

Microbial Networks and Immunometabolic Dysfunction in Diabetes: A Narrative Review

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<https://doi.org/10.67601/njbils.v3i2c.84>

Article info

Date received

23/08/2026

Date accepted

07/09/2026

Available online

30/09/2026

Keywords

Diabetes mellitus;
Microbiome;
Gut microbiota;
Oral microbiota;
Dysbiosis.

Abstract

Diabetes mellitus is a polyetiological disease with genetic predisposition and environmental factors, lifestyle, immune dysfunction and tissue specific metabolic disturbance playing a role. While hyperglycaemia and insulin resistance are hallmarks of diabetes, there is increased evidence that the microbial ecosystem plays a role in disease development and progression by interacting with host metabolism and immunity. Oral cavity, gastrointestinal tract and the interconnection of oral, gut and metabolic axes are important microbial interfaces between environmental factors and systemic metabolic regulation. This review addresses the emerging concept of microbial dysbiosis, epithelial barrier dysfunction, microbial metabolites, and immune activation in diabetics. Changes in oral and gut microbial communities can both lead to increased systemic inflammatory burden via periodontal inflammation and microbial component release, or by changes to intestinal permeability, endotoxin exposure, production of short-chain fatty acids, and bile acid metabolism. These processes may include, among many others, the impact on insulin sensitivity and β -cell function, as well as on the integrity of the vessels and on chronic inflammatory signalling. We will talk about evidence associating alterations in microbes with diabetes-associated metabolic dysfunction, and differentiate between known mechanisms from emerging hypotheses. We also discuss therapeutic potential related to diet manipulation, probiotics, prebiotics, and microbiome targeting, along with current challenges and the necessity for mechanistic validation. A holistic perspective of the oral-gut-metabolic axis may help to better understand diabetes as an environmentally triggered immunometabolic disease and could guide future prevention, risk stratification and targeted intervention.

Introduction

Diabetes mellitus is one of the greatest health and social problems in the world, affecting hundreds of millions of people around the world and causing a

large burden of cardiovascular disease, kidney failure, neurological problems, visual impairment and shortened lifespan. Diabetes is a clinically diagnosed disease in which there is chronic hyperglycaemia caused by inadequate insulin



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production or action or a combination of both, but the biological mechanisms involved in the onset of diabetes are much more complicated (Siam et al., 2024).

Older paradigms of diabetes have largely been centered on genetic risk factors, metabolic disturbances, obesity and lifestyle. Although these are basic factors, there is increasing evidence to indicate that interactions with the host's microbial environment are an extra layer of regulation that help shape metabolic health. The human microbiome – the collection of microbial communities found in anatomical locations such as the oral cavity and gastrointestinal tract – is an important biological interface between exposure to the environment and immune and metabolic processes (Ussar et al., 2016; Antar et al., 2023).

The microbiome concept as a metabolic control has revolutionized the understanding of chronic metabolic diseases. Microorganisms can alter host physiology in several ways, such as by acting on nutrient processing, influencing the production of bioactive metabolites, regulating the integrity of the intestinal barrier, and modulating immune responses. However, when host–microbe interactions are disrupted, they can cause metabolic imbalance and immune dysfunction. But this can turn into a dysbiosis that can foster inflammatory states linked with metabolic dysfunction (Li et al., 2026).

The oral cavity is one of the first microbial habitats colonized by humans and is home to complex microbial communities that constantly interact with mucosal immune tissues. Diabetic individuals have more severe and prevalent periodontal disease, and this is an important case where microbial inflammatory mechanisms are linked to systemic metabolic disturbances. Chronic periodontal inflammation can lead to raised levels of circulating inflammatory mediators and the inflammatory burden that is associated with metabolic disease (Peng et al., 2022).

Likewise, the gut microbiome has come to the fore as a crucial player in metabolic health. Microbial metabolites and interaction with intestinal epithelial and immune cells are involved in the regulation of glucose metabolism, lipid handling, immune development and energy balance by the gut microbiota. Diabetes related complications, insulin resistance and obesity related metabolic abnormalities have been linked to dysregulated microbial composition and function. The exact cause and effect, however, are still an area of investigation (Li et al., 2026).

Disruption of intestinal barrier is a major mechanism connecting microbial alterations with metabolic disease. Increased permeability can allow microbial components to enter the circulation, triggering innate immunity pathways and lead to chronic low-grade inflammatory activity. This process, also known as metabolic endotoxaemia, may serve to establish a mechanistic association between microbial imbalance and insulin resistance (Ghosh et al., 2020; Li et al., 2026).

In addition to microbial composition, there has been a growing interest in microbial function and metabolite production. Microbial metabolites such as short-chain fatty acids and bile acid derivatives interact with immune cells, endocrine signalling systems, and metabolic tissues to impact host metabolism. The results indicate that the metabolic impact of microbiome changes could be related to the metabolic activity of the microbes as well as the presence of specific microbes (Mu et al., 2026).

Although significant strides have been made, there are still issues to be addressed. Many studies of the microbiome have found associations, but not cause, and there are differences in diet, geographical location, medication, stage of disease and analytic methods between studies. Hence, there is a need for careful interpretation to distinguish established mechanisms from emerging hypotheses (Ece et al., 2026). The oral–gut–metabolic axis is presented in this review as a unified pathway that may affect the progression of diabetes, with an examination of

new therapeutic strategies utilizing the microbiome, and an identification of research priorities.

