotics has an average outcome with less or no side-effect on both mother and infant.[17]

The in vitro study by Wang G et al.,[18] to understand the protective effect of recombinant probiotic *Lactobacillus plantarum* on H_2O_2-induced oxidative stress in HUVEC cells, the *Lactobacillus plantarum* was constructed (NC8-pSIP409-alr-angiotensin-converting enzyme inhibitory peptide (ACEIP)). The MTT calorimetric assay was performed to check the viability of HUVEC cells which are pre-treated with oxidative stress inducer followed by treatment with recombinant probiotic. The survival rate of HUVEC cells after incubating with NC8-pSIP409-alr-ACEIP for a span of 1 hour its was found to be (57.78±0.40) %, which was slightly higher that positive control. As the incubation time was increased the cell viability was significantly increased (67.58±0.30) %. On performing the same experiment with empty vector NC8-alr has shown no protectivity against induced stress. Thus, this study hypothesises that the antioxidant property observed in the experiment is due to expression of fusion protein ACEIP.[18]

The probiotic effect can also be observed in normalizing GLP-1 and oxidative stress, which has been demonstrated by Pegah et al., With Wistar male rats. The histopathological, oxidative stress markers and biochemical analysis of test group has shown a significant decrease in insulin and glucose resistance ($p < 0.001$), increased GLP1 and antioxidant levels ($p < 0.001$) in diabetic rats in comparison with control.[19] In all these reports it is reported that all the different strains used are protective against oxidative stress. But it is also important to perform human trials and check for exact gene expressions.

Regulation of hormones

Since many years studies have a hypothesis on regulation of hormones from probiotics, though the clinical studies with human trails for effect of probiotics on imbalanced hormones is paltry, few studies show a promising result with this aim.

A study by Narmaki et al., aimed on supplementing probiotics to obese women with food addiction. On assessing the anthropometric indices, hormone levels and eating behaviour in randomized, double-blinded and placebo groups. It is observed that the group supplemented with probiotics has shown a significant anthropometric indices results compared to placebo group ($p<0.001$), and better outcome was observed in the eating behaviour. The serum levels of hormone oxytocin was increased and NYP (Neuropeptide Y) decreased significantly in group supplemented with probiotics and no significant reduction was observed in leptin levels in comparison with placebo group, which says multi strain probiotic supplementation has some beneficiary impact on appetite regulating hormones.[20]

On demonstrating the effect of probiotic Bifidobacterium lactis V9 for regulation and secretion of sex hormone in patients with PCOS (Polycystic Ovary Syndrome Patients). it was notably observed that on supplementing Bifidobacterium lactis V9 for 14 PCOS patients the levels of LH- luteinizing hormone, LH/FSH-LH-follicle-stimulating hormone was decreased significantly in 9 patients parallelly the levels of sex hormones were increased markedly, but the linear outcome was not observed in other 5 volunteers involved in the study.[21]

During the process of menopause ovarian hormone secretion decreases which results in increased body weight and mass of adipose tissue. The study by Chen et al., has demonstrated the effect of probiotics in ovariectomized mice with soy isoflavones diet. In the results it is found that the probiotic *Bifidobacterium longum* 15M1 used in the treatment has reversed the menopausal obesity, on the other hand the combination of *Lactobacillus plantarum* 30M5 along with soy isoflavones diet was found to be more effective in reducing the disorder of menopausal lipid metabolism. And it is also found that the probiotic *Lactobacillus plantarum* 30M5 alters the gut microbiota which results in increase circulation of estrogen followed by upregulation of expression of α estrogen receptor in adipose tissue which further improves the formation of short-chain fatty acids. And the study also states that the observed effect in ovariectomized mice is a synergetic effect of probiotics and soy isoflovenes diet, which is found to be associated with structure and diversity of intestinal metabolism for enhanced short chain fatty acid production and circulation of estrogen.[22]

The finding of all these studies suggest that the probiotics has a potential effect in regulating the imbalanced hormone. On the other hand, in some synergetic effects though the exact function of probiotic supplementation is not known the adaptability of the probiotics has to be considered. More studies have to be done with respect to treatment of PCOS from probiotics as the present-day treatment for PCOS has various side effects. In present day infertility is one of the major problems that people are going through, as probiotics contribute in regulating hormones studies can also be done to treat infertility.

Lipid and carbohydrates metabolism

Improves glycemic index

After eating the appearance of glucose in the bloodstream is understood as a glycemic response (GR). Normal physiological GR depends on the quantity of glucose intake, circulation, absorbance, and departure of glucose from circulation after absorption by tissues. Food with high carbohydrate content has an effect on glycemic response, which results in rapid increase and decrease of blood glucose levels.

