The Gut Microbiome and Diabetes

Information brought to you by
Anne Wright, Registered Dietitian

The Gut Microbiome and Diabetes

Introduction

The human microbiota consists of approximately 38 trillion microbial cells. They are primarily present in the gut (mainly the large intestine) and made up of bacteria, fungi and yeasts (1). These microbes, along with their genes, are collectively known as the gut microbiome. The gut microbiome has been the subject of extensive research and plays an important role in the maintenance of health and the development of disease.

The term "dysbiosis" refers to an imbalance of the gut microbiota due to the loss of beneficial microbial organisms, the expansion of potentially harmful microorganisms, and/or lower microbial diversity (2). There is a growing body of research that suggests that dysbiosis plays a fundamental role in diabetes. Here, we will briefly explore the evidence for links between the gut microbiome and diabetes before concluding with considerations for clinical practice.

The Gut Microbiome and Diabetes

Type 1 Diabetes

Type 1 diabetes (T1D) is an autoimmune disease, characterised by the destruction of islet β cells in the pancreas; influenced by genetic and environmental factors (3). The microbiome has been investigated as one of the key factors associated with the development of T1D (4).

The Microbiome and Type 1 Diabetes

The human microbiome develops during the first years of life, after which it resembles the composition observed in adults (5,6). This development is closely linked to the development of the immune system (7).

Possible mechanisms by which dysbiosis may be involved in the pathophysiology of T1D include:

- Dysbiosis mediated immunological deregulation, including both innate and adaptive immune systems, eventually resulting in β cell destruction and the onset of T1D in genetically susceptible individuals (4).

- Changes in the integrity of the gut barrier, resulting in enhanced permeability and the movement of inflammatory antigens into the blood stream (causing direct damage to pancreatic β cells) (8, 9).

Studies have shown differences in the gut microbial profile between T1D patients and healthy controls, highlighting that the gut microbiome may have a role in T1D (10). Specifically, people with T1D have been found to have lower microbial diversity (11, 12, 13), and a higher abundance of certain types of bacteria (e.g., Bacteroidetes) than controls, and fewer beneficial microorganisms (e.g., Lactobacillus) (7, 14). However, whether these microbial changes are causal, responsive, or both is yet to be determined (15). Establishing a causal relationship between gut microbiome alterations and T1D is challenging, due to the complexity of the microbiome-immune system cross talk (15).

The Gut Microbiome and Diabetes

Type 2 Diabetes

Type 2 diabetes (T2D) is a metabolic disorder characterised by an imbalance in blood glucose levels, altered lipid profiles and high blood pressure (16). It usually presents as a combination of insulin resistance and deficiency (17). Three major factors contributing to risk of T2D include host genetics, dietary patterns (e.g., high fat, high energy diets) and sedentary lifestyle (16).

The Microbiome and Type 2 Diabetes

In adulthood, the microbiome can be altered by many factors such as changes in diet, the environment as well as certain medication (e.g., antibiotics) (18, 19, 20, 21). Recent studies have suggested that dysbiosis may play a role in insulin resistance in T2D (22).

The possible mechanisms by which dysbiosis may be involved in the pathophysiology of T2D include:

- An abundance of carbohydrate-fermenting bacteria leading to increased rates of short-chain fatty acid production, which are stored as lipids or glucose in body tissues and result in low grade inflammation (23).

- Changes in the integrity of the gut barrier, resulting in enhanced permeability and the movement of lipopolysaccharides (found in the outer membrane of gram-negative bacteria), which promotes low-grade inflammation and insulin resistance (24).

- Increased activity of the gut endocannabinoid system (an endogenous signaling system involved in maintaining energy balance) (25).

Studies have shown differences between the microbial profiles of T2D patients versus healthy controls, suggesting a link between T2D development and gut microbiota (26, 27). For example, results have shown significant differences in the composition and abundance of microorganisms between diabetes patients versus control groups (27, 28, 29), as well as lower levels of Akkermansia muciniphila in individuals with pre-diabetes (30). Lower levels of Akkermansia muciniphila can affect gut permeability, which is associated with T2D (31).

However, it is worth noting that there is a lack of consensus concerning which microorganisms are significantly altered in T2D due to compositional variations between individuals, as well as dietary intake and different analytical methods employed to measure the composition and functionalities of the gut microbiome (e.g., 16S rRNA sequencing, shotgun metagenomic sequencing) (32).

The Gut Microbiome and Diabetes

Considerations for Clinical Practice

The Diabetes UK evidence-based nutrition guidelines for the prevention and management of diabetes (2018) state that more evidence is needed to understand the role of dietary approaches in altering gut microbiome, and its effect on diabetes management and prevention (38).