The Microbiome as an Immunometabolic Organ

Microbial Ecosystems as Regulators of Host Metabolism

The human microbiome is a complex ecosystem that plays a role in the regulation of metabolism, development of the immune system and maintaining physiological balance. While once regarded as passive residents of mucosal surfaces, there is compelling evidence that microbial communities are now thought to be an active metabolic organ that influences host energy metabolism and disease susceptibility (Sun et al., 2025; Aggarwal et al., 2022).

The gastrointestinal microbiome consists of billions of microorganisms that are involved in nutrient transformation, the production of metabolites and the regulation of host signalling pathways. These functions play a role in a number of processes that are important in diabetes, such as glucose homeostasis, lipid metabolism, energy extraction, immune regulation, and intestinal barrier maintenance (Wu et al., 2020).

Normally, microbial ecosystems are in dynamic equilibrium with the host. The beneficial microbial functions have a role in maintaining the integrity of the epithelium, in regulating immune tolerance, and in maintaining metabolic stability. But this balance can be disturbed, affecting host physiology and inducing inflammatory conditions related to metabolic disease (Cortés et al., 2025).

Microbial Regulation of Glucose and Energy Metabolism

One of the major ways that the microbiome affects metabolism is by affecting energy balance and nutrient processing. The intestine contains microorganisms which aid in the digestion of food components that cannot be degraded by human enzymes. These microbes produce metabolites

which interact with host metabolic pathways (Rowland et al., 2017). Key microbial derived metabolic signals include:

Short-chain Fatty Acids (SCFAs)

Microbial fermentation of dietary fibre creates SCFAs, such as acetate, propionate and butyrate. These metabolites have a variety of effects on epithelial function, immune control, glucose metabolism and insulin sensitivity within the intestine. Butyrate, especially, plays a role in maintaining the barrier integrity of the intestine, and promotes energy metabolism and regulates tight junction function in the epithelia. Therefore, a decrease in production of beneficial metabolites can lead to a compromise in the barrier and inflammatory activation (Kalkan et al., 2025).

Regulation of Host Hormonal Signalling

Microbial metabolites have the potential to affect the enteroendocrine pathways that regulate glucose. Interaction between microbial products and host receptors can influence the secretion of glucagon-like peptide-1 (GLP-1), insulin responses, appetite control and energy expenditure. These mechanisms create a biotic connection between the activity of microorganisms and the control of the metabolism systemically.

Microbiome-Immune System Communication

The microbiome is a key factor in regulating immune function. The intestinal immune system is in constant contact with microbial communities, balancing tolerance to beneficial organisms with defence against harmful organisms (Yurtseven et al., 2025). This interaction takes place in several ways; pattern recognition receptor activation, inflammatory signalling pathways, and immune cell regulation

Recognition of Patterns by Activation of Pattern Recognition Receptors

Microbial molecules engage the host immune receptors such as Toll-like receptors (TLRs), nucleotide-binding receptors, and other innate immune sensors. These interactions are important

for immune regulation under physiological conditions. But over-exposure to microbial inflammatory signals can lead to activation of chronic inflammatory pathways.

Inflammatory Signalling Pathways

A microbial imbalance could foster activation of metabolic inflammation pathways such as NF- κ B signalling, cytokine production, and inflammasome activation. These pathways share a high degree of overlap with the same pathways that mediate systemic insulin resistance, and show that subclinical microbial exposure exerts a close and bidirectional association with host immunometabolic dysfunction.

Immune Cell Regulation

The microbiome regulates the activity of macrophages, the maturation of regulatory T cells and inflammatory immune responses. The loss of diversities or the imbalance in functional groups of microbes can lead to a shift in immune activity towards a more inflammatory state, which can lead to insulin resistance and metabolic deterioration.

Dysbiosis and Metabolic Disturbance

Dysbiosis is a disturbance in the relationship between the microbial community and host. This can be associated with changes in microbes, decreased diversity, dysfunction of the microbes and abnormal production of metabolites. Diabetes has been linked to dysbiosis, which is linked to insulin resistance, obesity-associated inflammation, glucose regulation dysfunction, and cardiovascular risk.

Nevertheless, care should be taken when interpreting data from microbiomes studies. The changes in microbes seen in people with diabetes could be a factor which helps the disease develop, metabolic dysfunction or reactions to drugs, diet or lifestyle changes. Thus, the available evidence suggests that there is a complex, bi-directional relationship, which does not point exclusively in one direction.

Microbial Contributions to Insulin Resistance

The mechanisms linking changes in insulin sensitivity and microbial alterations are several:

Enhanced inflammatory signalling: Dysbiosis can lead to enhanced production or circulation of microbial components that activate inflammatory pathways, including lipopolysaccharide (LPS), microbial cell wall components and other microbial inflammatory molecules. These signals are able to trigger immune pathways that are able to disrupt insulin receptor signalling.

Metabolite production: Metabolite production is altered by changes in microbial metabolism, which impacts the production of metabolites involved in glucose regulation, lipid metabolism and inflammation. Metabolic imbalance is caused by a decreased amount of metabolites that are beneficial to the body and an increased amount of metabolites that are potentially harmful.

Healthy intestinal barrier function: Intake of microbial products is regulated to not pass through the intestinal barrier in excess. Breaches in the integrity of barriers increases exposure to microbes which leads to systemic inflammatory activation.