Oral consumption of probiotics lets them to amalgamate with intestinal flora either temporarily or indelibly. In addition, they also counterattack metabolic diseases related to diabetes.[8]

Modulation in microbiota of gut could be effective in managing type 2 diabetes mellitus. The study by Khalili et al., has demonstrated a trial to evaluate the effect of probiotics Lactobacillus casei on serum sirtuin1, fetuin-A and glycaemic control in patients with T2DM on 40 subjects divided into 2 intervention groups. The results with respect to FBS, concentration of insulin, and insulin resistance was found to significantly decreased in intervention group supplemented with probiotics in comparison with placebo group. But no evident reduction of HbA1c was observed. And also, the Lactobacillus casei supplementation has significantly increased sirtuin1, fetuin-A levels which further improved glycaemic response in patients with T2DM.

The observed effect of probiotics on sirtuin1, fetuin-A is not found to be linear, and its action mechanism in improving glycaemic response is found to be unclear. But the oral consumption of some probiotics has better outcome with respect to glycaemic responses. Here though the results for glycaemic responses on consumption of probiotics is found to be positive, but it is still unclear whether the mood of intake alters the outcome.[23]

The management of glycemic response and blood glucose levels followed by a meal is important and crucial component in every diabetic patient. To understand whether the oral administration of probiotics affects the glycemic response Chavkin et al., has demonstrated an animal experiment. Where *E. coli* Nissle 1917 (EcN) was evaluated for oral glucose tolerance test. It is observed that the oral gavage of *E. coli* Nissle 1917 along with a glucose bolus reduced the post-gavage glycemic response in mice. Thus, this study suggests that *E. coli* Nissle is eligible to alter glycemic response which is not directly mediated by uptake of glucose.[24]

Regulation cholesterol levels

A meta-analysis by Liang T et al 2020. on patients supplementing with multiple species of probiotics was found to have a statistical reduction in total cholesterol and patients supplemented with monospecies and monospecies with co-supplemented food have a comparatively lesser effect. And the effect of multiple species probiotics also depends on subjects like age, BMI, and duration of probiotic intake.[25] With randomized controlled trials the effect of the probiotic on lipid profile was assessed on young patients with mild/mildly hypercholesterolemia and the mean net change in total cholesterol of patients with type 2 Diabetes Mellitus on comparing with the control group after supplementing with probiotics for 6 weeks.[25] Probiotics have also shown a significant effect on patients with normal, borderline, and high cholesterol levels the mean net change in Borderline density lipoprotein and in high-density lipoprotein levels in comparison with the placebo group.[26] According to[27] Pourrajab B et al., study on the effect of probiotic yogurt on Group 1 patients with high lipid in blood, BMI less than 30, and no health complications and Group 2 with mild hypercholesterolemia and moderate hypercholesterolemia. This resulted in a reduction of total cholesterol and Low-Density Lipoprotein cholesterol (LDL-c) levels in participants with consumption of <300 mg/dl for more than 4 weeks and total cholesterol levels were high in the group after consumption of probiotics of the same dose for the duration of lesser than 4weeks. And no greater or significant impact was observed on the overall size of High-Density Lipoprotein cholesterol (HDL-c), and Triglyceride (TG) levels of participants.[27] Study on probiotics with high fat and high cholesterol diet-based rats by supplementing mixed probiotics (8 probiotics, 2 of each strain *L. casei, L.acidophilus, L. reuteri, Lactobacillus gasseri*) this symbiotic treatment showed a significant effect on total cholesterol and low-density lipoprotein compared to high-density lipoprotein cholesterol and triglycerides.[28]

Pellonpera O et al. Performed randomized and placebo-controlled trials on women with overweight and obesity, and it has not observed a significant gap in glucose level or insulin concentration between all intervention groups.[17] Investigated the effect of probiotic supplementation on lipid profiles and glycaemic control by randomized and placebo control trials with probiotic capsules (*L. acidophilus, L. casei, Bifidobacterium bifidum*) and cellulose capsule respectively for 6 weeks. And observed the effect

of probiotic supplementation on controlled glycaemic factor, stability in VLDL concentration, and triglycerides, and no effect was observed on lipid profiles.[29]. As per a study by Razmpoosh E et al., on performing randomized control trial on 60 patients by supplementing probiotics of combination *lactobacillus, streptococcus,* and *Bifidobacterium* for 6 weeks considerable decrease of FPG (fasting plasma glucose) and increase of HDL-C (high-density lipoprotein)was observed, and no significant variations were observed in the status of insulin resistance, cholesterol concentration, BMI.[30]

The present-day research has demonstrated that the cocktail of probiotics and their symbiotic combinations benefited the patients with T2DM by reducing cholesterol, triglycerides and reduction of cardiovascular disease risk. But no linear outcome has been observed in studies performed. However, with the happened studies it is clear that probiotics has got beneficiary effect on regulation cholesterol levels. Future, studies had to be concentrated on dose, span of treatment and mood of intake which may help to get the linearized results.