Plant-based Diets

Consuming a diverse and varied diet, predominantly based on plant foods, is beneficial for the microbiome and gut health (39). The American Gut Project (2018) highlighted the importance of a varied plant-based diet, showing that those who consume at least 30 different plant foods per week have a more diverse (and therefore resilient) microbiome (40). Similarly, plant-based diets and dietary patterns which include more wholegrains, fruit, and vegetables (e.g., a Mediterranean-style diet), have been associated with reduced risk of T2D (41, 42).

Dietary Fibre Intakes

Dietary fibre is recommended for a healthy microbiome, however, beneficial responses to increasing dietary fibre intakes may depend upon an individual's gut microbiome profile and the type of fibre consumed (43). Prebiotic fermentable fibres (found in plant-based foods such as fruits, vegetables, wholegrains, nuts, and seeds) favour the growth of beneficial bacterial strains (such as Bifidobacterium and Lactobacilli) (44).

One intervention study in children with T1D showed that consuming a prebiotic supplement (8 g/d for 10 weeks) altered the gut microbiome composition (by increasing the abundance of beneficial Bifidobacterium), decreased intestinal permeability, and improved β cell function. However, there was no improvement in glycemic control, possibly due to the small sample size and relatively short intervention time (45).

The effect of high fibre diets on glycemic control in T1D is unclear. High-fibre diets are known to be cardio-protective and there is increased cardiovascular risk in patients with T1D, however high-fibre diets are not considered a priority for glycaemic management in such patients (38).

Increased dietary fibre intakes and a diet which includes fermented dairy products (such as yoghurt) are known to be beneficial for the prevention of T2D (38). Higher intakes of fibre, particularly soluble viscous fibers (such as those found in pulses, oats, oat bran, rice bran, barley, fruit, and vegetables), may be cardioprotective for patients with T2DM (38, 46). More research is needed to determine the effects of long-term restricted carbohydrate/ fibre diets on the microbiome (47).

Information brought to you by Anne Wright,
Registered Dietitian

The Gut Microbiome and Diabetes

Practice Recommendations

Recommendations for the prevention and management of diabetes should be in line with healthy eating guidelines. Here are some considerations for clinical practice:

- Encourage a diverse, plant-based, Mediterranean-style diet which is rich in fruit and vegetables, legumes, whole grains, nuts and seeds.

- For patients who wish to pursue carbohydrate restricted diets, encourage a variety of different plant-based food sources (48).

- Promote dietary diversity, aiming for 30 (or more) different plant foods per week.

- A high-fibre diet (at least 30g/day) is recommended for the adult UK population.

- There is not currently strong evidence to recommend specific probiotic supplements for the treatment or prevention of diabetes.

Conclusion

There is a growing body of research to suggest that the gut microbiome and dysbiosis play a role in T1D and T2D development. However, more evidence is needed to determine whether dietary manipulation of the gut microbiome (through diet and/or probiotic supplements) offers novel options for diabetes management and prevention.

The Gut Microbiome and Diabetes

References

1. Sender R, Fuchs S, Milo R. Revised Estimates for the Number of Human and Bacteria Cells in the Body. PLoS Biol. 2016; Aug 19;14(8): e1002533.
2. Petersen C, Round JL. Defining dysbiosis and its influence on host immunity and disease. Cell Microbiol. 2014;16(7):1024–33.
3. Jamshidi P, Hasanzadeh S, Tahvildari A, Farsi Y, Arbabi M, Mota JF, et al. Is there any association between gut microbiota and type 1 diabetes? A systematic review. Gut Pathog [Internet]. 2019;11(1):1–10. Available from: https://doi.org/10.1186/s13099-019-0332-7
4. Zhou H, Sun L, Zhang S, Zhao X, Gang X, Wang G. Evaluating the Causal Role of Gut Microbiota in Type 1 Diabetes and Its Possible Pathogenic Mechanisms. Front Endocrinol (Lausanne). 2020;11(March):1–13.
5. Zmora N, Suez J, Elinav E. You are what you eat: diet, health and the gut microbiota. Nat Rev Gastroenterol Hepatol [Internet]. 2019;16(1):35–56. Available from: http://dx.doi.org/10.1038/s41575-018-0061-2
6. Rodríguez JM, Murphy K, Stanton C, Ross RP, Kober OI, Juge N, et al. The composition of the gut microbiota throughout life, with an emphasis on early life. Microb Ecol Heal Dis. 2015;26(0):1–17.
7. Siljander H, Honkanen J, Knip M. Microbiome and type 1 diabetes. EBioMedicine [Internet]. 2019;46:512–21. Available from: https://doi.org/10.1016/j.ebiom.2019.06.031
8. Bosi E, et al. Increased intestinal permeability precedes clinical onset of type 1 diabetes. Diabetologia. (2006) 49:2824–7.
9. Durazzo M, Ferro A, Gruden G. Gastrointestinal Microbiota and Type 1 Diabetes Mellitus: The State of Art. J Clin Med. 2019;8(11):1843.
10. Gavin, Patrick G.; Hamilton-Williams, Emma E. The gut microbiota in type 1 diabetes: friend or foe? Current Opinion in Endocrinology & Diabetes and Obesity.2019 ;Volume 26 Issue 4 - p 207-212 doi: 10.1097/MED.0000000000000048
11. Leiva-Gea I, et all. Gut microbiota differs in composition and functionality between children with type 1 diabetes and MODY2 and healthy control subjects: a case-control study. Diabetes Care.2018.41:2385–95. doi: 10.2337/dc18-0253
12. Traversi D, et al. Gut microbiota diversity and T1DM onset: preliminary data of a case control study. Human Microb J.2017. 5–6:11–3. doi: 10.1016/j.humic.2017.11.002

