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Original Article

Correlation between Gut Microbiota Composition and Glycemic Control Parameters in Patients with Type 2 Diabetes Mellitus: A Cross-Sectional Study

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ABSTRACT

Background: Gut microbial dysbiosis is increasingly linked to insulin resistance and low-grade inflammation in type 2 diabetes mellitus (T2DM), yet clinic-based evidence connecting community structure with routine glycemic indices remains limited in many Indian settings.
Objectives: To evaluate gut microbiota composition and diversity in adults with T2DM and to determine correlations between selected microbiota parameters and glycemic control.
Methods: A cross-sectional analytical study was conducted among 100 adults with T2DM (May–October 2025) at a tertiary-care center in Andhra Pradesh, India. Clinical profile, fasting plasma glucose (FPG), postprandial plasma glucose (PPPG), and glycated hemoglobin (HbA1c) were recorded. Stool samples underwent 16S rRNA gene sequencing. Relative abundance at phylum and genus levels, Firmicutes/Bacteroidetes (F/B) ratio, and alpha diversity indices were derived, and associations with glycemic indices were examined using group comparisons and correlation analysis.
Results: Mean age was 52.6 ± 8.9 years and 58% were male. Mean HbA1c was 8.2 ± 1.4%, with 62% having poor control (HbA1c ≥7%). Firmicutes (42.3%) and Bacteroidetes (36.8%) predominated overall. Poor control showed a higher F/B ratio (2.1 ± 0.6 vs 1.4 ± 0.4), lower alpha diversity (Shannon index 3.1 ± 0.5 vs 3.6 ± 0.4), and reduced beneficial genera (Bifidobacterium, Lactobacillus). The F/B ratio correlated positively with HbA1c (r = 0.46), FPG (r = 0.39), and PPPG (r = 0.42), while Bifidobacterium abundance correlated inversely with HbA1c (r = −0.41).
Conclusion: Poor glycemic control in T2DM was associated with a higher F/B ratio, relative enrichment of opportunistic taxa, and reduced microbial diversity, supporting a measurable link between gut community structure and routine glycemic indices.

Keywords: Type 2 diabetes mellitus; gut microbiota; dysbiosis; HbA1c; Firmicutes/Bacteroidetes ratio; microbial diversity.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder driven by progressive insulin resistance and beta-cell dysfunction, resulting in sustained hyperglycemia and multisystem complications. India carries a substantial and rising burden of T2DM, and even modest differences in glycemic trajectories translate into long-term cardiovascular, renal, and microvascular risk. Alongside genetic susceptibility and lifestyle factors, the intestinal microbiota has emerged as a relevant, potentially modifiable determinant of metabolic homeostasis. The gut microbial ecosystem participates in energy harvest, bile acid transformation, and short-chain fatty acid (SCFA) production and shapes mucosal immunity and barrier integrity. Dysbiosis can influence intestinal permeability and endotoxemia and can amplify low-grade inflammation that is closely tied to insulin sensitivity and glycemic control [1,7].

Landmark metagenome-wide and cohort studies have demonstrated that individuals with T2DM harbor distinct microbial signatures compared with non-diabetic controls, including enrichment of potentially pro-inflammatory taxa and depletion of taxa linked to butyrate production and anti-inflammatory effects [1-3]. Reduced representation of butyrate-producing organisms can be biologically important because butyrate supports epithelial energy supply and tight-junction function, and it modulates immune pathways that influence metabolic inflammation. Population-level analyses have further connected reduced gut microbial diversity with insulin resistance and T2DM, indicating that ecosystem stability and richness are clinically relevant phenotypes rather than incidental laboratory descriptors [6].

Among commonly reported compositional markers, the Firmicutes-to-Bacteroidetes (F/B) ratio has been linked to metabolic phenotypes in several reports, although direction and magnitude vary across populations, dietary patterns, and analytic pipelines [7-9,13]. At the genus level, Bifidobacterium and Lactobacillus are of interest because they contribute to barrier function, carbohydrate fermentation, and immunomodulation, and reduced abundance of these genera has been described in several dysbiosis frameworks for metabolic disease [9,13]. Medication exposure can also confound microbiome–glycemia associations: metformin produces reproducible shifts in microbial composition and metabolites, and some disease-associated patterns overlap with treatment signatures [4,5,11,12].