Reduction of gestational diabetes

The state of high glucose levels in the blood during pregnancy is known as gestational diabetes and defined as intolerance to glucose during pregnancy, piloted by high rates of obesity and overweight. And associated with complications like increased blood pressure and protein content in the urine leading to adverse pregnancy outcomes and c-section/ operative delivery. And it also affects the fetus by macrosomia, low blood glucose levels, per-term birth, respiratory disorders, and jaundice. GDM also increases the risk for both mother and infant of being diabetic in the later stage. According to the International Association of Diabetes and Pregnancy Study Group, about 18% of pregnant women are affected by gestational diabetes, which has increased the rates of fetal and maternal mortality and morbidity.

The case control study by Xiaoqian et al., to assess the effect of probiotic yogurt in 123 subjects with gestational diabetes. The study results that the consumption of probiotic yogurt before pregnancy has no effect of gestational diabetes, but the consumption of probiotic yogurt during pregnancy was found to be effective in reducing the risk of gestational diabetes.[31]

The demonstration by Shahriari et al. on probiotic supplementation in reducing the risk of gestational diabetes with 217 pregnant women, supplemented with cocktail of probiotics for a span of 24 weeks and compared with control. The result of this study says that pregnant women with gestational diabetes on supplementing with probiotics has not shown any significant results in glucose tolerance. The incidence of gestational diabetes in intervention group was found to be 41.9% and which is not significantly different from control group 40.2%.[32]

The four-week supplementation of probiotics to 28 subjects with gestational diabetes on control diet in late second and early third trimesters has significantly lowered the fasting glucose levels and insulin resistance has found to be increased. Parallelly the animal experiment on assessing the effect of probiotics on gestational diabetes mellitus rat has clearly indicated improved fasting blood glucose levels. Further for greater level understanding of action mechanism of probiotics 16s rRNA sequencing was performed and compared with control rats. On comparison, it is observed that in rats with gestational diabetes shows decreased diversity of gut microbiota. On supplementing with probiotics restored diversity of microbiota was observed. Particularly Actinobacteria and Firmicutes levels was found to be high after supplementation. Davidson et al. has assessed the effect of probiotics in the prevention of gestational diabetes and compared with other methods and reached the primary outcome with a considerable reduction in gestational diabetes rate with no statistical difference in rates of miscarriages.[33-35]

Few studies performed has proved a significant reduction in GDM where as other studies have not landed on the same conclusion, this variation is results might be due to type of the treatment and diet during supplementation. However, the effect of probiotics on GDM is still contradictory. As few studies has observed a better outcome and as probiotics are natural components it can be suggested as a novel approach for alleviation of gestational diabetes mellitus. Future, studies performed with the objective of designing

probiotics that get along with pregnancy treatment would help women to escape from gestational diabetes.

CONCLUSION

Probiotics are widely used to alleviate diabetes and related problems, and most of the results indicate that probiotics have a beneficiary effect. The present-day research and result analysis support the use of probiotics, the rich diversity of probiotics has found its accountability for major health benefits. Several in vitro and in vivo studies conducted using cell lines and animals by inducing pathogens have proved the efficiency of probiotics in treating disorders. Probiotics are found to be effective against many problems where the present-day available treatments have an adverse effect. Along with the proven aspects, there are several action mechanisms of probiotics that are yet to be reported. This review highlights the ameliorating impact of probiotics on diabetes mellitus as well as its symptoms and complications. This has been an integrated effort for the summation and reviewing of the available literature on probiotic intervention on diabetes. However, more studies on probiotics for resolving health issues could definitely help people as they are natural, safe, economical and reliable.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

RR conceptualized and designed the study. NS and MKJ performed data acquisition and analysis. SNB and SJC performed the supervision and wrote the original draft. All authors read and approved the final manuscript for publication.

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DATA AVAILABILITY

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ETHICS STATEMENT

Not Applicable.

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