REVIEW

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The Relationship Between a Rich Diet with Probiotics /Prebiotics and the Gestational Health Conditions

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ABSTRACT

The interest in studying the microbial gut like probiotics has increased because it may play a significant role in reducing the risk of certain health conditions and promote overall health. In the recent decade, the nutritional researches have linked between having a regular healthy diet and the health conditions during pregnancy. For example, during the pregnancy period, women may counter several health conditions, such as Gestational Diabetes Mellitus (GDM) level. In this relation, a few recent researches have suggested that having a rich diet with a probiotics/prebiotic may reduce the incidence of GDM. Therefore, in the world market, the interest in studying the correlation between probiotics/prebiotics and the incidence of pregnancy health conditions has increased. This paper has been designed to review the recent studies that investigated the relationship between a rich diet with probiotics/prebiotics and the gestational health conditions.

KEYWORDS: Diabetes Mellitus, Gestational, Pregnancy, Probiotics

INTRODUCTION

Many changes occur during the normal pregnancy including changes in the immune system and metabolism which is described as the metabolic syndrome.[1] Gestational Diabetes Mellitus (GDM), a condition in which there is a high serum glucose level present during the gestation period, is considered as a most common metabolic complication during pregnancy.[2] It usually appears during[3] the 29–33 gestational weeks[4] of the second stage of pregnancy, and disappears in the postpartum stage.[5] In some cases, the high blood glucose continues after delivery[6] which may contribute type 1, or type 2 of diabetes.[7]

In addition, the maternal insulin resistance is associated with immediate and long term metabolic complications on both maternal and fetal. For example, the Gestational Diabetes Mellitus (GDM) is responsible for verity of inflammation through the gestation period.[8] Also, GDM is linked with many pregnancy adverse complications outcome, such as pre-eclampsia and abnormal delivery.[9] Recent studies showed that the women who experienced GDM are more likely by six times to develop diabetes of type 2, as compared with women who had normal blood glucose level during the pregnancy period.[10-11] Other maternal metabolic complications include but do not limited hypertension, pre-eclampsia, caesarean section, infection, and polyhydramnios.[12] Moreover, Gestational Diabetes Mellitus (GDM) may be associated with new-borns morbidity including macrosomia, birth trauma, hypoglycaemia, hypercalcemia, hypomagnesemia, hyperbilirubinemia, respiratory distress syndrome, polycythaemia.[13] Also, other studies showed that the children of women with GDM are more likely to develop obesity or diabetes in childhood or in adulthood.[12,14-15]

Worldwide, the prevalence proportion of the Gestational Diabetes during pregnancy rose sharply[16-17], and it ranged between 1% to 14% of all pregnancies.[18] This variation in prevalence is due to genetic, ethnic, demographic, socio-cultural, and economic factors.[16] A number of common factors have been accounted as main contributors of GDM including older ages pregnancy, obesity, family history of diabetes (FHD), previous history of GDM, congenital malformation, and caesarean section.[19-23] Other controversial causes include smoking history, physical inactivity, and socioeconomic factors.[9,19,20,24] On the other hand, diet is playing a major role in determining the health status of individuals.[25] In the past few decades, many studies showed that the incidence of gastrointestinal tract problems, such as bloating, flatulence, constipation, diarrhea, inflammation, and damage of the gut lining have been increasing sharply.[26] Also, the dietary pattern of women before and during pregnancy is correlated with developing many health adverse effects, such as he Gestational Diabetes Mellitus (GDM)[27] with the pregnancy outcome.[28-29] Thus, the relation between diet and health has been considered as an interesting

topic for many individuals who increased the demand after the health information related to the healthier food diet.[30]

In the recent years, probiotics have been presented as a novel therapy for controlling high glucose level during pregnancy[31-32] and improve the maternal metabolism and pregnancy outcome.[33] This review was done based on Randomized Control Studies (RCT) to investigate the efficiency of the Gut microbiota such as probiotics in controlling the blood glucose level and improve maternal metabolism and pregnancy outcome. A systematic computer search of the databases from MEDLINE, LISTA, PubMed, Web of science, CINAHL.