Despite the expanding literature, Indian data that concurrently report community composition, diversity indices, and correlations with routine glycemic parameters remain limited. Local diet, antimicrobial exposure, and baseline microbiome structure can influence observed associations, underscoring the need for region-specific evidence using standardized microbiome profiling. Such evidence is essential for interpreting microbiome signals within routine diabetes care. Therefore, this study evaluated gut microbiota composition and alpha diversity in adults with T2DM and assessed correlations between key microbiota parameters (phylum-level proportions, F/B ratio, selected genera, and diversity indices) and glycemic control parameters (HbA1c, fasting plasma glucose, and postprandial plasma glucose).

METHODOLOGY

Study design and setting

A cross-sectional analytical study was undertaken in the Department of Microbiology, NIMRA Institute of Medical Sciences, Jupudi, Vijayawada, Andhra Pradesh, India, over six months (May 2025 to October 2025). Adult patients with known T2DM attending the affiliated outpatient and inpatient services during the study period were screened consecutively.

Participants and eligibility

Adults aged 30–70 years with a physician diagnosis of T2DM for at least 6 months were eligible for enrollment. Exclusion criteria included acute febrile illness, chronic inflammatory bowel disease, gastrointestinal malignancy, pregnancy, and recent hospitalization for diabetic emergencies. Participants reporting systemic antibiotic exposure or probiotic/prebiotic supplementation within the preceding 4 weeks were excluded to minimize short-term microbiome perturbations [12]. After obtaining written informed consent, 100 participants meeting eligibility criteria were included.

Clinical and laboratory assessment

Demographic variables, duration of diabetes, comorbidities, and current antidiabetic therapy were recorded using a structured proforma. Anthropometry (height, weight) was measured using standard procedures, and body mass index (BMI) was calculated as kg/m². Venous blood sampling was performed after an overnight fast for fasting plasma glucose (FPG). Postprandial plasma glucose (PPPG) was measured 2 hours after a standardized meal. HbA1c was measured using a National Glycohemoglobin Standardization Program–aligned method. Glycemic control was categorized as good (HbA1c $<7.0\%$) or poor (HbA1c $\geq 7.0\%$) for comparative analyses [6].

Stool collection and microbiota profiling

Participants provided a fresh stool sample in a sterile, labeled container. Samples were transported to the microbiology laboratory under cold chain conditions and stored at −80°C until processing. Microbial DNA was extracted using a bead-beating step followed by silica-membrane spin column purification. The V3–V4 hypervariable region of the bacterial 16S rRNA gene was amplified and sequenced on an Illumina platform. Quality filtering, chimera removal, and amplicon sequence variant inference were performed using QIIME2, with taxonomic assignment against a curated reference database. Relative abundance at phylum and genus levels was computed, and the Firmicutes/Bacteroidetes (F/B) ratio was derived per participant [1,3].

Diversity indices and statistical analysis

Alpha diversity was assessed using Shannon and Simpson indices and observed species richness, derived from rarefied feature tables. Continuous variables were summarized as mean ± standard deviation (SD) or median (interquartile range), and categorical variables as frequency and percentage. Between-group comparisons (good vs poor glycemic control) used appropriate parametric or non-parametric tests based on distributional assumptions. Correlations between microbiota parameters (phylum proportions, F/B ratio, and selected genera) and glycemic indices (HbA1c, FPG, and PPPG) were evaluated using correlation coefficients. Two-sided p values <0.05 were considered statistically significant. Analyses were performed using standard statistical software.

Ethical considerations

The study protocol was approved by the Institutional Ethics Committee of NIMRA Institute of Medical Sciences. Participant confidentiality was maintained through de-identification of datasets, and microbiological processing followed standard biosafety procedures.

RESULTS

A total of 100 patients with T2DM were analyzed. The mean age was 52.6 ± 8.9 years, with a male predominance (58%). The median duration of diabetes was 6 years (IQR: 3–10). Mean BMI was 26.1 ± 3.4 kg/m². Mean HbA1c was 8.2 ± 1.4%, fasting plasma glucose (FPG) was 156 ± 38 mg/dL, and postprandial plasma glucose (PPPG) was 228 ± 54 mg/dL. Based on HbA1c, 38 participants (38.0%) had good glycemic control (HbA1c <7.0%), whereas 62 (62.0%) had poor control (HbA1c ≥7.0%) (Table 1).