The Oral Microbiome–Diabetes Connection

The Oral Cavity as a Metabolic–Immune Interface

The oral cavity is one of the biggest microbiological ecosystems in the human body and is also important interface between the exposure to the external environment and systemic physiology. The oral cavity is not only a local microbial environment, but also continuously interacts with immune tissues, vascular networks and metabolic pathways (Sedghi et al., 2021).

The oral microbiome is a collection of different bacteria species, living in complex biofilm communities that are in a normal and balanced relationship with the host. Physiologic conditions, the microbial communities play roles in immune

education and maintenance of mucosal homeostasis. But when the balance is disturbed, it can lead to a chronic inflammatory condition, not just in the oral cavity, but in the whole body (Rajasekaran et al., 2024).

The association of microbial imbalance with systemic metabolic dysfunction is highlighted by the example of diabetes. Diabetics are more prone to periodontal disease and periodontal inflammation can lead to systemic inflammatory burden and metabolic control problems. This bidirectional relationship indicates that oral health is closely intertwined with metabolic health, highlighting the essential role of oral health in the overall immunometabolic system (Zhao et al., 2023).

Diabetes and Increased Susceptibility to Periodontal Disease

Periodontal disease is an ongoing inflammatory condition that attacks the supporting structures of the teeth and is a common inflammatory disease globally. The prevalence, severity and progression of periodontal disease has been consistently shown to be higher among people with diabetes (Hasan et al., 2025). There are several reasons why this occur, for example impaired immune regulation occur because diabetes affects immune function by affecting neutrophil function, inflammatory response and the resolution of inflammation. Immune activation is necessary to deal with microbial exposure; however, dysfunctional response results in excessive tissue inflammation and destruction.

Chronic metabolic stress leads to altered tissue repair processes, affecting collagen metabolism, vascular function and wound healing. These alterations make the periodontal tissues less susceptible to repair from inflammatory injury. Consequences of High Glucose: Hyperglycaemic Environment – causes changes in the oral environment which affect the growth of microbes, the production of inflammatory mediators and host

defence mechanisms, favouring the maintenance of periodontal inflammation.

Periodontal Inflammation as a Contributor to Systemic Metabolic Dysfunction

Diabetes raises the risk of periodontal disease, and there is evidence of the reverse effect, too: periodontal inflammation affects systemic metabolic regulation. A proposed mechanism is the transfer of inflammatory mediators and microbial components from periodontal tissues to circulation. The process may be briefly described in Figure 1.

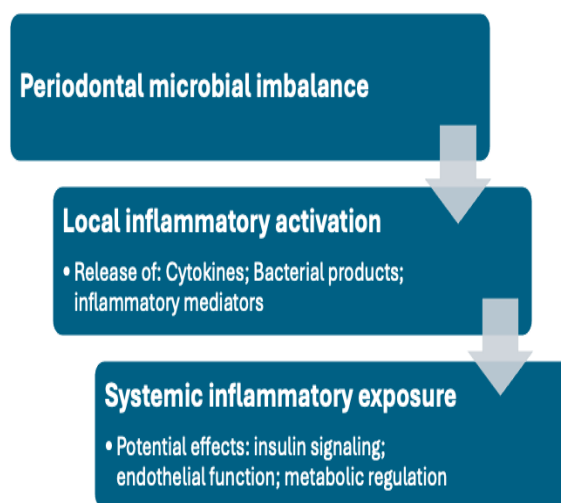


Figure 1: Metabolic Dysfunction Pathway
Microbial Components Linking Oral Dysbiosis to Inflammation

Some periodontal microorganisms have received interest due to their effect on host immune responses:

Porphyromonas gingivalis: A significant periodontal pathogen that can influence immune responses, inflammatory signalling and tissue homeostasis. Experimental research indicates that *P. gingivalis* contact can impact systemic inflammatory pathways, but as of yet it is not possible to conclude that a single organism straightaway causes diabetes (Mei et al., 2020).

Tannerella forsythia and *Treponema denticola*: These organisms increase the complexity of periodontal biofilm and activation of inflammation. They are relevant to metabolic disease due to their association with increased inflammatory signalling, changes in host-microbial interactions and contribution to the severity of periodontal disease.

Biological Pathways Connecting Oral Inflammation and Diabetes

The connection between periodontal disease and metabolic dysfunction is due to multiple mechanisms that are interlinked:

Cytokine-Mediated Inflammation: Periodontal inflammation leads to increased production of mediators including IL-1 α , IL-6 and TNF- α . These molecules have the potential to act as signals of systemic inflammatory processes and to affect insulin sensitivity.

Chronic periodontal inflammation increases production of Reactive Oxygen Species increasing tissue damage, endothelial dysfunction and amplifying inflammation.

Microbial Translocation: Inflammatory periodontal tissues increase the exposure of microbial components, which can lead to activation of systemic immune responses through activating Toll-like receptor, NF- κ B signalling and activation of inflammasome.

The Bidirectional Relationship between Periodontal Disease and Diabetes

The bidirectional link between diabetes and periodontal disease is becoming more and more realised. Diabetes can affect oral disease in several ways: decreased immunity, a different oral microbial environment, and delayed repair. In turn, periodontal disease affects the diabetes by systemic inflammation, elevated levels of inflammatory mediators, and possible impact on insulin sensitivity. This correlation implies that there is a link between oral health management and comprehensive metabolic management.

