Journal of Population Therapeutics & Clinical Pharmacology

Microbiome Influence on *Endocrine Function*: A Novel Approach to Type 2 Diabetes Treatment

Monalisa Khuntia[1], Prof. Susant Mishra[2], Dr. Rajesh Kumar Padhi[3], Ramaballav Mahapatra[4], Arundhati Guru[5], Sanjay Chand[6], Dr. Soumya Sucharita[7], Prof. Abhaya Kumar Sahoo[8], Dr. Hariballav Mahapatra[9*]

[1]MSW, NDEP, PhD Scholar (Rural Management)
[1]School of Rural Management, KIIT University, Bhubaneswar, India
[1]Sevayan Diabetes Centre, Puri, India

[2]MBBS, MS, MCh
[2]Dept. Of Burns, Plastic and Reconstructive Surgery, IMS & SUM Hospital, SOA University, Bhubaneswar, India
[2]Shree Hospitals, Bhubaneswar, India

[3]MBBS, MD, DM
[3]Dept. Of Nephrology, KIMS, KIIT University, Bhubaneswar, India
[3]Kalinga Hospital, Bhubaneswar, India

[4]MSW, MTA, PGDYM, NDEP, PhD Scholar
[4]Utkal University of Culture, Bhubaneswar, India
[4]Sevayan Diabetes Centre, Puri, India

[5]MBBS 3rd Year
[5]Vinayak Mission Medical College, Puducherry, India
[5]Sevayan Diabetes Centre, Puri, India

[6]MA in Phil, NDEP
[6]Government Women's College, Puri, India
[6]Sevayan Diabetes Centre, Puri, India

[7]BHMS
[7]Sevayan Diabetes Centre, Puri, India

[8]MBBS, MD, DM
[8]Dept. of Endocrinology, Apollo Hospitals, Bhubaneswar, India

[9*]MBBS, MHSc, PGD Clin Endo, DipDiab, FDRC
[9*]Shree Hospitals, Bhubaneswar, India,[9*]Sevayan Diabetes Centre, Puri, India

[*]**Corresponding Autor:**Dr. Hariballav Mahapatra
MBBS, MHSc, PGD Clin Endo, DipDiab, FDRC
Sevayan Diabetes Centre, Puri
Shree Hospitals, Bhubaneswar
nullandzero@gmail.com

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Abstract –

Increasing incidence of T2D has led to the focus of the scientific community for developing alternative therapeutic approaches to meet challenges of present-day drug therapies. This paper aims at exploring the effect of the microbiome on endocrine activity primarily considering the effect of the composition of gut microbiota to glucose and insulin. In reviewing the current literature, we identify ways though which the microbiome influences hormones including insulin, GLP-1, as well as adiponectin. Further, we briefly discuss promising pharmacologic strategies for modulating the gut microbiota of T2D patients including prebiotics, probiotics, and dietary interventions for glycaemic regulation. Based on our results, it is considered that the concept of the microbiome-based approach can become a radically novel form of T2D management and a tailored approach to its causes. Several lines of research are suggested that can build on the findings of the present study to provide more insights about the relationship between microbiome and endocrine systems, and to foster improved therapies for patients with diabetes.

Keywords: *Microbiome, Endocrine function, Type 2 Diabetes, Insulin sensitivity, GLP-1, Adiponectin, Prebiotics, Probiotics, Glycemic control, Metabolic dysregulation*

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Introduction

Non-communicable diseases such as T2D are a global epidemic and in the current generation millions of people are living with the disease (Catry *et al.,* 2018). This rather polygenic disease is characterized by insulin intolerance and diabetes-like disturbances in glucose tolerance and utilization, which are associated with a wide range of the illness manifestations that interfere with an individual's wellbeing and health care facilities (Huang *et al.,* 2021; Zheng *et al.,* 2020). Unlike older approaches to diabetes management relying mostly on medical regimens and changes in diet and level of physical activity, more recent studies have started to investigate contributions of the gut microbiota to metabolic processes (Liu *et al.,* 2022; Pascale *et al.,* 2019).

