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The Relationship between Gut Microbiota Composition and Type 2 Diabetes Mellitus

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Gut microbiota, type 2 diabetes mellitus, *Escherichia coli*, dysbiosis, insulin resistance, inflammation

ABSTRACT

Introduction: Type 2 diabetes mellitus (T2DM) is a growing global health issue influenced by gut microbiota composition. Alterations in gut bacteria impact metabolic regulation, insulin sensitivity, and inflammation, making microbiota a potential target for therapeutic intervention.

Methodology: A case-control study in Kirkuk City (November 2024 – March 2025) included 100 T2DM patients and 40 apparently healthy individuals as a control group. Stool and blood samples were analyzed for microbiological and immunological markers. Bacterial identification was performed using culture and biochemical tests, and interleukin (IL)-38 levels were measured via enzyme linked immunosorbent assay (ELISA). Statistical significance was set at $p < 0.05$.

Results: patients with T2DM exhibited increased *Escherichia coli* abundance, indicating gut dysbiosis linked to inflammation and impaired gut barrier function. Microbial diversity declined with disease duration, and differences in microbiota composition were observed in patients with hyperlipidemia and hypertension. Age-related variations suggested a higher metabolic risk in older diabetics.

Discussion: The study confirmed gut dysbiosis as a contributor to T2DM by promoting systemic inflammation and metabolic endotoxemia. Increased *E. coli* levels align with previous findings on intestinal permeability and insulin resistance. The impact of age and comorbidities on microbiota highlights its potential as both a biomarker and a therapeutic target. Microbiota-based interventions, such as probiotics and dietary modifications, may enhance insulin sensitivity and glycemic control.

Conclusion: This study highlights the link between gut microbiota dysbiosis and T2DM, emphasizing its role in disease progression. Future research should explore microbiota-targeted therapies to improve diabetes management.

Keywords: Gut microbiota, type 2 diabetes mellitus, *Escherichia coli*, dysbiosis, insulin resistance, inflammation

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INTRODUCTION:

Diabetes mellitus: Diabetes mellitus (DM) is possibly one of the oldest illnesses known to man. It was initially described in Egyptian text over 3000 years ago [1]. The fast evolution of contemporary civilization has resulted in significant changes in the lifestyles of individuals, particularly in their food preferences. The increasing prevalence of chronic metabolic illnesses, including obesity and diabetes, is a direct result of the excessive consumption of salt, sugar, and fat in the diet. Diabetes mellitus has evolved into a societal health issue that is becoming more prominent on a global scale. According to the eighth edition of the International Diabetes Federation (IDF) Diabetes Atlas in 2017, the global population of people with diabetes was around 425 million. It predicted that the number of diabetes patients will rise to 700 million by 2045[2]. Diabetes mellitus is a diverse collection of conditions that are distinguished by hyperglycemia as a result of an absolute or relative deficiency in insulin synthesis or activity. End organ damage, malfunction, and failure are all connected with the chronic hyperglycemia of diabetes mellitus, which affects the retina, kidney, neurological system, heart, and blood vessels. In 2011, the International Diabetes Federation (IDF) reported that the global prevalence of diabetes mellitus was 366 million, with a projected increase to 552 million by 2030[3].

Classification of diabetes mellitus : There are four types of diabetes mellitus: type 1 diabetes mellitus, Type 2 diabetes mellitus, gestational diabetes mellitus, and Maturity Onset Diabetes of the Young (MODY) [4].

Type 2 diabetes mellitus: Type 2 DM was initially characterized as a component of metabolic syndrome in 1988[5]. Type 2 DM (previously known as non-insulin dependent DM) is the most frequent form of DM, characterized by hyperglycemia, insulin resistance, and relative insulin insufficiency [6]. The long-term consequences of the fast advancement of global urbanization and modernity are evident in lifestyle characteristics, including bad eating habits, inadequate physical activity, elevated stress levels, and environmental issues. These variables are responsible for the worrisome increase in obesity and type 2 diabetes on a global scale. Insulin resistance is a condition that is distinguished by decreased insulin activity in the liver and reduced glucose absorption in fat and muscle in obese persons [7]. The interplay of genetic, environmental, and behavioral risk factors is the cause of type 2 diabetes [6].