Gut Microbiome Dysfunction in Diabetes

Psychosocial Stress and Mental Illness

The gastrointestinal microbiome is a highly influential regulator of host metabolic physiology, and is a key factor in diabetes susceptibility and progression. Gut dysbiosis is a more global shift in the microbial composition, diversity and functional activity that impacts the host-microbiota metabolic interaction (Mendis et al., 2025). Metabolic disease in people is linked to changes in gut bacteria, which affect glucose control, insulin resistance, obesity-related inflammation, lipid metabolism and heart and blood vessel risk.

But there are many other factors that significantly influence microbiome changes in diabetes such as diet, geographic location, drug use, duration of the disease, obesity, and glycaemic control. Thus, the association between gut microbiota and diabetes must be considered as a dynamic interaction (not as a single microbial signature that causes diabetes).

Mechanisms Linking Gut Dysbiosis to Diabetes

Reduced Microbial Diversity and Functional Imbalance

Healthy microbial communities are highly diverse and redundant, and can adapt to shifts in nutrition and environment. In metabolic diseases, a decreased diversity is linked to the decrease in production of beneficial metabolites, increase in inflammatory potential and decrease in intestinal resilience. The functional changes could be more relevant than just differences in the abundance of microorganisms. If there is a similarity of microbial function, the microbial constituents of two individuals might be different yet achieve the same metabolic results.

Intestinal Barrier Dysfunction and Metabolic Endotoxaemia

The intestinal barrier is a key point of interaction between the microbial community and host tissues. A healthy gut barrier allows for regulated inter-

communication between microbes and immune cells, and limits the transfer of microbial elements from the gut into the bloodstream (Neurath et al., 2025). Metabolic disease leads to increased breach of barrier integrity, and systemic inflammation.

Loss of Intestinal Barrier Integrity

Barrier dysfunction is caused by changes in tight junction proteins, increased permeability and loss of mucosal defence. The occludin, claudins and zonula occludens proteins are important structural components. Impaired integrity provides access to microbial molecules into the circulation triggering immune responses.

Lipopolysaccharide and Metabolic Inflammation

Lipopolysaccharide (LPS) is a part of the cell wall of Gram-negative bacteria that may be involved in the connection between alterations in gut microbiota and metabolic inflammation. LPS levels in circulation are increased (metabolic endotoxaemia), which results in the activation of Toll like receptor 4 signalling, NF- κ B activation, and inflammatory cytokine production. The inflammatory environment that is created leads to impaired insulin signalling, adipose inflammation and endothelial dysfunction. The clinical significance of metabolic endotoxaemia in the different studies is however varied and additional studies are needed to understand the role of metabolic endotoxaemia at different phases of diabetes.

Microbial Metabolites as Mediators of Host Metabolism

Chemical communication between microorganisms and host tissues is a key factor in microbial function (Aggarwal et al., 2022). The effects of microbial metabolites on immune regulation, glucose metabolism, lipid handling and endocrine signalling are listed in Table 1.

Short-Chain Fatty Acids

The SCFAs are major products of fermentation by gut bacteria of dietary fibre, these are primarily

acetate, propionate and butyrate. These metabolites have several mechanisms to regulate metabolism:

Butyrate is a major energy source for intestinal epithelial cells; maintains tight junctions, protects mucosa and barrier stability. Less production of SCFA leads to greater intestinal permeability and inflammation.

Table 1: Microbial Factors Associated with Diabetes-Related Metabolic Dysfunction

Microbial Factor	Mechanism	Potential Metabolic Effect
Reduced microbial diversity	Loss of functional balance	Increased metabolic vulnerability
Reduced SCFA production	Impaired barrier and immune regulation	Insulin resistance
Increased LPS exposure	TLR4 activation	Chronic inflammation
Altered bile acid metabolism	FXR/TGR5 signalling changes	Glucose dysregulation
Periodontal dysbiosis	Cytokine activation	Increased inflammatory burden

Immune Regulation: SCFAs modulate immune responses via their ability to regulate the generation of regulatory T cells, production of inflammatory cytokines and tolerance, which can help to regulate systemic inflammatory states in diabetes.

Metabolic Signalling: SCFAs are able to bind to host receptors such as G protein coupled receptors and modulate metabolic signalling pathways, impacting on glucose metabolism, insulin sensitivity and energy metabolism.

Microbial Regulation of Bile Acid Metabolism

Another important pathway between gut microorganisms and host metabolism is the bile

acids. Secondary bile acid metabolites, created by microbial metabolism in the intestine, affect host signalling pathways; their production is linked to the production of primary bile acids in the liver. Important pathways include:

Farnesoid X receptor (FXR): Tonic control of bile acid metabolism, glucose homeostasis and lipid metabolism.

Takeda G-protein receptor 5 (TGR5): Regulates energy expenditure, GLP-1 secretion, and metabolic regulation.

Therefore, the altered microbial modification of bile acids could be a factor in the metabolism of diabetes-related pathways.

Trimethylamine-Related Pathways

Trimethylamine (TMA) can be generated by dietary components through microbial metabolism, and then form trimethylamine N-oxide (TMAO) in the liver. High levels of TMAO have been linked to cardiovascular risk, changes in lipid metabolism, and inflammatory responses. While the connection between TMAO and diabetes is still multifaceted, this pathway serves as an example of the production of a systemic signal that is associated with metabolic health and comes from microbial metabolism.