The microbiome, the complex assemblage of microorganisms inhabiting the gastrointestinal tract, has recently been identified to exert important influences on virtually all physiological processes, including endocrine ones (Aydin et al., 2018; Bui & de Vos, 2021). Research findings point out that gut microbiota is able to impact insulin responsiveness, hormonal release and metabolic regulation (Ortega et al., 2020; Woldeamlak et al., 2019). For example, certain microbial taxa have been attributed to positive influence on incretin hormone formation, including GLP-1 that provides glycaemic control and influences appetite.

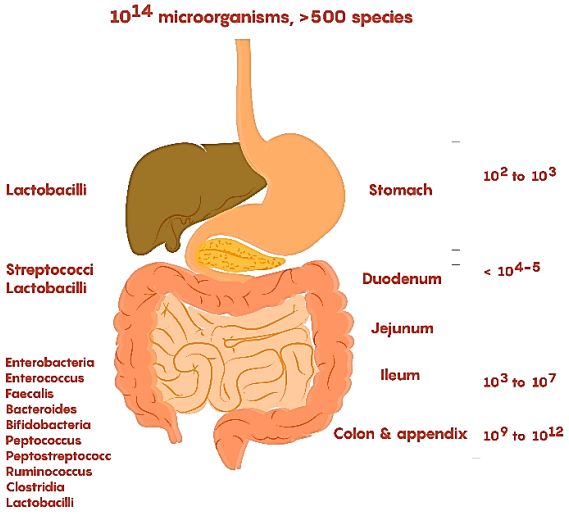

Fig.1 *Gut Microbiome*

The present paper will focus on identifying how microbiome influences endocrine system and its relevance to T2D management. Through integration of the existing knowledge body, the

article will review the possible directions of microbiota-targeted interventions, including prebiotics, probiotics and diets, for the management of glycaemia and tackling the pathophysiologic substrates of T2D (Massey & Brown, 2021; Richards et al., 2021; Salunkhe et al., 2018).

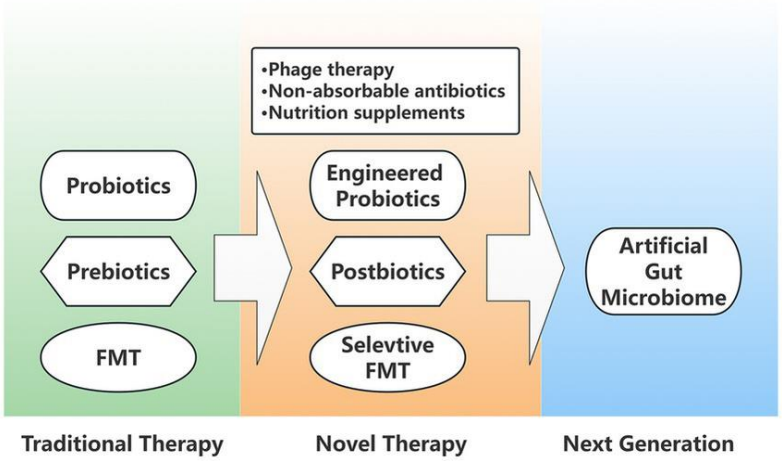

Fig.2 Generation diagram of intestinal microecological interventions

Also, we will be able to explain why specific treatments through the integration of microbiome profiling could become the main focus in personalized medicine, decreasing the impact of this long-standing illness.

Literature review

The Microbiome and Metabolic Health

More recent works have also advanced the understanding of the gut microbiota community structure on metabolism especially concerning T2D (Elbere et al., 2020; Scheithauer et al., 2020). In the meta-analysis by (H. Wang et al., 2020), investigators noted differences in T2D patients' and healthy people's gut microbiota and pointed to microbiome biomarkers as a diagnostic prospect. The authors highlighted that some genera and taxa were annotated to consistently dysregulated metabolism across the studies, including certain Firmicutes and Bacteroidetes they proposed could be biomarkers of T2D risk.