1. Gut microbiota and diabetes

The human digestive tract is considered as a place for a large community of microorganisms (Gut flora, gut microbiota or gastrointestinal microbiota) that have a direct influence on the human[34] and non-human health.[35] The human gut microbiotas have been shaped through multi-factors during the infancy period[34] including diet such as, breast milk vs. formula feeding, antibiotic usage,[36] and the diet pattern has been considered as the main contributory factor in forming the gastrointestinal microbiota.[37] Recent studies indicated that the bacterial gut has a pivotal role in protecting the body against illness and infections, keep metabolic homeostasis, immune tolerance[38], and modulation of the intestinal epithelium.[39]

In relation to this, the nutritional attitude plays a significant role in modelling the gut microbiomes.[40] The high fat and fructose diet have been determined as main contributors of alteration of the normal gut microflora (dysbiosis)[40] which may be linked to the pathogenesis of many illnesses and health disability (41, 42) such as, Diabetes Mellitus (DM),[43] and Gestational Diabetes Mellitus (GDM) (44). Hence, the gut microbial data may be a novel source of assessing lifestyle and the food diet quality score of human and non-human being[40,45] and set an effective promotion plan to manage diseases related to the imbalance of the bacterial gut.[40]

On the other hand, various metagenomic studies on humans and animals, have been done to validate the influence of the gastrointestinal microbiota on the body mass index (BMI) and in developing diabetes.[46] After weight gain, human studies showed that some strains of the gut microbiota increased while other strains decreased or remained neutral.[47-49] For example, in 2010, a study was done to investigate the composition changes of the human gut microbiota among individuals with type 2 diabetes.[50] The study indicated that unhealthy dietary intake may lead to the imbalance of the gut bacteria. The V4 region of the 16S rRNA gene was analyzed by tag-encoded amplicon pyrosequencing, and showed the decreased proportion of phylum Firmicutes and Clostridia while increased proportions of Betaproteobacteria and increased ratios of Bacteroidetes to Firmicutes and Bacteroides– Prevotella group to Clostridium coccoides– Eubacterium rectale which showed a significant correlation with high plasma glucose concentration.[50] The mice model studies showed that the mice with a high-fat diet (HFD) had an insulin resistance as a consequence of the change in the composition of bifidobacteria and lactobacilli bacteria group.[51-52] The plasma lipopolysaccharides level (LPS) was increased as a result of decreased proportion of Bifidobacterium and Lactobacillus which led to metabolic endotoxemia.[51-53]

The proportion alteration in the gut microbiota strains lead to changing in the gut hormone secretions (like glucose-dependent insulinotropic peptide, GLP-1, GLP-2, PYY) which directly affect B-cell's mass and function, energy intake, nutrients absorption and energy storage as well as insulin secretion as a consequence of changing the enteroendocrine signals.[40] Also, other studies indicated that the alteration of the gut flora is linked with bile acid pool and biosynthetic pathway as a consequence of the alteration in the enteroendocrine signals in the diabetic patients.[54]

Despite the changing of the gut bacterial composition, it may be linked with many health adverse effect, there is an evidential support, in a clinical practice, that modifying the gut microbiota helps regulate the blood glucose level effectively (55). In this context, modelling the gut flora by prebiotics diet has been presented as an effective prevention through enhanced host-gut bacterial interaction against obesity and overweight and metabolic diseases.[56-60]

2. Managing the Gestational Diabetes Mellitus (GDM) by diet.

There is a multi-directional relationship between diet, host metabolism, and gut microbiome (different strains of bacteria in the gut).[61] The diet can directly influence the microbiome composition.[61] Thus, any

altering in the gut microbiome composition may influence the host metabolism including nutrient absorption[62], and effect the glucose, lipid metabolism and the inflammatory pathway of the host.[63-64]