Gut Microbiome and Insulin Resistance

Microbial imbalance, barrier dysfunction, and changes in the production of metabolites are all thought to play a role in insulin resistance, in the following proposed sequence (Figure 3).

Gut Microbiome and Diabetes Complications

There is growing evidence that gut microbial disturbances are involved in the development of diabetes and in the complications of diabetes such as cardiovascular complications (through inflammatory activation, and through altered lipid metabolism); kidney disease (through increased circulating microbial products and altered clearance of metabolites); vascular inflammation (due to endothelial dysfunction and oxidative stress).

The Oral–Gut–Metabolic Axis: An Integrated Disease Model

Conceptual Framework of the Oral–Gut–Metabolic Axis

It is important to consider the oral cavity, gastrointestinal tract and microbial ecosystems together when understanding the relationship between microbial ecosystems and diabetes. Recent studies have shown that various microbial communities in the body are tightly coupled and communicate with other host immune and metabolic systems, establishing a body-wide network of oral–gut–metabolic axis communication (Ni et al., 2026). This axis encompasses an oral microbial community, gastrointestinal microbiota, epithelial barrier function, immune signalling, microbial metabolites, and systemic metabolic regulation.

Environmental Factors as Initiators of Microbial Disturbance

Microbial ecosystems change rapidly as a response to changes in environment. Diabetes risk factors can act in concert to affect microbial composition and host metabolism. One of the most potent regulators on microbial structure and function is diet. A high intake of refined carbohydrates, saturated fats and ultra-processed foods could favour microbial patterns associated with decreased diversity, decreased production of metabolites and increased inflammatory signalling. In contrast, a dietary pattern with a high amount of dietary fibre, plant-derived nutrients and a variety of food sources fosters bacterial populations capable of generating metabolites beneficial for human health, such as short-chain fatty acids.

Implications for the Sub-Saharan African Lifestyle Transition

The shift from traditional agrarian diet to westernised, ultra processed diet experienced in Nigeria provides an acute epidemiological mirror to this microbial change. The typical Nigerian diet has been rich in complex carbohydrates,

fermentable fibres, and a variety of plant-based nutrients (including sorghum, millet and indigenous yams), which in the past, has promoted a diverse microbial ecosystem in the gut and facilitated the production of short-chain fatty acids (SCFAs). Moreover, fermented functional foods are naturally introduced in the region, such as Ogi (fermented maize/sorghum sludge), Ugba (fermented African oil bean seeds) and Dawadawa/Iru (fermented locust beans), which strengthen the intestinal barrier integrity along with the introduction of beneficial lactic acid bacteria and prebiotics. On the other hand, the surging trend of consumption of highly processed carbohydrates and sugary drinks in contemporary urban centres of Nigeria throw this balance out of whack. This dietary change leads to a condition of local dysbiosis that compromises the mucosal defence mechanisms and sets in motion a cascade of metabolic endotoxemia, leading to the increasing incidence of Type 2 Diabetes Mellitus (T2DM) in the region.

From Oral Dysbiosis to Systemic Inflammation

Oral cavity is a first point of contact of environmental exposure and host immunity. The imbalance in oral microbiota brought about by environmental exposure causes periodontal inflammation. This local inflammatory reaction results in systemic release of microbial components, inflammatory cytokines and immune mediators into the blood stream. This prolonged exposure has direct effects on insulin sensitivity, the function of the vascular endothelial cells, and regulation of broader metabolism.

Gut Microbial Dysfunction as a Metabolic Amplifier

Exposed to environmental and dietary stress, changes to gut microbial communities exacerbate metabolic dysfunction by disrupting gut permeability, producing different metabolites, and leading to chronic immune activation. This decreased barrier function leads to more leakage of microbial products into the blood stream and

continual activation of the innate immune system. At the same time, shifts in microbial activity leads to the production of shorter-chain fatty acids, bile acid conjugates and other bioactive metabolites, which helps to further exacerbate systemic insulin resistance.

Integrated Oral–Gut–Metabolic Disease Model

The suggested integrated model consists of four successive phases:

Stage 1: Environmental Influence: Diet, obesity, lifestyle, medication exposure, and genetics.

Stage 2: Microbial Ecosystem Alteration: Perturbs periodontal tissue, generating microbial inflammatory signals and dysbiosis in the oral microbiome and disruption of the gut microbiome, along with altered metabolites.

Stage 3: Immune and Metabolic Consequences: Triggers inflammatory pathways, oxidative stress responses, and immune signalling networks, thereby impacting insulin sensitivity, β -cell function and vascular health.

Stage 4: Diabetes Progression: Associated with the progression of metabolic dysfunction and the increased risk of complications, with a changed disease course.

Evidence Strength and Current Knowledge Gaps

While the oral–gut–metabolic axis is a promising mechanism, there are some key caveats to be noted. Many ongoing microbiome research projects now report the presence of difference between diabetes patients and those without diabetes, but are not able to determine if the differences are a cause of diabetes, a consequence of metabolic issues or simply a difference between lifestyles. In order to establish directionality, longitudinal studies are needed. Moreover, there is also considerable inter-person variability in the microbial community resulting from geographic, dietary, genetic, medication, and age differences among people, suggesting that there may not be a common "diabetes-associated microbiome signature". In future studies, the emphasis should not just be on

the microbial classification, but also on the activity of the microbes, production of metabolites, and interactions between the host and the microbes.