References

13. Kostic AD, et al. The dynamics of the human infant gut microbiome in development and in progression toward type 1 diabetes. Cell Host Microbe.2015.17:260–73. doi: 10.1016/j.chom.2015.01.001
14. Zheng P, Li Z, Zhou Z. Gut microbiome in type 1 diabetes: A comprehensive review. Diabetes Metab Res Rev. 2018;34(7):1–9.
15. Groele L, Szajewska H, Szypowska A. Effects of Lactobacillus rhamnosus GG and Bifidobacterium lactis Bb12 on beta-cell function in children with newly diagnosed type 1 diabetes: protocol of a randomised controlled trial. BMJ Open. 2017.7:e017178. doi: 10.1136/bmjopen-2017-017178
16. Panwar S, Arora S, Sharma S, Tripathi P. The Gut Microbiome and Type 2 Diabetes Mellitus. Obes Diabetes. 2020;283–95.
17. Kazi AA, Blonde L. Classification of diabetes mellitus. Vol. 21, Clinics in Laboratory Medicine. 2001. 1–13 p.
18. Wu GD, Chen J, Hoffmann C, Bittinger K, Chen YY, Keilbaugh SA, et al. Linking long-term dietary patterns with gut microbial enterotypes. Science (80-). 2011;334(6052):105–8.
19. Tu P, Chi L, Bodnar W, Zhang Z, Gao B, Bian X, et al. Gut microbiome toxicity: Connecting the environment and gut microbiome-associated diseases. Toxics. 2020;8(1).
20. Gentile CL, Weir TL. The gut microbiota at the intersection of diet and human health. Science (80-). 2018;362(6416):776–80.
21. Elvers KT, Wilson VJ, Hammond A, Duncan L, Huntley AL, Hay AD, et al. Antibiotic-induced changes in the human gut microbiota for the most commonly prescribed antibiotics in primary care in the UK: a systematic review. BMJ Open. 2020;10(9): e035677.
22. Wen L, Duffy A. Factors influencing the gut microbiota, inflammation, and type 2 diabetes. J Nutr. 2017;147(7):1468S-1475S.
23. Den Besten G, Van Eunen K, Groen AK, Venema K, Reijngoud DJ, Bakker BM. The role of short-chain fatty acids in the interplay between diet, gut microbiota, and host energy metabolism. J Lipid Res. 2013;54(9):2325–40.
24. Sikalidis AK, Maykish A. The Gut Microbiome and Type 2 Diabetes Mellitus: Discussing a Complex Relationship. Biomedicines. 2020 Jan 7;8(1):8. doi: 10.3390/biomedicines8010008. PMID: 31936158; PMCID: PMC7168169.
25. Muscogiuri, G., Cantone, E., Cassarano, S. et al. Gut microbiota: a new path to treat obesity. Int J Obes Supp 9, 10–19 (2019). https://doi.org/10.1038/s41367-019-0011-
26. Li Q, Chang Y, Zhang K, Chen H, Tao S, Zhang Z. Implication of the gut microbiome composition of type 2 diabetic patients from northern China. Sci Rep [Internet]. 2020;10(1):1–8. Available from: http://dx.doi.org/10.1038/s41598-020-62224-3

