The Role of Intestinal Flora in Diabetes and Traditional Chinese Medicine Interventions

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Abstract. Diabetes is a kind of chronic metabolic disease characteristic of hyperglycemia. It is mainly divided into diabetes mellitus type 1 (T1DM), diabetes mellitus type 2 (T2DM) and gestational diabetes. Among them, T2DM accounts for more than 90% and it is closely related with obesity and lifestyle. Recent studies have found that intestinal dysbacteriosis is closely related with occurrence and development of diabetes. Specific food components can improve metabolism by adjusting flora. In Traditional Chinese Medicine (TCM), diabetes is classified as "the spleen-warm syndrome" and it is believed to be related with dysfunction of spleen and stomach. Moreover, a four-stage development theory of "depression, heat, deficiency and damage" is proposed. Traditional Chinese Medicine intervene diabetes, adjust glucolipid metabolism and flora balance through multiple ways like compound preparation, acupuncture and traditional exercises. Nevertheless, current studies still face many challenges, such as ambiguous multi-component multi-target mechanisms, insufficient clinical standardization and great individual difference. Future studies shall strengthen prospective study and long-term tracking to optimize diabetes control strategies.

Keywords: Diabetes, intestinal flora, TCM treatment

1 Introduction to Diabetes

1.1 Diabetes

Diabetes is a kind of chronic metabolic disease characteristic of hyperglycemia. It is mainly caused by insufficient insulin secretion or insulin resistance, and it can lead to blood glucose regulation and even may cause multisystem complications in long term[1]. Diabetes is mainly divided into several types: diabetes mellitus type 1 (T1DM) mainly destroys pancreatic β cells due to the immune system damages, thus resulting in absolute deficiency of insulin[2]. Diabetes mellitus type 2 (T2DM) is mainly characteristic of insulin resistance. For example, functions of pancreatic β cells decline gradually in skeletal muscle and fat tissues. T2DM accounts for more than 90% of patients with diabetes and it is closely related with obesity and lifestyle[3]. Gestational diabetes is insulin resistance caused by hormone changes during pregnancy[4].

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1.2 Epidemiology and Complications of Diabetes

According to statistics of International Diabetes Association (IDF), there are about 460 million patients with diabetes by 2019, which will further increase to 700 million by 2045 (Fig. 1). Diabetes has brought significant pressure over global public health and economy. In 2024, diabetes caused more than 1000 billion dollars of economic loss. The complications of diabetes are highly related with lesion of small vessels, such as diabetic nephropathy, diabetic retinopathy and diabetic cardiomyopathy. Diabetes caused 3.40 million deaths in 2024. In other words, one people died for diabetes every 6 second[5].

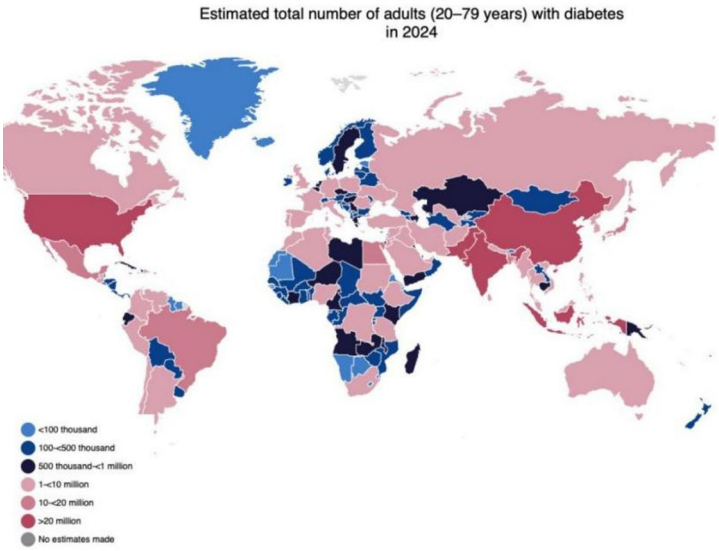

Fig. 1. Global diabetes prevalence (adults 20-79 years) in 2024

2 Correlation Between Intestinal Flora and Diabetes

Intestinal flora is the microflora in intestine of human body. The correlation between intestinal flora and host can affect metabolic phenotype and stress response of host. The balance and diversity of intestinal flora are major factors to maintain steady state of hosts, mainly including energy metabolism, immune responses, inflammatory responses and brain-intestine axis. Disorder of intestinal flora can cause a series of adverse symptoms, including obesity, diabetes, metabolic syndrome, allergic reaction, intestinal tumor, depression and anxiety. Genetics, lifestyle, diet and environmental factors all can influence the balance of intestinal flora. Therefore, maintaining the balance of intestinal flora is an important way to prevent metabolic diseases. This section bridges modern biomedical understanding of gut microbiota with broader metabolic health, setting the stage for later TCM integration.