Biotechnological and Infrastructural Challenges in Regional Research

While these microbial dynamics can be translated to actionable clinical biomarkers, this calls for new levels of molecular surveillance which poses unique infrastructural challenges to the Nigerian research ecosystem. Most research in Africa is limited by the frequency of power outages, cold-chains for sample storage, and the high cost of sequencing reagents as well as a lack of bioinformatic pipelines that are specifically designed for African microbiome profiles which is heavily used in Western paradigms for deep shotgun metagenomics and untargeted metabolomics. New tools to fill the existing knowledge gaps and overcome these limitations

require the use of cost-effective, high-throughput biotechnology tools such as targeted sequencing of the 16S rRNA gene and targeted organic acid chromatography at the regional level. The establishment of local biorepositories and open-access metagenomic databases of Nigerian cohorts is a crucial step in the progression from microbial identification to real precision metabolic medicine.

Implications for Diabetes Research

Implications of the oral-gut-metabolic axis: Diabetes prevention strategies could take into account microbial health along with the established metabolic risk factors; and oral health is a neglected aspect of metabolic disease management.

In addition, microbiome research could also play a role in the future in the prediction of disease risk, biological stratification, and targeted intervention.

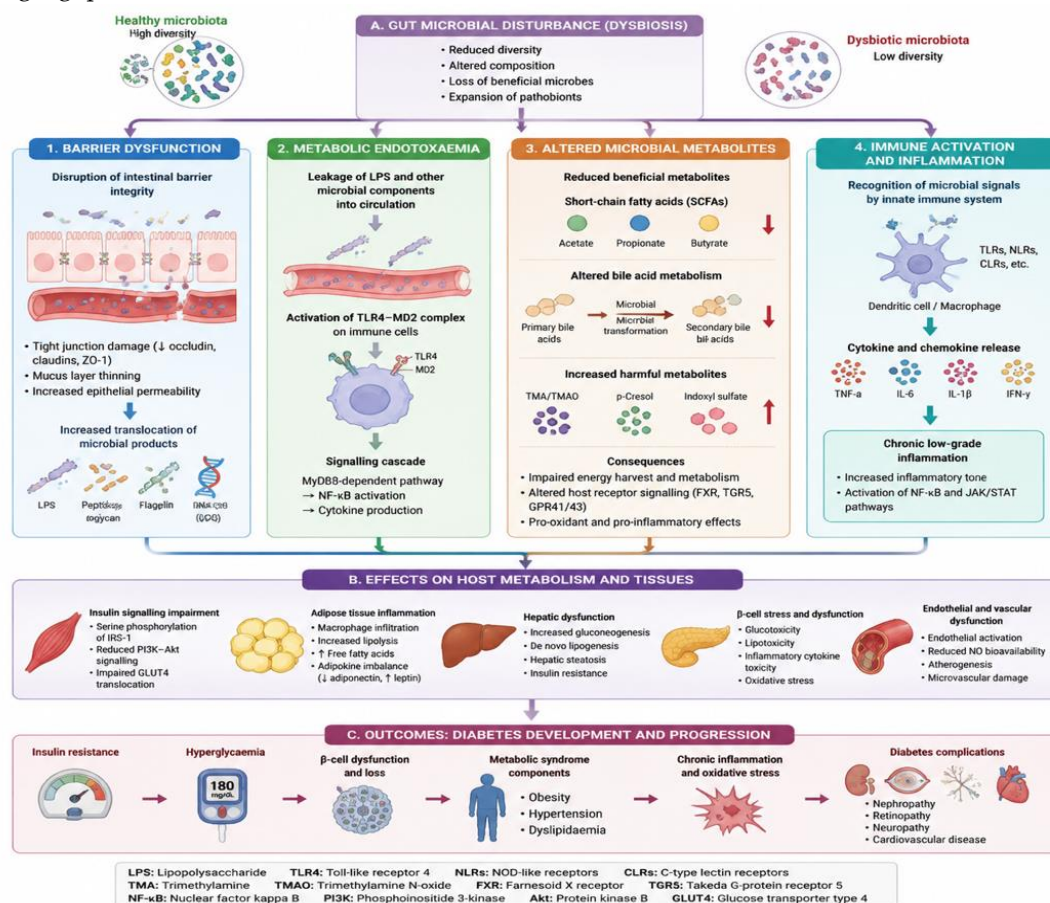


Figure 2. Microbial mechanisms contributing to diabetes-related metabolic dysfunction