Gut microbiota:

The gastrointestinal (GI) tract of the human body is one of the greatest interfaces (250–400 m2) between the host, ambient variables, and antigens. Around 60 tons of food travel through the human gastrointestinal system during an average lifetime, in addition to a plethora of bacteria from the environment that constitute a significant danger to gut integrity [8]. The gut microbiota is a complex and mutually beneficial association that has evolved over thousands of years in conjunction with the host, consisting of bacteria, archaea, and eukaryotes that colonize the gastrointestinal tract [9]. The estimated number of microorganisms in the gastrointestinal system exceeds 10^{14}, which is approximately 10 times the number of bacterial cells and over 100 times the amount of genetic material (microbiome) in the human genome [10]. Nevertheless, a recent revision of the estimate has indicated that the ratio of human to bacterial cells is closer to 1:1[11]. The host and the microorganisms that inhabit it are sometimes referred to as a "superorganism" due to the extensive number of bacterial cells in the body [12].

Relationship between gut microbiota and type 2 diabetes mellitus: It was discovered that T2DM was closely associated with gut flora [13]. For the first time, a substantial disparity in gut microbiota was found between diabetes and the general population [14]. Microbiome changes in individuals with diabetes or insulin resistance as compared with people without modifications in carbohydrate metabolism. In addition, alterations in the number of bifid bacteria, *Lactobacillus*, and *Clostridium*, as well as a lower *Firmicutes* to *Bacteroides* ratio in gut microbiota, have also been identified in type 1 diabetic children. This study also demonstrated that bacteria important in the preservation of gut integrity were considerably fewer in diabetes patients than in healthy controls. Similar alterations in the makeup of gut microbiota have also been found in TDM2 [15].

Aim of the study:

The aim of the study is to elucidate the complex association between gut microbiota and T2DM, inflammation, and metabolism,

Objectives:

1-Evaluate the pathogenic association between microbiota and T2 DM.

2- Explore any new therapeutic agents. Including nutraceuticals that may modulate the microbiota.

3- Detect the association between gut microbiota alteration and obesity which lead to T2DM .

MATERIAL

1. Study Design

A case-control study was conducted between November 1, 2024, and March 15, 2025, involving 100 T2DM patients and 40 apparently healthy individuals as a control group recruited from Kirkuk City.

2. Sample Collection

Stool samples were collected from all participants after obtaining informed consent and ethical approval. Samples were processed immediately or stored appropriately for later analyses.

3. Culture and Identification

Stool samples were cultured using Nutrient agar, MacConkey agar, Blood agar, and EMB agar. Gram staining and biochemical tests, including oxidase, catalase, urease, coagulase, indole, methyl red, and citrate utilization tests, were performed following standardized microbiological procedures (6).

Statistical Analysis:

Statistical significance was assessed using SPSS software version 25. Differences with a p-value <0.05 were considered statistically significant.

RESULTS

This study found significant differences in gut microbiota composition between type 2 diabetic patients and control group. Specifically, patients with type 2 diabetes demonstrated a higher abundance of *Escherichia coli* compared to controls, indicating a state of dysbiosis that may contribute to impaired gut barrier function and chronic inflammation. Additionally, an increased presence of pathogenic bacterial species was observed in diabetic patients, which correlated with advancing age, longer disease duration, and comorbid conditions, including hypertension and hyperlipidemia, as shown in tables 1,2,3and4,and figures 1and 2 .

DISCUSSION

The current study reinforced existing evidence of significant alterations in gut microbiota composition among T2DM patients. These alterations include increased *E. coli* abundance, potentially indicating dysbiosis and intestinal barrier dysfunction associated with chronic low-grade inflammation, a hallmark of T2DM pathogenesis [16].

Emerging literature consistently reports a lower microbial diversity in T2DM patients compared to healthy individuals, correlating

with impaired glucose metabolism and increased systemic inflammation [17, 18]. The higher abundance of *E. coli* observed in this study aligns with findings indicating that pathogenic strains of *E. coli* contribute to increased intestinal permeability and metabolic endotoxemia, exacerbating insulin resistance [19, 20].

The study also highlights age-dependent variations in gut microbiota composition, aligning with previous observations that gut microbiota diversity decreases with age, exacerbating metabolic disturbances and inflammation [21,22]. These age-related microbial shifts may further compromise glucose homeostasis in older diabetic populations, emphasizing the need for tailored therapeutic approaches in elderly diabetic patients [23].

Interestingly, this study uncovered significant microbiota differences associated with hyperlipidemia and hypertension, common comorbidities in T2DM. Such comorbidities have been previously linked to specific microbiota signatures, suggesting an intricate microbiota-host interaction influencing T2DM complications [24, 25].

The notable reduction in gut flora diversity with increasing T2DM duration suggests progressive gut dysbiosis, reinforcing the role of chronic hyperglycemia in shaping microbiota composition [26].This finding underscores the potential benefit of early interventions targeting gut microbiota to delay T2DM progression and associated complications [27].