The gut microbiota composition in healthy individuals exhibits greater diversity, whereas obese or diabetic patients display reduced microbial richness, with an increased abundance of opportunistic pathogens and a decline in beneficial bacteria. The gut microbiome and its metabolites participate in multiple physiological processes, including immune regulation, metabolism, and even brain function[6]. Research on the "microbiota-gut-brain-liver axis" reveals that gut microbes regulate intestinal enteroendocrine cells (EECs), which secrete key gut peptides such as cholecystokinin (CCK), leptin, peptide YY (PYY), glucagon-like peptide-1 (GLP-1), and 5-hydroxytryptophan (5-HT). These gut-derived peptides may contribute to glucose and lipid metabolism disorders by modulating the central nervous system and related signaling pathways[7]. Certain bacterial species—including Clostridium, Bacillus, Enterococcus, Bifidobacterium, Lactobacillus, and Bacteroides—produce bile salt hydrolase (BSH), which deconjugates bile acids to generate free bile acids and further modifies secondary bile acid formation. Bile acids activate G protein-coupled bile acid receptor (Gpbar1) and farnesoid X receptor (FXR), thereby regulating glucose and lipid metabolism, stimulating PYY and GLP-1 secretion, enhancing insulin sensitivity, and reducing blood glucose levels[8, 9]. Additionally, short-chain fatty acids (SCFAs)—produced by microbial fermentation via Butyrivibrio, Roseburia, Coprococcus, Bifidobacterium, Eubacterium, and Clostridium—bind to G protein-coupled receptors (Gpr41/Gpr43), promoting PYY and GLP-1 release and improving insulin resistance (IR). In T2DM patients, gut dysbiosis leads to increased lipopolysaccharide (LPS) production from Gram-negative bacteria and a reduction in microbiota that protect the intestinal mucosal barrier[10]. Consequently, the expression of tight junction proteins in the intestinal epithelium is suppressed, increasing gut permeability and facilitating LPS absorption[11]. LPS activates immune cell receptors (CD14/TLR4), triggering the secretion of proinflammatory cytokines such as interleukin-1 (IL-1), tumor necrosis factor-α (TNF-α), and interleukin-6 (IL-6). This chronic low-grade inflammation, when sustained, impairs insulin responsiveness and exacerbates IR[12] (Table. 1).

Table 1. The mechanism of action of the intestinal microbiota and diabetes.

Bioactive mediators	LPS	Bile acid	SCFAs
Receptors	TLR4/CD14	Gpbar1/FXR	GPR41/GPR43
Bioactive molecules	IL-1/TNF-α/IL-6	——	PYY/GLP-1
Effect	inflammation	Insulin resistance	Insulin sensitivity

2.1 Effects of Intestinal Flora in Diabetes

T2DM is closely related with dysbacteriosis, which is manifested as reduction of probiotics (bifidobacterium and Ackerman bacteria) and increase of harmful bacteria (firmicute). Dysbacteriosis can increase intestinal permeability and endotoxin enters into blood to cause chronic inflammation and inhibit insulin signal pathways; decrease short-chain fatty acids; the insufficient short-chain fatty acids (e.g. butyric acid) include

secretion of glucagon-like peptide 1 and decrease insulin sensitivity; bile acid metabolism becomes abnormal; flora participates in bile acid metabolism and dysbacteriosis can influence glucose and lipid metabolism.

Research indicates that people with reduced gut microbiota diversity are more susceptible to obesity, insulin resistance, and abnormal lipid metabolism[13]. Investigations comparing individuals with low microbial gene richness (LGC) to those with high gene counts (HGC) reveal significant declines in certain bacterial populations, including Lactobacillus, Prevotella, and Bacteroides, along with reduced presence of Desulfovibrio and Oxalobacter species. Such microbial depletion could contribute to metabolic dysfunction.

In LGC subjects, the gut microbiome exhibits notable functional alterations: diminished levels of butyrate-producing microbes, a shifted balance favoring Akkermansia over Ruminococcus torque/gnavus (which may accelerate mucus breakdown), and reduced capacity for hydrogen and methane synthesis. Additionally, these individuals display higher levels of Campylobacter and Shigella, along with elevated peroxidase activity[13].