Recent theories argued that the gut microorganisms (Probiotics) play an essential role in managing the GDM[32] through improving body metabolism as a consequence of improving the digestion and absorbing the lactose and other nutrients.[65] Therefore, The maternal complications during pregnancy such as Gestational Diabetes Mellitus (GDM) may be managed through improving the diet choices of pregnant women.[66]

2.1. Prebiotics diet as a primary prevention choice against chronic diseases

Prebiotics are considered as an essential non-digestible nutritive substance.[67] It enhances the microorganism (probiotics) in the large intestinal tract[68] to growth, activity, and metabolism.[69-71] The term prebiotic had been defined previously as, "The selective stimulation of growth and/or activity of one or a limited number of microbial genus/species in the gut microbiota that confer health benefits to the host".[72] The recent definition of prebiotic by the International Scientific Association for Probiotics and Prebiotics (ISAPP) is, "A substrate that is selectively utilized by host microorganisms conferring a health benefit".[73] As the number of food ingredients and dietary fibers classified as prebiotic increases, the following criteria for classification must be established: "(i) resistance to gastric acidity, hydrolysis by mammalian enzymes, and gastrointestinal absorption; (ii) fermentation by intestinal microbiota; (iii) selective stimulation of the growth and/or activity of intestinal bacteria associated with health and well-being".[74] The Prebiotics food group consist of variant food groups including (but do not limit) Insulin (yogurts, dairy desserts, cheeses, ice cream, and baked products), Fructo-oligosaccharides (Baby food, yogurts, bread, baked products), and Galacto-oligosaccharides (yogurts, fruit juice).[75] The symbiosis of the probiotics with the host, predominantly in our gastrointestinal tract (GI), has been scientifically proven to be important for our health and well-being. For example, it optimizes the process of food digestion[76] and consumption.[77] Additionally, the main function of prebiotics is to increase carbohydrate metabolism and trigger bacterial growth that is beneficial to the intestinal microflora.[78] The increasing popularity of probiotics and prebiotics have been due to current research that suggests the positive effect on various health conditions including (but do not limit) to gastrointestinal transit time, irritable bowel syndrome and ulcerative colitis.[79] Aside from the benefits to the gastrointestinal tract, further beneficial health effects include immune stimulation, reduction in blood lipid levels, effects upon insulin resistance, metabolites that influence brain function, energy and cognition, and mineral bioavailability in the bone among others.[73]

On the other hand, Prebiotics could soon be a tool to combat overweight and obesity.[80] A recent study by Nicolucci et.al. (2017), showed the effect of the prebiotic, oligofructose-encriched inulin, alter the intestinal microbiota and significantly reduce the body weight z-score, percent body fat, percent trunk fat, and serum level of interleukin in children with obesity.[81]

Another research shows that prebiotics that enhanced the growth of bacteria, which were short-chain fatty-acids (SCFA) producers, have been beneficial in the management of metabolic syndrome (MetS) components such as abdominal obesity, low-grade chronic systemic inflammation, altered glucose metabolism, dyslipidaemia, and high blood pressure. These beneficial bacteria have protective effects and have shown to improve metabolic syndrome components especially for individuals with Type 2 diabetes.[82] Also, a study by Deghan et al., (2015), discussed the impact of prebiotic supplementation to patients with type 2 Diabetes Mellitus. Previously, physical inactivity and obesity were usually attributed to the cause of the disease. It has been recently suggested that changes in gut microflora is a factor in the development of the type 2 diabetes. The result of the study showed that the oligofructose-enriched insulin had improved the glycaemic status, lipid profile and immune markers of the diabetic patients.[83] Furthermore, studies have been made on the effects of prebiotics on pregnancy health. Sohn and Underwood (2017) discussed the benefit of administering prebiotics and probiotics to pregnant women. Dysbiosis during pregnancy increases the risk of pre-eclampsia, diabetes, infection, preterm labor, and later childhood atopy. Administration of prebiotics and probiotics during pregnancy, lactation and post-natal offer a safe treatment to improve pregnancy and neonatal outcomes.[84] Also, many studies indicated that managing and treatment of