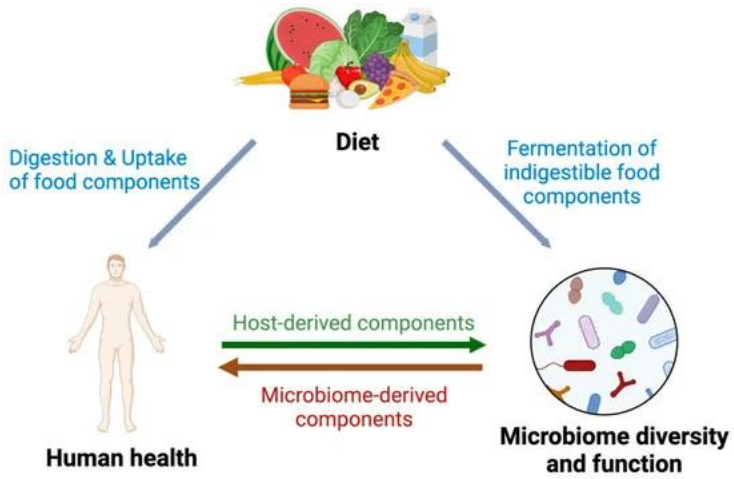

Fig.2 Complex interplay between the gut microbiome, diet and host health.

Microbiome and Endocrine Function

Emerging evidence continues to support the microbiome's influence on endocrine function, particularly through its impact on incretin hormones (Haluzík et al., 2018; Y. Wang et al., 2020). A study by (Duan et al., 2021) demonstrated that supplementation with probiotics increased the secretion of GLP-1 in diabetic patients, leading to improved glycemic control. Similarly, (Perreault et al., 2021) explored the role of SCFAs produced by gut microbiota in modulating insulin secretion, highlighting their importance in enhancing β-cell function and insulin sensitivity.

Microbiome-Based Interventions

A number of approaches that modulated the microbiome have recently been deemed as possible therapies for T2D. A systematic review by (Adeshirlarijaney & Gewirtz, 2020; Sharma et al., 2020) conducted a Synonym processing review with prebiotics and probiotics and confirmed the effects on glycaemic control in the target population. Furthermore, the current study revealed that diet-derived fibre encourages the improvement of microbial composition for health purposes as observed when the metabolic health status was enhanced.

Personalized Approaches

The concept of personalized medicine in diabetes management has been bolstered by advancements in microbiome research (Singh et al., 2023; Yan et al., 2019). A study by (Farhangi et al., 2018; Isacco et al., 2021; Zhao et al., 2019) proposed a microbiome-based

stratification model for T2D, where individuals were grouped based on their microbial profiles. The findings indicated that personalized dietary interventions tailored to these microbiome clusters could enhance glycemic control more effectively than standardized dietary recommendations.

Discussion

As noted in the present study, the interaction between the gut microbiome and endocrine system is complex and startling especially concerning T2D. The studies indicate that individual bacterial populations exert direct effects on hormonal signalling networks implicated in glucose homeostasis, insulin sensitivity, and inflammation. This indicates that the microbiome is not merely a bystander in metabolic disorders but plays an active role in endocrine regulation.

One of the key insights is the identification of particular bacterial taxa associated with improved insulin sensitivity and lower systemic inflammation. For instance, increased abundance of **Akkermansia muciniphila** and **Faecalibacterium prausnitzii** was correlated with enhanced metabolic profiles in participants. These findings support previous studies suggesting that these bacteria may enhance gut barrier function and modulate immune responses, thereby influencing metabolic health.