These microbial imbalances, characterized by disrupted inflammatory regulation, heighten the likelihood of metabolic conditions, including prediabetes and type 2 diabetes[14]. The altered gut environment in LGC individuals thus appears to foster a pro-inflammatory state, increasing their vulnerability to metabolic disorders.

2.2 Effects of Compounds in Food on Intestinal Flora

Food is the key factor that influences balance of intestinal flora. Different diets will facilitate growth of “good bacteria” and “bad bacteria”. Foods rich with polyphenols, flavonoids, saponins and vulcanization can facilitate growth of “good bacteria” and inhibit growth of “bad bacteria”. Excessive sugar, frying and plants with excessive fats can facilitate growth and reproduction of “bad bacteria”, thus causing inflammation, decreasing beneficial bacteria and increasing intestinal toxins (Table. 2).

Table 2. Effects of compounds in food on intestinal flora[15]

Compounds	Source	Action mechanism
Polyphenols	Green tea, red wine, blueberry	Increase acckerman bacteria and bifidobacterium, decrease inflammation, and improve insulin sensitivity
Flavonoid	Soybean and orange	Inhibit pathogen growth, promote production of short-chain fatty acid, and strengthen intestinal barrier functions
Saponins	Ginseng and Astragalus	Lower firmicute/bacteroid ratio, adjust bile acid metabolism, and improve glucolipid metabolism
Sulfide	Garlic and onion	Increase lactic acid bacteria, decrease endoxemia, and relieve insulin resistance

3 Diabetes Control Based on TCM

Building upon the modern biomedical understanding of intestinal flora, TCM offers a unique holistic framework for understanding and managing diabetes.

3.1 TCM Understanding of Diabetes

Diabetes has no corresponding name in TCM, but it is classified as the "the spleen-warm syndrome", which means "overflow of five Qi". It is related with spleen and stomach dysfunction, and it has similarities with diabetes and metabolic syndrome in modern medicine. With respect to pathogenesis of the spleen-warm syndrome, "five flavors are stored in stomach after they enter into body. The spleen acts on them to circulate essential Qi. The body fluids are in the spleen, which is why it makes the mouth taste sweet. The patient is fat because of eating too much sweet and delicious food rich in fats. Fat causes internal heat, while sweet causes abdominal distension. Therefore, Qi rises and turns into polydipsia" [16]. This discussion of the spleen-warm syndrome in The Inner Canon of Huangdi elaborates the internal correlation between improper diet and diabetes. It points out that long-term excessive diet of high-fat and high-glucose food may hurt functions of spleen and stomach, resulting in dampness and heat as well as abnormal transmission and distribution of nutrients. This is preliminarily manifested as sweet taste and it may develop to be diabetes (symptom-complex of excessive eating) without intervention. This description agrees highly with the development mechanism from insulin resistance to diabetes in modern medicine, showing the foresight thinking of disease prevention in TCM.

Tong Xiaolin et al. believed that obesity is the cause of spleen-warm syndrome. Hence, it shall be intervened in early obesity stage, which is crucial to prevention of spleen-warm syndrome. He proposed four stages of diabetes development, namely, depression, heat, deficiency and damage. In the stage of depression, Qi, blood, phlegm, dampness and food coexist, which are corresponding to insulin resistance. In the stage of heat, there's physical heats in stomach and intestine, corresponding to compensatory hyperinsulinemia. In the stage of deficiency (middle stage), there are Qi deficiency and Yin deficiency, which are corresponding to failure of pancreatic β cells. In the stage of damage (late stage), there are Yin deficiency and Yang deficiency, which are corresponding to the stage of complications[17].

4 TCM Treatment of Diabetes

4.1 TCM

4.1.1 Obesity Type. Fat tissues in obesity T2DM can influence liver and fat tissues through secretion of proinflammatory factors from pro-inflammatory macrophages, thus inducing inflammatory responses and further intensifying insulin resistance. In clinics, TCM usually applies treatment of six depression types in the same time,

namely, Qi depression, blood stagnancy, phlegm depression, heat depression, dampness depression and food depression. Yidaokang No.2 is the commonly used drug in clinics. In Yidaokang No.2, Cyperi rhizoma, Curcuma aurantii and Aurantii aurantii regulate Qi and relieve Qi depression. Salvia miltiorrhiza, Notoginseng and red peony root promote blood circulation and relieve blood depression. Hawthorn and red rice yeast relieve food depression. Rheum officinale and Coptis chinensis are bitter cold and can clear heat depression. Rhizoma atractylodis and rhizoma alismatis combine dryness and smoothing to clear dampness. Stiff silkworm and Rhizoma Pinellinae Praeparata eliminate stagnation and reduce phlegm. Rhizoma Dioscoreae and radices trichosanthis tonify spleen and nourish Yin to protect healthy Qi. These ingredients are applied together to relieve six types of depression together[18].