Recent advances highlight gut microbiota modulation as a promising therapeutic strategy in T2DM management, including probiotics, prebiotics, and dietary modifications to restore gut microbiota balance [19]. Such interventions may improve insulin sensitivity and glycemic control and reduce systemic inflammation, enhancing overall diabetes management [28, 29].

Interleukin -38, an anti-inflammatory cytokine recently implicated in metabolic disorders, was included to investigate immunological links with microbiota changes. Although limited studies exist, emerging In conclusion, this study demonstrates a clear relationship between gut microbiota dysbiosis and T2DM. Future research should focus on longitudinal studies to understand causal relationships and interventional trials exploring microbiota-targeted therapies.

CONCLUSION

This research revealed a significant relationship between gut microbiota composition and type 2 diabetes mellitus, suggesting that gut dysbiosis plays a critical role in disease pathogenesis. Further longitudinal studies are warranted to elucidate causal mechanisms and develop effective microbiota-targeted interventions in diabetes management.

Recommendations

- Future studies should aim to use advanced techniques such as metagenomics and longitudinal monitoring to better understand how microbiota changes over time in response to disease and treatment. It would also be valuable to examine how gut microbial alterations relate to other common comorbidities in diabetes, such as hypertension and digestive disorders.
- A more personalized approach to treatment, guided by individual microbial profiles and immune responses, could enhance the effectiveness of T2DM management. Finally, public health strategies should promote gut-friendly diets and lifestyle choices as part of comprehensive diabetes care.
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Conflict Of Interest

This study has no conflict of interest to be declared by the author.

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TABLES

Table 1: Distribution of intestinal tract bacteria in T2 DM patients and control group.

Type of bacteria	**Study groups**				**P value**
	T2DM patients		**Control group**		
	No	**%**	**N**	**%**	
Escherichia coli	85	62.	4	43.	
Citrobacter koseri	24	17.	2	28.	
Klebsiella pneumoniae	8	5.8	4	4.4	0.1
Enterobacter cloacae	7	5.1	6	6.5	
Citrobacter freundii	4	2.9	4	4.4	
Acinetobacter lwoffii	4	9.9	5	5.5	
Acinetobacter baumannii	2	1.5	1	1.0	
Klebsiella oxytoca	2	1.5	5	5.5	
Total	13	100	9	100	
P value	0.003				

Table 2: Distribution of Total count of intestinal flora according to age in DM patients.

Age group (year)	Diabetic patients		
	No.	%	Total count of intestinal flora \ Cfu
35-45	21	21	2051142 [a]
46-55	38	38	2213184 [a]
56-65	29	29	1584206 [b]
>65	12	12	1023500 [c]
Total	100	100	6872032
P value	0.03		

Table 3: Distribution of intestinal tract bacteria in DM patients according to the presence or absence of other disorders

Type of bacteria		T2DM patients					P value
		Hypertension	Hyperlipidemia		No other disorder		
	No.	%	No.	%	No.	%	
Escherichia coli	38	61.3	7	77.78	40	61.54	0.0012
Citrobacter koseri	14	22.6	1	11.11	9	13.85	
Klebsiella pneumoniae	1	1.61	0	0	6	9.24	
Enterobacter cloacae	3	4.83	1	11.11	4	6.15	
Citrobacter Freundii	1	1.61	0	0	1	1.54	
Acinetobacter lwoffii	1	1.61	0	0	1	1.54	
Acinetobacter baumannii	2	3.22	0	0	2	3.07	
Klebsiella oxytoca	2	3.22	0	0	2	3.07	
Total	62	100	9	100	65	100	
P value		0.0007					

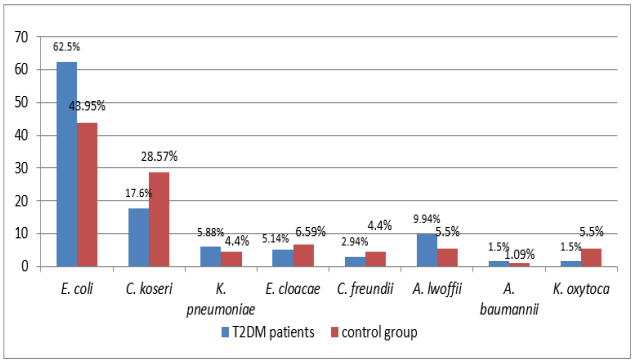
Table 4: Total count of intestinal flora in type 2 DM according to duration

Duration	Total count of intestinal flora \ Cfu
<1Y	5360000 [a]
1-5Y	1692117 [b]
6-10Y	1587500 [b]
11-15Y	1542684 [b]
>15Y	769833 [c]
P value	0.02

* Different letters mean there is a significant differences at p-value<0.05

FIGURES

Figure 1: Distribution of intestinal tract bacteria in T2 DM patients and control group.



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