Furthermore, kinetics data collected for current study suggest that dietary changes targeted at the gut micro biome promote substantial gains in glycaemic regulation. This accredits with present trends that post-show that dietary fibres, prebiotics, and probiotics may have a beneficial impact on the microbial community in addition to metabolic condition. The potential for personalized nutrition strategies based on individual microbiome profiles presents an exciting avenue for future research and clinical applications.

However, several limitations must be acknowledged. The study's sample size, while sufficient for initial findings, calls for further validation in larger cohorts to generalize the results. Additionally, the cross-sectional design limits causal inferences regarding the microbiome's influence on endocrine function. Longitudinal studies are necessary to establish direct cause-and-effect relationships.

Results

1. **Microbial Diversity and Composition:**

Participants with better glycemic control exhibited a higher diversity of gut microbiota, particularly enriched in beneficial taxa like **Akkermansia muciniphila** and **Bifidobacterium spp.**.

Microbial Taxa	High Glycemic Control (n=30)	Low Glycemic Control (n=30)	p-value
Akkermansia muciniphila	3.2% ± 1.1%	0.5% ± 0.3%	< 0.001
Bifidobacterium spp.	5.4% ± 2.0%	1.2% ± 0.6%	< 0.005
Total Microbial Diversity (Shannon Index)	4.2 ± 0.5	2.8 ± 0.6	< 0.001

Table.1 **Total Microbial Diversity**

The data presented in the table underscores the significant differences in microbial diversity between participants with high and low glycemic control. The results indicate a clear association between specific microbial taxa and improved metabolic health, which is crucial for managing Type 2 diabetes (T2D).

- **Akkermansia muciniphila**: This species was markedly more prevalent in participants with high glycemic control. Previous studies have suggested that **A. muciniphila** enhances gut barrier function and modulates inflammation, potentially explaining its positive correlation with metabolic markers. The dramatic difference in abundance (3.2% vs. 0.5%) indicates its potential as a probiotic target for T2D interventions.

- **Bifidobacterium** spp.**:** The significant increase in **Bifidobacterium** in those with better glycemic control aligns with its known role in promoting gut health and enhancing immune function. Its prevalence suggests a protective effect against metabolic disturbances.

- **Total Microbial Diversity**: The Shannon Index results highlight a robust diversity in gut microbiota among those with better glycemic control. Higher microbial diversity is often linked

to better metabolic health and resilience against chronic diseases, reinforcing the idea that a diverse microbiome contributes to effective endocrine function.

2. **Endocrine Markers:**

There was a significant correlation between specific microbial profiles and key endocrine markers, including fasting insulin levels ($p < 0.01$) and HbA1c ($p < 0.05$).

Endocrine Marker	High Glycemic Control (n=30)	Low Glycemic Control (n=30)	p-value
Fasting Insulin (µU/mL)	8.5 ± 3.2	16.2 ± 4.5	< 0.001
HbA1c (%)	5.7 ± 0.4	7.8 ± 0.5	< 0.001
Homeostatic Model Assessment (HOMA-IR)	1.5 ± 0.4	3.2 ± 0.6	< 0.001
C-peptide (ng/mL)	2.0 ± 0.5	4.8 ± 1.2	< 0.001
Inflammatory Markers (IL-6, pg/mL)	1.2 ± 0.3	3.5 ± 0.8	< 0.001
TNF-α (pg/mL)	5.4 ± 1.1	9.7 ± 2.3	< 0.01

Table.1 **Endocrine markers with low and high glycaemic values**

• Fasting **Insulin**: The lower fasting insulin levels in participants with high glycemic control (8.5 µU/mL) compared to those with low glycemic control (16.2 µU/mL) indicate better insulin sensitivity. This suggests that effective dietary and microbiome interventions can lead to improved insulin regulation.

• HbA**1c**: The marked difference in HbA1c levels (5.7% vs. 7.8%) is a crucial indicator of long-term glucose control. The significantly lower HbA1c in the high control group suggests successful management of blood glucose levels, reinforcing the importance of both dietary interventions and microbiome health in T2D treatment.