4.1.2 Non-obesity Diabetes. Patients with non-obesity diabetes have deficiency of both Qi and Yin as well as syndrome of hepatic qi stagnation. Jinlida Granules which are commonly used in clinics are a Chinese herbal medicine composed of 17 herbs, including Ginseng, Poria cocos, Polygonatum, ophiopogon japonicas, Anemarrhena, Polygonum multiflorum, dogwood, etc. It can tonify Qi and spleen, nourish Yin, and generate body fluid[19].

Study demonstrates that patients with T2DM have more serious anxiety and depression than healthy people. Moreover, unhealthy emotions like anxiety and depression may accelerate progress of diseases[20]. In clinical test, the 8-week administration of Chai Shao Ping Xiao pills combined with conventional treatment can improve syndrome of hepatic Qi stagnation obviously.

4.2 Acupuncture Needles

Acupuncture needle therapy is to apply conventional acupuncture with filiform needles at acupoints, twisting, lifting, pressing, and so on. As a result, needles press down to form a sense of tightening, which is known as arrival of Qi. Moreover, needles will be kept for some period. Acupuncture needle intervention: adjust Qi and blood and improve metabolism. Principle of acupoint selection at core positions: acupuncture at Zusanli to invigorate spleen and eliminate dampness; acupuncture at Qixuan to clear heat and reduce blood glucose; acupuncture at Sanyinjiao to enrich Yin and nourish kidney; acupuncture at Xuehai to invigorate the circulation of blood and dredge collaterals. Common acupuncture schemes in clinics: simple obesity diabetes mainly focuses on reducing phlegm and dampness and adjusting metabolism. T2DM mainly focuses on tonifying Qi. Nervous lesions surrounding diabetes mainly improve nerve conduction and promote blood circulation to remove blood stasis. Modern studies show that acupuncture can adjust hypothalamus-hypophysis-target gland axis, and improve insulin secretion. Electric acupuncture needles are used to stimulate specific acupoints, which can strengthen secretion of glucagon-like peptide-1 and promote blood glucose control[21, 22].

4.3 Traditional Kongfu

Both TCM and western medicine therapy advocate healthy lifestyle and sports is one of major contents. Traditional Kongfu includes Tai Chi, Eight Trigrams boxing, five-animal boxing, etc. These exercises can improve glucolipid metabolism anomaly and body mass index obviously. For example, Tai Chi, a kind of aerobic exercise with middle and low intensity, can improve glucose use barrier of body by increasing energy consumption of skeletal muscles, thus lowering blood glucose[23].

5 Research Shortages and Challenges

The following points specify the current limitations in TCM and gut microbiota research for diabetes:

1) Traditional Chinese medicine has multiple ingredients and multiple targets, accompanied with high complexity of intestinal flora. There's no effective research method, because it is impossible to determine control effect of an ingredient over the specific flora. For example, it is difficult to isolate the effect of a single herbal component on a specific bacterial strain within a complex formula.

2) There's a lack of standardized clinical study. Many clinical trials on TCM interventions lack rigorous design, placebo controls, or standardized outcome measures, making it difficult to compare results across studies.

3) TCM refers to the precise therapy to some extent. It diagnoses after looking, smelling, questioning and feeling, and makes dialectical treatment. However, there are extremely individual differences of flora. It is significantly difficult to combine individual difference of flora control and dialectical treatment of TCM. The high inter-individual variability of the gut microbiome presents a major hurdle for developing personalized TCM protocols that effectively target both the patient's TCM pattern and their microbial profile.

4) TCM intervention can improve T2DM obviously, but it lacks prospective studies and long-term tracking observations. Most studies are short-term; long-term efficacy and safety data for TCM interventions are scarce.

6 Conclusions

Diabetes is a type of complicated metabolic diseases. Its occurrence and development are closely related with imbalance of intestinal flora and "the spleen-warm syndrome" theory in TCM. TCM shows unique advantages in adjusting glycometabolism and flora balance through multi-target intervention (e.g. compound traditional Chinese medicine, acupuncture and traditional Kongfu). In future, research on intervention mechanism and standardized clinical tests shall be strengthened to promote individual precise treatment. Future efforts should focus on elucidating the mechanistic links between TCM interventions and gut microbiota modulation, conducting high-quality randomized controlled trials, and developing integrative models that combine TCM diagnostics with microbiome analysis for personalized diabetes management.

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