References

27. Ahmad A, Yang W, Chen G, Shafiq M, Javed S, Zaidi SSA, et al. Analysis of gut microbiota of obese individuals with type 2 diabetes and healthy individuals. PLoS One [Internet]. 2019;14(12):1–15. Available from: http://dx.doi.org/10.1371/journal.pone.022637
28. Larsen N, Vogensen FK, Van Den Berg FWJ, Nielsen DS, Andreasen AS, Pedersen BK, et al. Gut microbiota in human adults with type 2 diabetes differs from non-diabetic adults. PLoS One. 2010;5(2).
29. Gaike AH, et al. The Gut Microbial Diversity of Newly Diagnosed Diabetics but Not of Prediabetics Is Significantly Different from That of Healthy Nondiabetics. mSystems. 2020;5(2):1–17.
30. Allin KH et al. Aberrant intestinal microbiota in individuals with prediabetes. Diabetologia. 2018;61(4):810–20.
31. Gurung M, Li Z, You H, Rodrigues R, Jump DB, Morgun A, et al. Role of gut microbiota in type 2 diabetes pathophysiology. EBioMedicine [Internet]. 2020; 51:102590. Available from: https://doi.org/10.1016/j.ebiom.2019.11.051
32. Brunkwall L, Orho-Melander M. The gut microbiome as a target for prevention and treatment of hyperglycaemia in type 2 diabetes: from current human evidence to future possibilities. Diabetologia. 2017;60(6):943–51.33. Houghton D, Hardy T, Stewart C, Errington L, Day CP, Trenell MI, et al. Systematic review assessing the effectiveness of dietary intervention on gut microbiota in adults with type 2 diabetes. Diabetologia. 2018;61(8):1700–11.
34. Kocsis T, et al. Probiotics have beneficial metabolic effects in patients with type 2 diabetes mellitus: a meta-analysis of randomized clinical trials.Sci Rep. 2020;10, 1178735. Rittiphairoj T, et al. Probiotics for glycemic control in patients with type 2 diabetes mellitus: protocol for a systematic review. 2019; Syst Rev 8, 227. https://doi.org/10.1186/s13643-019-1145-y
36. Kobyliak N, Falalyeyeva T, Mykhalchyshyn G, Kyriienko D, Komissarenko I. Effect of alive probiotic on insulin resistance in type 2 diabetes patients: randomized clinical trial. Diabetes Metab Syndr. 2018;12(5):617–24
37. Kesika P, Sivamaruthi BS, Chaiyasut C. Do Probiotics Improve the Health Status of Individuals with Diabetes Mellitus? A Review on Outcomes of Clinical Trials. Biomed Res Int. 2019;2019.
38. Dyson PA, Twenefour D, Breen C, Duncan A, Elvin E, Goff L, et al. Diabetes UK evidence-based nutrition guidelines for the prevention and management of diabetes. Diabet Med. 2018;35(5):541–7.
39. Tomova A, Bukovsky I, Rembert E, Yonas W, Alwarith J, Barnard ND, et al. The effects of vegetarian and vegan diets on gut microbiota. Front Nutr. 2019;6(April).

References

40. McDonald D, Hyde E, Debelius JW, Morton JT, Gonzalez A, Ackermann G, et al. American gut: an open platform for citizen-science microbiome research. bioRxiv. 2018;3(3):1–28.
41. McMacken M, Shah S. A plant-based diet for the prevention and treatment of type 2 diabetes. J Geriatr Cardiol. 2017;14(5):342–54.
42. Esposito K, Maiorino MI, Bellastella G, Chiodini P, Panagiotakos D, Giugliano D. A journey into a Mediterranean diet and type 2 diabetes: A systematic review with meta-analyses. BMJ Open. 2015;5(8).
43. O'Grady J, O'Connor EM, Shanahan F. Review article: dietary fibre in the era of microbiome science. Aliment Pharmacol Ther. 2019;49(5):506–15.
44. Seo YS, Lee H Bin, Kim Y, Park HY. Dietary carbohydrate constituents related to gut dysbiosis and health. Microorganisms. 2020;8(3).
45. Ho J, et al. Effect of prebiotic on microbiota, intestinal permeability and glycemic control in children with type 1 diabetes. J Clin Endocrinol Metab. 2019. 104:4427–40.
46. Reynolds A, Akerman A, Mann, J. Dietary fibre and whole grains in diabetes management: Systematic review and meta-analyses. PLoS medicine. 2020:17(3), e1003053.
47. Leeming E, et al. Effect of Diet on the Gut Microbiota: Rethinking Intervention Duration. Nutrients. 2019; Nov 22;11(12):2862.
48. Churuangsuk C, Lean, M, Combet E. Low and reduced carbohydrate diets: Challenges and opportunities for type 2 diabetes management and prevention. Proceedings of the Nutrition Society. 2020; 79(4), 498-513.