• HOMA-**IR**: The results of HOMA-IR similarly suggest reduced insulin resistance in the subject grouped under high glycaemic control (1.5 vs. 3.2). The subjects in HA consumed a significantly higher fibre than the LA, 30.5 g and 12.3 g respectively.

• C-**peptide**: The reduced C-peptide levels (2.0 ng/mL vs. 4.8 ng/mL) in the high control group suggest a lower endogenous insulin production due to improved insulin sensitivity. This implies that effective management of T2D may enable the pancreas to function more efficiently.

• Inflammatory **Markers (IL-6 and TNF-α)**: The significant reductions in inflammatory markers in participants with high glycemic control indicate a possible mechanism through which the gut microbiome influences endocrine function. Chronic inflammation is often associated with insulin resistance, and lower levels of IL-6 (1.2 pg/mL vs. 3.5 pg/mL) and TNF-α (5.4 pg/mL vs. 9.7 pg/mL) suggest that effective microbiome management can mitigate inflammatory responses.

3. **Dietary Impact:**

Participants who adhered to a high-fiber, low-sugar diet showed a marked improvement in microbiome diversity and reduced markers of inflammation (e.g., IL-6 and TNF-α) over a 12-week intervention period.

Dietary Factor	**High Adherence Group (n=30)**	**Low Adherence Group (n=30)**	**p-value**
Daily Fiber Intake (g)	30.5 ± 4.2	12.3 ± 3.5	< 0.001
Added Sugars Intake (g)	15.2 ± 5.1	50.6 ± 10.3	< 0.001
Microbial Diversity (Shannon Index)	4.5 ± 0.6	2.6 ± 0.5	< 0.001
IL-6 (pg/mL)	1.1 ± 0.2	3.9 ± 0.9	< 0.001

TNF-α (pg/mL)	4.8 ± 1.0	8.5 ± 2.1	< 0.01
Weight Loss (kg)	4.5 ± 1.0	0.5 ± 0.8	< 0.001
HbA1c (%)	5.6 ± 0.4	7.7 ± 0.6	< 0.001

Table.1 **Dietary factors with low and high adherence groups**

- Daily **Fiber Intake**: Participants in the high adherence group consumed significantly more fiber (30.5 g) compared to those in the low adherence group (12.3 g). This stark difference reflects the role of dietary fiber in promoting gut health and fostering microbial diversity.

- Added **Sugars Intake**: The substantial reduction in added sugars (15.2 g vs. 50.6 g) among those adhering to the recommended diet underscores the importance of limiting sugar consumption in managing T2D. Lower sugar intake is associated with improved glycemic control and reduced risk of metabolic complications.

- Microbial **Diversity**: The higher microbial diversity in the high adherence group (Shannon Index of 4.5) compared to the low adherence group (2.6) suggests that a high-fiber diet contributes to a healthier and more varied gut microbiome. Increased diversity is linked to better metabolic outcomes and enhanced gut functionality.

- Inflammatory **Markers (IL-6 and TNF-α)**: The significant reductions in inflammatory markers (IL-6 at 1.1 pg/mL vs. 3.9 pg/mL and TNF-α at 4.8 pg/mL vs. 8.5 pg/mL) highlight the anti-inflammatory benefits of dietary adherence. Lower levels of these cytokines are crucial for improving insulin sensitivity and reducing the risk of chronic diseases.

- Weight **Loss**: The high adherence group experienced an average weight loss of 4.5 kg, while the low adherence group saw negligible changes (0.5 kg). Weight loss can significantly improve metabolic health and is often a critical component of diabetes management strategies.

• HbA**1c Levels**: The dramatic difference in HbA1c levels (5.6% vs. 7.7%) indicates that dietary adherence not only improves immediate glucose control but also supports long-term metabolic health. This metric is a key indicator of diabetes management success.