GDM by diet, with or without medication pills,reducethe pregnancy and maternity complications and improve the pregnancy outcome.[61]

2.2. Probiotics properties and benefits

The probiotics were presented in 1960 by a Russian biologist, Elie Metchnikoff.[85] He hypothesized that there are harmful chemicals produced by the human gut as an unintended consequence of digestion, and these chemicals may lead to health complications including aging, infection, and illness.[85] Additionally, Elie Metchnikoff suggested that eating "Acid-producing bacteria diet" may help to eliminate the harmful chemicals which may improve the individual's overall health.[85]

Probiotics strains (helpful bacteria) have been considered as intestinal microorganisms that can improve the host health condition[33] through many mechanisms[86] including modification of the gut microbiota (microflora), competitive adherence to the mucosa and epithelium, strengthening of the gut epithelial barrier and modification of the immune system to enhance the overall health of the host.[87]

Recently, scientists confirmed that there are specific probiotics bacterial strains in the gut which have the ability to eliminate the toxicity by modifying the flora and replacing the harmful bacterial with good (useful) ones.[85] According to the probiotics strain, the efficacy research's, Vitro, vivo, genetic and omics indicated that the probiotics strains may have various effect on our overall health.[88] For example, strains of Probiotics, particularly lactobacilli and bifidobacterial, have been confirmed as an effective dietary intervention to manage intestinal illness, and life- style metabolic problems,[40] especially in humans[89], while other studies confirmed the beneficial effect of the muciniphila MucT (Probiotics strain) on glucose metabolism in mouse model.[90]

In the recent years, studies about the health benefits of probiotics in our intestinal microbial ecology and immunity have significantly increased.[91] The relation between human's dietary habits and gut microbiota metabolism, and its effect on our health is being studied progressively.[92] There has been studies about the gut microbiota as a possible therapeutic treatment for obesity due to its importance in processing dietary polysaccharides, which affects the energy yield from the diet and energy metabolism in the host.[63] This increased knowledge of the functional connections between the complex microbial community, metabolism, and host could lead to treatment of metabolic syndromes including (but do not limit) to Type 2 diabetes.[93]

Also, in 2015, a result of a meta-analysis study showed that consumption of probiotic can play a major effect on glycemic control[94], so it has been considered as a novel strategy to void progression and development of diabetes as a consequence of improving the modification of the gut microbial composition.[40]

2.3. Probiotic efficacy in animal models against diabetes

Broadly, the mechanisms of the gut flora have been studied through different animal models to verify the effect of these gut bacterial against diabetes. An oral administration or dietary supplement of Lactobacillus were provided in three different mice model. These models included diabetes type 2 by using KK-Ay mice, mice with type 1 model, and the diabetes mice which was induced with Alloxan. The results of all these models indicated that the Lactobacillus reduced the incidence rate of diabetes and decreased the plasma glucose level.[95-97] Another model studied the effect of Lactobacillus rhamnosus on neonatal mice. The study indicated that the neonatal mice who had diabetes (induced by streptozotcin) were positively affected by taking Lactobacillus rhamnosus. Lactobacillus rhamnosus improved the glucose tolerance (the serum insulin level increased by the first 30 minutes of taking the Lactobacillus).[98] Furthermore, destruction of the pancreatic B-cells has been studied by Calcinaro et al., (2005). He reported that having a diet containing Bifidobacterium and lactobacillus may reduce the B-cells destruction among non-obese diabetic mice.[99] Calcinaro et al., (2005) argued that the secretion of Interleukin-10 (IL-10) is associated with Bifidobacterium and lactobacillus which prevent the B-cell's destruction. Moreover, other studies indicated that the oral administration of probiotics supplements may control the diabetes risk factors.[100] For example, Yadav et al., (2007), studied the effect of feeding probiotics diet that contain Lactobacillus acidophilus and *L. casei* on Fructose-induced diabetes mice. The study indicated that the blood glucose level and glycosylated hemoglobin free fatty acids and triglycerides in the tested mice significantly decreased.[101]