Table 1. Baseline Clinical and Glycemic Characteristics of the Study Population (N = 100)

Variable	Value
Age (years), mean ± SD	52.6 ± 8.9
Male sex, n (%)	58 (58.0)
Duration of diabetes (years), median (IQR)	6 (3–10)
BMI (kg/m²), mean ± SD	26.1 ± 3.4
HbA1c (%), mean ± SD	8.2 ± 1.4
Fasting plasma glucose (mg/dL), mean ± SD	156 ± 38
Postprandial plasma glucose (mg/dL), mean ± SD	228 ± 54
Good glycemic control (HbA1c <7%), n (%)	38 (38.0)
Poor glycemic control (HbA1c ≥7%), n (%)	62 (62.0)

Phylum-level profiling showed a predominance of Firmicutes (42.3%) and Bacteroidetes (36.8%), followed by Actinobacteria (11.2%) and Proteobacteria (9.7%). Compared with the good-control group, poorly controlled participants demonstrated higher Firmicutes and Proteobacteria and lower Bacteroidetes and Actinobacteria proportions. The F/B ratio was significantly higher in poor control (2.1 ± 0.6) than good control (1.4 ± 0.4; p <0.001) (Table 2).

Table 2. Relative Abundance of Major Gut Microbiota Phyla According to Glycemic Control

Microbiota phylum	Overall (%)	Good control (n=38)	Poor control (n=62)	p value
Firmicutes	42.3	38.1 ± 6.4	45.0 ± 7.2	<0.001
Bacteroidetes	36.8	40.5 ± 5.9	34.2 ± 6.1	<0.001
Actinobacteria	11.2	13.8 ± 3.1	9.6 ± 2.8	<0.001
Proteobacteria	9.7	7.6 ± 2.4	11.2 ± 3.0	<0.001
Firmicutes/Bacteroidetes ratio	—	1.4 ± 0.4	2.1 ± 0.6	<0.001

Correlation analysis demonstrated a moderate positive association between the F/B ratio and HbA1c (r = 0.46, p <0.001). Similar positive associations were observed with FPG (r = 0.39, p <0.001) and PPPG (r = 0.42, p <0.001). In contrast, the relative abundance of Bifidobacterium showed an inverse association with HbA1c (r = −0.41, p <0.001) and FPG (r = −0.34, p = 0.002). Lactobacillus abundance also correlated negatively with glycemic indices, whereas Proteobacteria abundance correlated positively (Table 3).

Table 3. Correlation Between Gut Microbiota Parameters and Glycemic Indices

Microbiota parameter	HbA1c (r)	FPG (r)	PPPG (r)
Firmicutes/Bacteroidetes ratio	0.46*	0.39*	0.42*
Bifidobacterium abundance	−0.41*	−0.34*	−0.37*
Lactobacillus abundance	−0.29*	−0.26*	−0.31*
Proteobacteria abundance	0.33*	0.28*	0.35*

*p <0.01 for all correlations

Alpha diversity analysis showed significantly lower diversity in participants with poor glycemic control. The Shannon index was 3.1 ± 0.5 in poor control compared with 3.6 ± 0.4 in good control ($p < 0.001$). Simpson index and observed species richness were similarly reduced in the poor-control group (Table 4).

Table 4. Gut Microbial Diversity Indices in Relation to Glycemic Control

Diversity index	Good control (n=38)	Poor control (n=62)	p value
Shannon index	3.6 ± 0.4	3.1 ± 0.5	<0.001
Simpson index	0.89 ± 0.03	0.83 ± 0.05	<0.001
Observed species (richness)	212 ± 36	176 ± 42	<0.001

DISCUSSION

This cross-sectional study demonstrated that adults with T2DM and poor glycemic control displayed a distinct gut microbial profile compared with those achieving HbA1c <7.0%. Although Firmicutes and Bacteroidetes dominated the overall community, poor control was characterized by a higher Firmicutes proportion, lower Bacteroidetes proportion, and a significant increase in the F/B ratio, alongside expansion of Proteobacteria and reduction of Actinobacteria. These patterns align with foundational metagenomic observations of T2DM-associated dysbiosis and enrichment of taxa linked to inflammatory signaling [1-3,7,13].