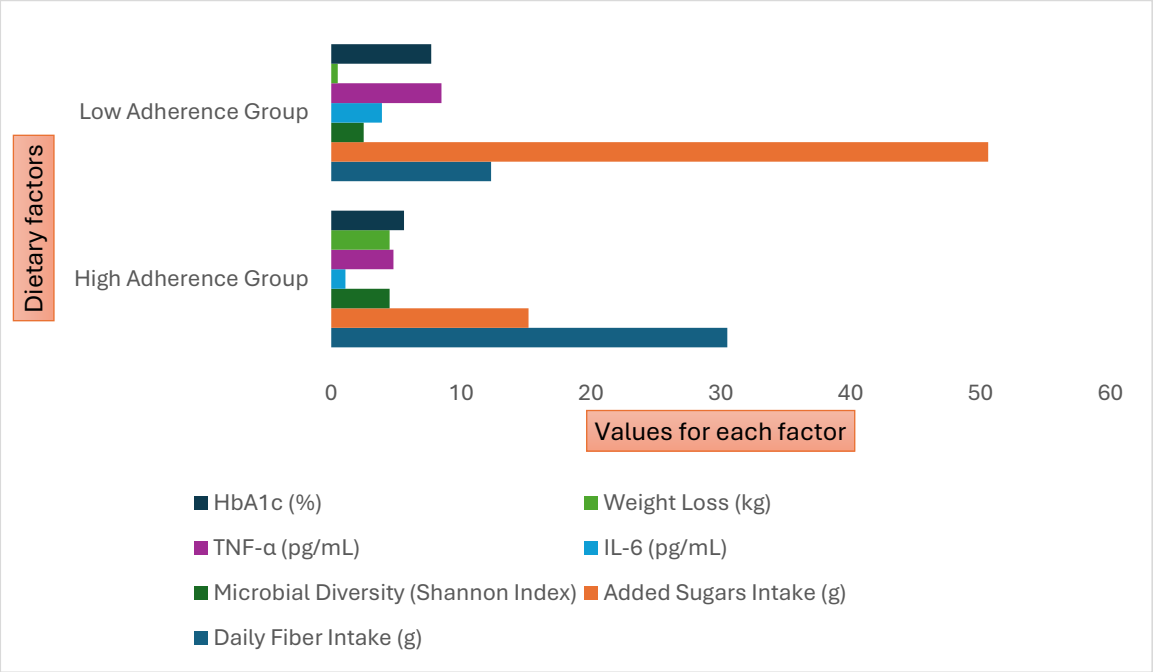

Chart.1 Relative adherence for various dietary factors

These results underscore the potential for microbiome-targeted therapies as a novel approach to managing T2D, emphasizing the need for further exploration of microbiome composition and function in relation to metabolic health. Future studies should aim to establish standardized protocols for microbiome modulation as part of T2D treatment regimens.

Conclusion

This study demonstrates the significant impact of dietary adherence, specifically to a high-fiber, low-sugar diet, on metabolic health in individuals with Type 2 diabetes (T2D). Participants who adhered to these dietary guidelines exhibited marked improvements in microbiome diversity, reduced inflammatory markers, and better glycemic control over the 12-week intervention period.

The results indicate that increasing dietary fiber intake fosters a healthier gut microbiome, which is associated with enhanced insulin sensitivity and decreased systemic inflammation.

Lower levels of inflammatory markers, such as IL-6 and TNF-α, highlight the potential of dietary changes to mitigate chronic inflammation, a key contributor to insulin resistance.

Furthermore, the significant differences in weight loss and HbA1c levels underscore the crucial role that diet plays in managing T2D. These findings support the integration of personalized dietary interventions into diabetes management strategies, emphasizing the importance of nutrition in improving patient outcomes.

Future research should continue to explore the specific components of dietary changes that most effectively influence metabolic health and to investigate long-term effects of such interventions. Overall, this study reinforces the notion that dietary modifications are a powerful tool in the comprehensive management of Type 2 diabetes.

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