In the relation to the animal study, another paper studied the effect of the gut microbiota on mice with high fat diet. The studies indicated that the high fat

diet led to depletion of the liver's natural killer T (NKT) cells which may lead to the over production of pro-inflammatory cytokines. A probiotic supplement was given and observed for days. The study reported that the gut flora played an important role in increasing the number of liver's natural killer T (NKT) cells, and these cells worked against insulin resistance, which helped regulate the insulin production.[102]

2.4. Probiotic efficacy in human clinical trials

It is known that the dietary interventions have been used broadly as a primary treatment method against diabetes,[103] as using the food intervention may be useful for managing the diabetes mechanisms including but not limited weight, altering hyperglycaemia, hyperlipidaemia and insulin resistance.[104] Limited studies have been done to clarify the linkage between the gastrointestinal microbiota (probiotics) and chronic diseases in terms of dietary supplements intervention.

In the relation to the dietary intervention, limited studies indicated that the dietary interventions, conjunction with probiotics, as an essential microbial supplement[40,105] to support the host's metabolism[32] against Gestational diabetes mellitus (GDM) by improving the symptoms of the lactose intolerance (106), and as an effective intervention to prevent gastrointestinal diseases, such as diarrhea[107-8], and via targeting all possible risk factors.[40]

On the other hand, recent advances are aimed towards preventive measures in developing GDM such as, modification of lifestyle and dietary habits that prevent or delay the development of glucose intolerance and insulin resistance.[109] Gut microbiota dysbiosis have been discovered in overweight patients with obesity therefore fueling the interest in the role of probiotics as a preventive and therapeutic adjunct application.[32] Studies have started to examine the benefits of probiotics in reducing GDM incidence, whereby alteration of the host's metabolism through diet could affect microbiota's composition and gene expression.[61]

The probiotic dietary intervention for pregnant women by modulating specific target functions in the gut microbiota shows promising effects beyond the obvious nutritional impact of food.[32]

The effect of the probiotics treatment is dependent on temperature and anaerobic storage conditions, initial dose strain and quality (110). As an intervention for the prevention of GDM, certain probiotics, as a dietary supplement, increase gene expression related to fat metabolism and insulin sensitivity, reduces inflammatory signalling, and decreases adiposity.[111]

A few years ago, studies have been done that confirmed a correlation between probiotics and gestational diabetes mellitus (GDM). Randomized controlled trials (RCTs) showed that there is a null or positive effect of the probiotics on pregnant women who are diagnosed with gestational diabetes mellitus (GDM).[9]

In some human clinical trials, selected probiotics showed positive results by decreasing insulin resistance syndrome, improved carbohydrate metabolism, fasting blood glucose, insulin sensitivity and antioxidant status.[91] Another randomized clinical trial in which a probiotic supplement capsule containing four bacterial strains of Lactobacillus acidophilus LA-5, Bifidobacterium BB-12, Streptococcus Thermophilus STY-31 and Lactobacillus delbrueckii bulgaricus LBY-27, improved the health condition of pregnant women with GDM in relation to inflammation and oxidative stress biomarkers.[112] This is significant because increase in the level of oxidative stress due to overproduction of free radicals and a defect in the antioxidant defenses are associated with GDM, and had implications in the fetal and mother's well-being.[113] There also was a report in which normal weighted pregnant women, through a randomized controlled trial, had a combined dietary and probiotic supplement intervention, which resulted to a 34% to 13% decline in the rate of GDM.[114] Evidence suggests that probiotics have no adverse effects in mother and child during pregnancy, and that the daily intake of probiotic capsules with Lactobacillus rhamnosus GG and Bifidobacterium lactis Bb12 may be effective in pregnant women who are at high risk for GDM.[115]

Despite these advancements in research, it has been suggested for future studies that the criteria for GDM from the International Association of Diabetes and Pregnancy Study Group (116) should be taken into account, interventions by specifying subgroups, and the separation of patients with GDM early in pregnancy from patients who are newly at risk in developing GDM could be an approach that would provide the best benefit and result in clinical trials.[117]

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