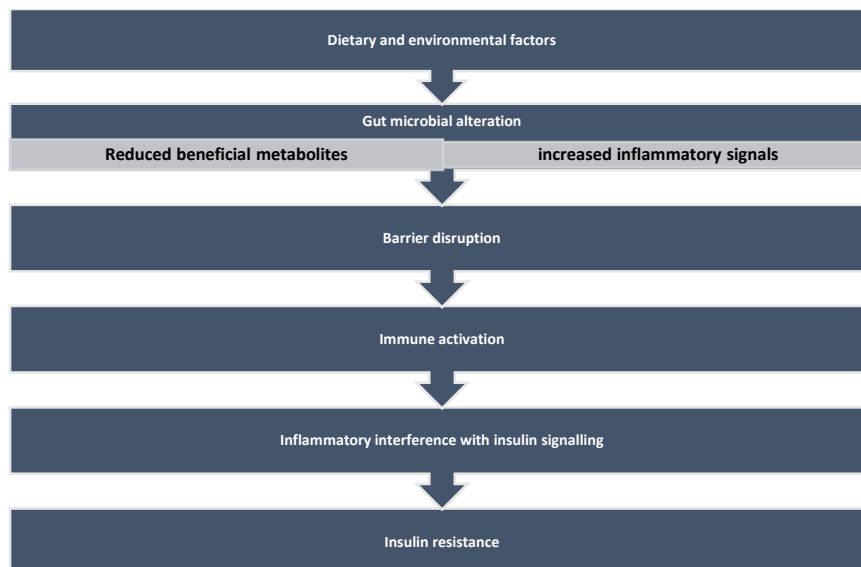


Figure 3: Combined effect of Microbiome on Insulin Resistance

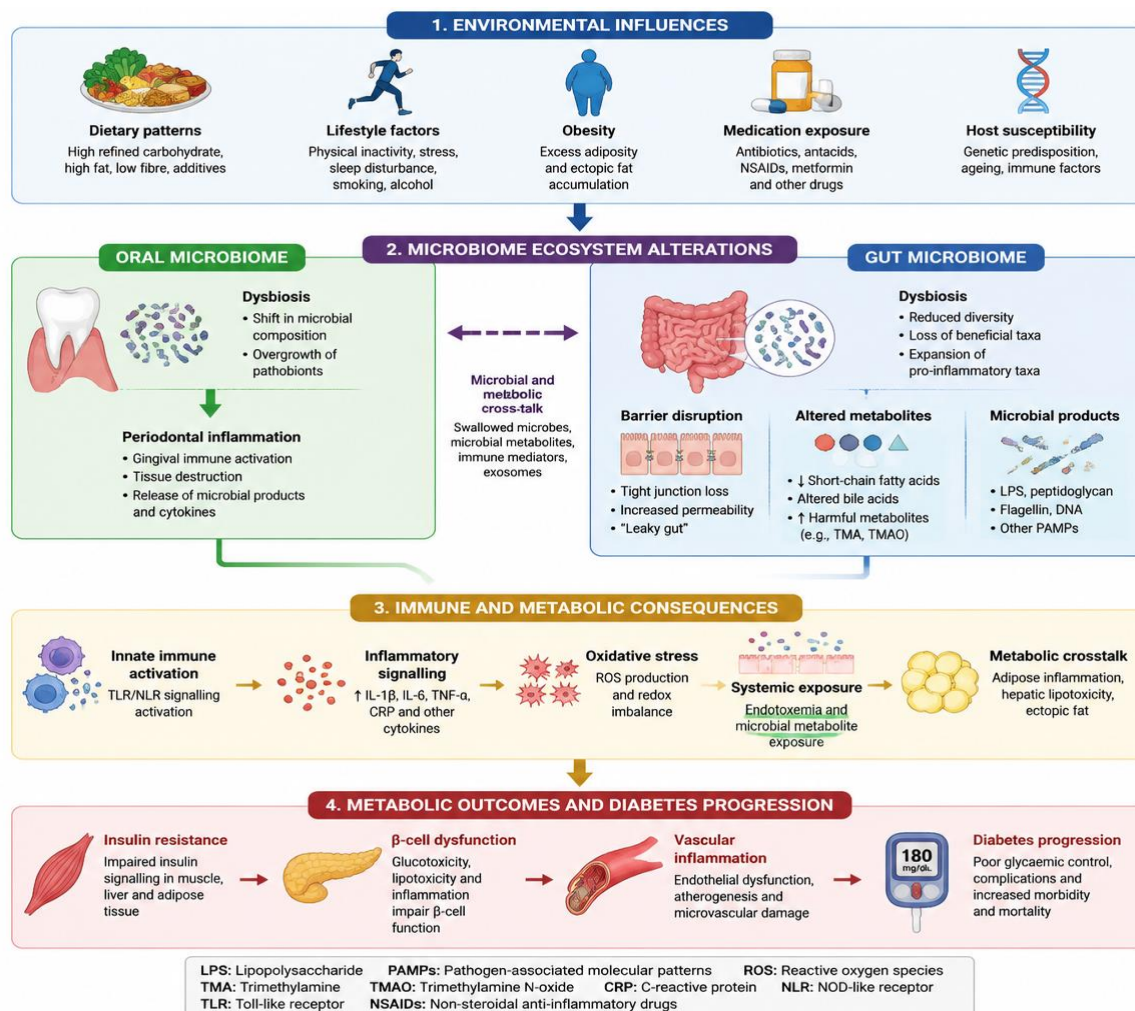


Figure 4. The oral–gut–metabolic axis linking microbial ecosystems with diabetes progression

Therapeutic Opportunities and Limitations in Microbiome-Targeted Diabetes Management

Rationale for Microbiome-Directed Therapeutic Strategies

The idea of using microbiome-based strategies is to have an impact on upstream biological processes such as the structure of the microbiome, production of metabolites, function of the intestinal barrier, regulation of the immune system, and inflammatory signaling—processes that are different from what is done by traditional strategies aimed at glucose regulation. The challenge to translate to clinical therapies is still challenging however due to the individualisation of microbial ecosystems. So, for now, microbiome-based treatments must be seen as a complement, not a substitute, to current diabetes care plans.