The F/B ratio correlated positively with HbA1c, fasting glucose, and postprandial glucose, suggesting that broad community shifts track with metabolic dysregulation in this cohort. While several studies report an increased F/B ratio in metabolic disorders, the marker is not universally consistent and can vary with geography, diet composition, sequencing depth, and bioinformatic pipelines [7-9]. Mechanistically, shifts in dominant phyla can alter SCFA availability, bile acid pools, and intestinal barrier integrity. These downstream changes influence hepatic glucose output, peripheral insulin signaling, and systemic inflammatory tone, thereby providing plausible routes linking dysbiosis with glycemic measures [7,11]. The relative enrichment of Proteobacteria in poor control is noteworthy because Proteobacteria expansion is often interpreted as a signal of microbial imbalance and can be associated with increased lipopolysaccharide-driven inflammation [7,13].

At the genus level, reduced abundance of Bifidobacterium and Lactobacillus in poorly controlled T2DM is consistent with reports describing depletion of beneficial fermenters and barrier-supporting taxa in dysbiotic states [9,13]. In the present analysis, Bifidobacterium abundance correlated inversely with HbA1c and fasting glucose, supporting a protective association. Interventional evidence provides added plausibility: meta-analyses of randomized trials indicate that probiotic and synbiotic supplementation can improve glycemic indices in prediabetes and T2DM, although effect sizes vary by strain selection, dose, and baseline therapy [10]. A preliminary clinical trial of Bifidobacterium breve also reported improvements in metabolic and microbiome measures among T2DM participants, reinforcing the concept that targeted taxa can influence host metabolism [14].

Alpha diversity was significantly lower in the poor-control group, consistent with population-based microbiome-wide analyses linking reduced microbial diversity with insulin resistance and T2DM [6]. Lower diversity can indicate ecological fragility and reduced functional redundancy, potentially limiting resilience to dietary perturbations and inflammatory stressors. From a translational perspective, diversity indices and summary ratios such as F/B are attractive because they reduce complex ecosystems into interpretable metrics, but they should be interpreted alongside taxon-level and clinical context rather than as stand-alone biomarkers [8,9].

Medication exposure remains a key consideration in microbiome research. Metformin produces reproducible shifts in microbial composition, including enrichment of Akkermansia and SCFA-producing taxa, and large-scale analyses have shown that some “diabetes signatures” partially reflect treatment exposure [4,5,11,12]. Future work in this setting should incorporate medication stratification, detailed dietary assessment, and functional outputs (metagenomic pathways and metabolite profiling) to distinguish disease-associated dysbiosis from treatment-driven changes and to strengthen causal inference [4,5,8].

Limitations

This single-center cross-sectional design cannot establish temporal direction between dysbiosis and hyperglycemia. Dietary intake, physical activity, and detailed drug exposure (including dose and duration of metformin, antibiotics beyond the exclusion window, and other antidiabetic agents) were not quantified with standardized instruments, leaving residual confounding. Microbiota profiling relied on 16S rRNA sequencing, which limits species-level resolution and functional inference. Sampling at one time point does not capture within-person microbiome variability.

CONCLUSION

In this hospital-based cohort of adults with T2DM, gut microbiota composition and diversity differed markedly by

glycemic control status. Poor control was associated with higher Firmicutes and Proteobacteria proportions, lower Bacteroidetes and Actinobacteria, and a significantly elevated F/B ratio. The F/B ratio correlated positively with HbA1c, fasting glucose, and postprandial glucose, whereas Bifidobacterium abundance correlated inversely with key glycemic indices. Lower alpha diversity in poor control further supports a link between ecosystem instability and metabolic dysregulation. These findings reinforce the relevance of microbiota-informed risk stratification and support future studies integrating diet, medication stratification, and functional profiling to guide microbiota-targeted adjunctive strategies in regional clinical practice in tertiary-care settings**.**

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