Dietary Modulation of the Microbiome

Diet is one of the most potent and accessible tools to manipulate microbial ecosystems. The diet influences the diversity of microbes, the production of metabolites, the integrity of the gut barrier and inflammatory responses.

Intestinal barrier integrity: Dietary Fibre offers substrates for microbial fermentation and stimulates the production of beneficial metabolites such as short-chain fatty acids which in turn positively affects immune regulation and the integrity of the intestinal barrier.

Plant-based Dietary Patterns: Dietary patterns that are high in fruits, vegetables, legumes, and whole grains are linked to higher diversity of microbes and more metabolites that are beneficial, which leads to better glycemic control, inflammation, and cardiovascular risk.

Probiotics and Prebiotics

Probiotics

Probiotics are active microbes that are taken to give health benefits. This can occur through a variety of mechanisms such as strengthening of the intestinal

barrier, inhibiting the growth of pathogenic microorganisms, immune modulation, and changing the production of metabolites. A few clinical trials have shown a modest beneficial effect of probiotics on glucose control, inflammatory markers, and lipid parameters, but results have been variable, depending on the types of bacteria used and their dosage, length of the intervention, and characteristics of the participants.

Prebiotics

Prebiotics are foods that selectively promote the growth of beneficial microorganisms, e.g. inulin, resistant starch and fermentable fibres. The benefits may be an improved production of short-chain fatty acids, an improved gut barrier function, and a better metabolic signalling. Prebiotic strategies work by helping to maintain the microbial community that already exists in a person's body, while probiotic strategies involve adding specific microorganisms to the body.

Microbiota-Directed Therapeutic Approaches

Faecal Microbiota Transfer (FMT): has shown potential to modify microbial make up, is being used in metabolic diseases to restore microbial diversity and to regulate inflammation. But remains very experimental in the field of diabetes because of donor selection, long-term safety and regulatory concerns.

Targeted Microbial Engineering: The development of new techniques in biotechnology has renewed interest in targeted modification of microbial functions through the use of engineered microorganisms and precision microbial modulation, which are still in the early research stages.

Metabolite-Based Therapeutic Strategies

The use of targeting microbial metabolites is an attractive therapeutic approach:

Short-Chain Fatty Acid Pathways: Focusing on pathways that enhance the production of beneficial SCFAs can lead to enhanced epithelial integrity, immune regulation and metabolic signalling.

This could involve modulation of bile acid transformation by microbes which could affect FXR pathways, TGR5 signalling and glucose metabolism.

Pathways of inflammatory metabolites – Microbial metabolites could produce harmful metabolites leading to systemic inflammatory activation – Reduced production or effects of harmful metabolites could reduce systemic inflammatory activation.

Table 2: Microbiome-Based Therapeutic Strategies in Diabetes

Strategy	Proposed Mechanism	Current Evidence	Major Limitation
Dietary modification	Improves microbial diversity and metabolites	Moderate evidence	Individual variability
Probiotics	Modulates microbial balance	Emerging evidence	Strain-specific effects
Prebiotics	Supports beneficial microbes	Emerging evidence	Variable response
Microbial metabolites	Targets host signalling pathways	Experimental	Translation challenges
Faecal microbiota transfer	Microbial ecosystem replacement	Early-stage evidence	Safety and durability

Integration of Oral Health into Diabetes Management

Possible interventions involve periodontal screening and improved oral hygiene habits, treating periodontal inflammation, and integrated dental and metabolic care. Since periodontal disease and diabetes impact each other, treatments for periodontal disease can have a positive impact on the entire metabolic picture and may help to lessen the inflammatory impact.

Challenges in Translating Microbiome Science into Clinical Practice

Several factors impede immediate clinical use: biological complexity (thousands of interacting organisms), absence of universal microbial signatures (profiles change by age, geography, diet, medications and genetics), potentially unspecified causality (based on associative data) and standardisation issues (explainable by the differences in sequencing methods and analytical pipelines).

Conclusion

The new paradigm of the oral–gut–metabolic axis offers a more comprehensive perspective on diabetes as a disease that is shaped by environmental, microbial, immune and metabolic interactions. Although genetic susceptibility, insulin resistance and hyperglycaemia remain the main factors examined by traditional models, there is emerging evidence that the microbial community is a significant biological interface between external exposures to internal systems regulating metabolism.

Disruption of these microbial ecosystems could facilitate inflammatory activation via periodontal inflammation, intestinal permeability, changes in microbial metabolisms and increased exposure to microbial-derived inflammatory signals. There is a significant link between microbial dysfunction and the progression of diabetes as suggested by the current evidence; however, there are numerous suggestions on how these factors may be involved as mechanism that still need to be tested with long-term human studies. Going beyond just identifying differences in microbes to understanding microbial function, host–microbe interaction, and relevant clinically useful biomarkers should be the subject of future research.

Acknowledgement

The authors have no acknowledgement to declare.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of the paper.

Author Contribution

The authors confirm contribution to the paper as follows: Conceptualization and draft manuscript: Author A.A.I., Author S.I.; manuscript writing and editing: Author S.I., Author F.Y.M., Author S.S.D. All authors reviewed and approved the final version of the manuscript.

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